The Master Illusionist

A Theory of Neuropsychology

by

Federico Sanchez

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The Master Illusionist
A Neurological Theory of Psychology
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Neurons, Now You Feel Them, Now You Don't

Single Neurons

I am deeply indebted to the coherent and logical presentations and insights of others that have come before me. Without the tireless research of countless scientists, without the brilliant ideas of brain theorists and philosophers, this work would not be possible. Without intending comparison with Isaac Newton, his words come to mind and are truer in my case, "I stand on the shoulders of giants" -- a whole slew of them.

In the last few decades brain research has reached new heights. It is time to synthesize the information coming in from many varied fields and to propose a coherent and logical brain theory. A good neuropsychological model is needed to guide future research. Otherwise, brain research will continue to be a compilation of facts, a cataloguing of new species, much as biology was a couple of centuries ago. Any model of the brain will have to contend with causes operating at several levels simultaneously, with signals propagated upward and downward, and in a chaotic sense, of emerging properties at some levels, combined with random and deterministic processes. Thus, the minute, exact neural details that lead to predictable responses in the brain might prove too complex to unravel in the near future. However, I feel confident that the basic cytoarchitecture, brain structures, mechanisms and circuits with their corresponding chemistries, which the brain uses to achieve all the wondrous results it does, is within our grasp. This model should be altered and modified to fit the new facts that future research uncovers. The brain model presented here is intended to serve as base-starting point to guide future neurological research. The similarities between the model and reality can be easily tested, at minimum by using its predictive power. Hopefully it will lead to a better understanding of the cause of psychological disorders and consequently to a more rational pharmacology and the development of more efficient therapeutic methods.

I have highlighted in yellow my own hypothesis, slight deviations from others' theories, or when I propose a different twist or interpretation of facts discovered by others, hoping to assist the reader in separating what I am proposing from what is "standard knowledge" (among neurologists, psychiatrists or psychologists). Otherwise, I am just presenting known facts or accepted theories.

To begin to understand the mysteries of the brain and the central nervous system, it is necessary to start with a discussion of neurons and their connections. Neurons are the basic unit of the brain and the nervous system. They essentially send electro-chemical signals to one another. In large groups, or coordinating between large groups, they store memories, interpret information from the senses, learn, think, deduct, love, govern reproductive behavior, control body movement, and perform all the homeostatic functions necessary for the functioning of the body in an optimal state. Somehow, neurons, with their multiple and complicated interactions, in an emergent sense, are responsible for all the magnificent things the brain performs.[3]

The neuron is a cell specializing in sending and processing information. There are many different types of neurons, but they all have four components: the cell body or soma, where all the proteins and chemicals are manufactured, the axon, the dendrite and the synapse.

The soma comes in various sizes, but is typically about 20 microns in diameter. The axon is a delicate tubular extension from the soma. The nerve impulses are sent down the axon to the synaptic terminal. Axons can have several branches allowing a single neuron to send impulses to many others. The result is that the messages sent out from one cell can affect many; this is called divergence. At the same time, each neuron can receive inputs from numerous others; this is called convergence. The axons can vary in length from a fraction of a millimeter to more than a meter, as is the case of neurons that activate muscles in our arms or legs.

Dendrites, in contrast to axons, are multiple tubular extensions of the cell body. They are the receivers of impulses from other neurons. Some are branched with multiple receptor sights that enable them to make contact with many neurons.

The general style of dendritic branching varies from one type of neuron to another but a neuron usually has several main branches, each of which branches a few times into sub branches and so on. A small neuron may have as few as five hundred dendrites; a large pyramidal cell may have as many as twenty thousand. The average numbers of dendrites per neuron in the cortex are roughly six thousand.

The synapse or synaptic cleft is defined as the minute space between the axon and the dendrite. The synapse is about one fortieth of a micron. The space between the membranes of the neurons is called the extracellular space. This space is filled with liquid with all sorts of chemicals. This liquid allows neurotransmitters to cross the extracellular space between presynaptic and postsynaptic sites – the synapse. The distance they diffuse through is very small (measured in angstroms).

Inside the neuron membrane is a concentrated aqueous solution of chemicals and structures that make communication between neurons possible. The flow of information from one nerve cell to another involves the passage of ions through separate, minute channels in the membrane. Variations in these concentrations generate the nerve impulse or action potential.

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[3] Even though we still don't know exactly how a group of neurons can represent an object or an idea, we can infer that they must do so. For this section I am drawing primarily from three secondary sources: ***Receptors***, By Richard M. Restak, MD, and ***The Astonishing Hypothesis***, by Francis Crick, and ***Synaptic Self*** by Joseph LeDoux, otherwise see the footnotes.

Four ions are most important in this process: sodium, potassium, calcium and chloride. Each ion passes in or out through its own channels in the neuron's membrane. A part of the membrane acts as an ion pump that releases two sodium ions for every potassium ion. The uneven distribution of ions – high intracellular potassium and low extracellular potassium, coupled with high extracellular sodium and low intracellular sodium – produces a voltage difference between the outside and the inside of the nerve cell. This voltage difference confers on the neuron its capacity to generate and transmit the wave of electrochemical depolarization that is the nerve impulse. The nerve impulse travels down the axon and when it reaches the synapse, releases neurotransmitters.

The ion channels can be open or closed "gates", meaning that a small change in the configuration of the proteins that make the channels can let the ions pass or not. To generate a nerve impulse, a neuron's membrane must first depolarize. Depolarization begins when a sodium channel across the membrane is briefly opened and sodium ions pass through it into the cell. This produces a voltage reduction. When the voltage reduction reaches a critical level – 35 millivolts – adjacent sodium channels are opened, generating an action potential. This impulse spreads down the axon, as the voltage-controlled sodium channels open sequentially.

Calcium ions enter neurons through voltage-gated channels. This, along with their diffusion, buffering, and release from intracellular stores, leads to rapid local modulations of the calcium concentration. The concentration of calcium can, in turn, influence the membrane potential (via calcium-dependent membrane conductance) and—by binding to buffers and enzymes—turn on or off intracellular signaling pathways that initiate plasticity and form the basis of learning.[4]

The impulse is different than an electric current in a wire. In a wire a cloud of electrons carries the current. In a neuron the electrical effect depends on ions moving in or out through the molecular gates of its membrane. This signal is a regenerative one, requiring energy. As a result the impulse traveling down the axon does not decay, but retains the same amplitude and frequency. This allows the impulse to travel long distances and still produce an appreciable effect. Once the impulse reaches the end of the axon, the electrical message ceases and is turned into a chemical message as the presynaptic membrane releases neurotransmitters into the synaptic cleft. The neurotransmitters diffuse across the synaptic cleft and bind to their receptors on the postsynaptic membrane on the dendrite of the target neuron, again opening or closing channels that initiate a current flow.

Depending on the type of channel the neurotransmitter has "gated", the action potential exerts either an excitatory effect, influencing the neuron to generate an impulse of its own, or an inhibitory effect, preventing it from "firing". Neurons are continuously adding and subtracting excitatory and inhibitory inputs to determine whether an action potential will be generated. The full sequence of communication between neurons is thus, usually, electrical-chemical-electrical.

The arrival of a neurotransmitter from a single presynaptic terminal is typically not sufficient to produce an action potential in the postsynaptic (target) cell. Only if the target neuron is bombarded with neurotransmitters from many presynaptic terminals at about the same time – within milliseconds – will an action potential result.

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[4] Christof Koch, *The Quest for Consciousness.*

A given target neuron receives relatively few synaptic contacts from any one presynaptic neuron. As a result, much of the convergence that drives a target cell toward action potentials comes from the convergence of different presynaptic cells at roughly the same time. In order for inputs to arrive at the target about the same time, action potentials have to be triggered in the various presynaptic cells at about the same time. The timing has to be adjusted for different lengths of axons; the longer the axon, the longer it takes for the action potential to travel down it. The role of the target shifts from a receiver to a sender when it generates an action potential. It now becomes a presynaptic neuron that helps fire action potentials in other cells.

There are also synapses through which communication between presynaptic and postsynaptic sites is purely electrical, but chemical transmission is by far the most prevalent. Much of what the brain does involves electrical-to-chemical-to-electrical coding of experience.

There is a systematic flow of molecules along the axon in both directions. Some travel faster than others, but all these flows are far slower than the speed of the axonal impulses. Impulses travel at different speeds: within the cortex, speeds of one to five meters/sec; down the spinal cord, speeds are 20 meters/second (but sometimes up to 100 meters/second). This means that messages between two sides of the brain take as long to travel as a message going all the way to the leg.

Neurons are in different states of preparedness to “fire”. Some might be very close to reaching a minimum “threshold”, while others might be in a preponderant inhibitory mode that needs to be overcome in order for the nerve impulse to be generated.

Every neurotransmitter molecule and receptor molecule on the target neuron have a unique three-dimensional structure. The neurotransmitter is somewhat like a “key” fitting into its “lock”. However, a particular neurotransmitter might find itself competing with a slightly different neurotransmitter for a particular receptor site.

There are four main chemical types of neurotransmitters. The most prevalent are simple amino acids, which are involved in rapid communication between neurons: glutamate, glycine and aspartate are the most important of the twenty amino acids that function as neurotransmitters. Glutamate is the primary excitatory neurotransmitter in the brain. Gamma-amino-butyric acid (GABA) is the most prevalent inhibitory neurotransmitter. GABA is synthesized from glutamate with the help of a single enzyme. About a fifth of all neurons in the neocortex release GABA. Of these, about twenty per cent also release large organic molecules, called peptides. These transmitters probably implement rather general processes, such as keeping the cortex “awake” or remembering something, rather than dealing with the vast, intricate information handled by the fast processes.

The three other classes of neurotransmitters are present at far fewer synapses. The monoamines consist of two classes: the catelchomines, which include epinephrine, norepinephrine and dopamine with a common chemical structure; and the indoleamines, which are synthesized from the amino acid tryptophan and include serotonin and melatonin. All of these are present in groups of neurons that are primarily located in the brain stem. The groups of neurons, or nuclei, of the brain stem that connect to the cortex use transmitters such as serotonin, norepinephrine and dopamine.

Receptors are proteins on the surface of cells. Serotonin acts through many different receptors; some are fast acting, others slow, and one inhibitory.[5] Multiple 5-hydroxytriptamine (5-HT) receptors have been identified; five different subtype 5-HT1, three 5-HT2, two 5-HT3, two 5-HT4, two 5-HT5, one 5-HT6, and four 5-HT7. Dopamine acts through excitatory receptors (D1, the most common), and inhibitory receptors (D2, D3, D4 and D5). Serotonin and dopamine can be excitatory or inhibitory, depending on the receptors they act upon.

Acetylcholine, the major transmitter at the junction between nerves and muscles (including the heart), originates in subcortical structures above the brain stem. Acetylcholine is the only major neurotransmitter that isn't derived from an amino acid. It is employed at many synapses throughout the brain (in the cortex, the hippocampus, the substantia nigra and the globulus Pallidus), but most of the neurons that synthesize acetylcholine are in an area in the lower part of the basal ganglia, named after its discoverer, the nucleus basalis of Meynert.

Acetylcholine uses two basic different types of receptors: nicotinic and muscarinic. Acetylcholine produces an influx of sodium through a ligand-gated ion channel and is fast and excitatory in action through nicotinic receptors. Acetylcholine, through muscarinic receptors, produces slower responses and can be excitatory or inhibitory and involves a second messenger system, rather than a direct opening of ion channels. Muscarinic receptors are found in the parasympathetic nervous system. Muscarinic receptors control smooth muscle in cardiac contractions, gut motility and bronchial constriction; they also control exocrine glands that stimulate gastric acid secretion, salivation and lacrimation. Muscarinic receptors are also found in the cortex, the striatum, the hippocampus, thalamus and brain stem.

Last is a chemically heterogeneous group of neurotransmitters that includes histamine, nitric oxide, and the neuropeptides. Among the neuropeptides are the endorphins, enkephalins, Substance P and Substance K. Peptides function as modulators, rather than producing stimulation or inhibition on their own; they facilitate such actions for other neurotransmitters. Neurons may employ one or more neuropeptides along with any of several neurotransmitters. The endorphins and the enkephalins are triggered by pain and stress.

Peptides are actually made in various parts of the body aside from the brain. Pituitary peptides are also used in the gut. The same peptides that bind to receptors in the kidney to change blood pressure operate receptors in the lung and the brain. Peptides include insulin, prolactin (signals a woman's breast to secrete milk) and gut cell substances that guide every step of digestion. Although peptide structures are deceptively simple, the responses they elicit are extremely complex. This has led to their being classified under a wide variety of categories like hormones, neurotransmitters, neuromodulators, growth factors, gut peptides, interleukins, cytokines, chemokines and growth inhibiting factors.

The immune system communicates with the endocrine system as well as the nervous system by using neuropeptides endorphins and their receptors.[6] It is important to make note that many other cells (aside from neurons) have receptors on their membranes.

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[5] Deborah Haber, News Office, *Newfound receptor responds to serotonin,* Dec 6, 2000.
[6] Candace B. Pert, *Molecules of Emotion,* 1997.

These receptors are used to activate or deactivate many processes and can be used to send information throughout the body.

There are receptors on immune cells for virtually every peptide or drug identified in the brain, such as Valium, Substance P, and many others. Conversely, neuropeptides used in the immune system are also used by the nervous system. Interleukin-1 (Il-1) is a polypeptide produced mainly by macrophages in the immune system and is one of fifty or so identified peptides that mediate the inflammatory reactions caused by injury, trauma or an activated immune system. In a chemical cascade, interleukin-1 causes fever, activates T cells, induces sleep, and puts the body in a generally healing state of being, allowing it to mobilize energy reserves to fight pathogenetic intruders. Il-1 receptors in the hypothalamus mediate fever and are also found in the cortex and higher brain centers (mainly on glial cells and the tough membranes around the brain).

Candace Pert has been developing the idea that various systems, the nervous, endocrine and immune systems and their organs – the brain; the glands; and the spleen, bone marrow and lymph nodes – are joined in a multidirectional network of communication, linked by neuropeptides acting as information carriers.[7]

Norepinephrine and dopamine-containing neurons are prominent in another brain stem nucleus called the locus ceruleus. Serotonin is formed in cells in a nucleus called the midline raphe. Fibers from these cells and the locus ceruleus are widely distributed throughout the brain. The action of dopamine, norepinephrine and serotonin can affect large numbers of neurons because of their diffuse distribution.

There are three main classes of ion channels: one sensitive to voltage only, another sensitive to a neurotransmitter only, and the third sensitive to voltage and glutamate, called the NMDA channel (N-methyl-D-aspartate is an agonist of this receptor and is named after it). The NMDA channel rarely opens even in the presence of glutamate if the local membrane potential is near its resting value. If this potential becomes less negative, then glutamate will open the channel. Thus it only responds to the association between the presynaptic activity (the release of glutamate) and the postsynaptic activity (the alteration of the voltage across the local membrane produced by the other inputs).

When the NMDA channel opens, it allows the passage of not only sodium and potassium ions but also an appreciable amount of calcium ions. These incoming calcium ions (at this moment this process is only partially understood) produce a net result, which alters the strength of the synapse, probably for days, weeks, and months or even longer. With frequent usage, a synaptic connection can be strengthened, and more important, these changes can be enduring. The production of changes in synaptic strength as a result of brief stimulation is usually referred to as long-term potentiation (LTP).

Another interesting property of LTP is what has been called specificity. Specificity is when neuron A receives inputs from neurons B and C and the input from B produces induction of LTP between A and B, and doesn't change anything between A and C. In this way, neuron A is more sensitive to inputs from B, but not from C. In order for LTP to occur, a certain minimum number of inputs to a neuron have to be stimulated to activate enough synapses. This property is called cooperativity. In other words, neurons that tend to fire together tend to stay together. This can be the foundation of a theory of learning and memory.

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[7] Ibid.

There are at least seven types of potassium channels; some open fast, others more slowly. Some channels, when opened, inactivate rapidly, others slowly. Some are used to form the traveling impulse along the axon; others produce more subtle effects in the soma and dendrites.

All brain impulses are the same, whatever information they may carry. Brain activity at every level, from the anatomical to the molecular, must be thought of in terms of messengers and receptors.

Eric Kandel, of Columbia University, has proposed another mechanism for learning and laying down long-term memories involving a sort of prion, which is a type of protein that can exist in various shapes. Unlike other proteins, some prions whose shape acts as a catalyst cause neighboring proteins of the same type to take up the same shape. He has shown that long-term memory is the result of new proteins being made at the synaptic connections. Electrical stimulation of these synapses releases serotonin, which in turn, somehow stimulates the manufacture of memory-forming proteins.

It is still difficult to understand how these changes happen. The templates from which new proteins are made, the messenger RNAS (mRNAS), are manufactured in the cell nucleus. Most cells are small, so mRNAS, and the proteins made in them, flood the whole cell. Neurons, on the other hand, are huge, relatively, and consist mainly of filaments that can reach several centimeters long. The puzzle is how exactly the cell knows where to make memory-forming proteins. Prions could be a possible explanation.

Some types of mRNA are not translated into protein unless a special molecular tag is added to them by an enzyme called a cytoplasmic poly (A) element binding protein (CPEB). The presence or absence of CPEB therefore acts as a local switch for the production of these proteins. And CPEB is known to be present in synapses. A part of CPEB looks similar to the part of known prions, which is responsible for their curious properties. It has also been shown that when a synapse is exposed to serotonin, the levels of CPEB increase.

The more a synapse is stimulated, the more it produces CPEB. The more CPEB that is present, the greater the chance that some will take on the prion form. Once that happens, the prion form takes over rapidly. In this proposed model, mRNA molecules go everywhere in the neuron, but only those that reach the stimulated connection marked with activated CPEB are translated into proteins and bring about some of the changes necessary for long-tem memory formation.[8]

Different neurons fire in different ways. Some fire very rapidly, others more slowly. Some fire a single impulse; others tend to fire in bursts. Sometimes a neuron can do both, depending on its incoming signals and on its recent history.

All terminals of the axon of a particular neuron are either all excitatory or all inhibitory, never a mixture of both. The long distance connections from one cortical area to another area are provided by pyramidal cells and are always excitatory. The axons of most inhibitory neurons are rather short and only influence neurons in the same neighborhood. Quite different classes of neurons can produce excitation and inhibition. However, all neurons receive both excitation and inhibition, which prevents them from being always silent, or alternately, going wild.

One thing is evident: a single neuron can fire at different rates and, to some extent in different styles. At any one moment it can only send a limited amount of information.

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[8] *Prion Proteins, A New Twist in the Tale*, The Economist, January 3rd 2004.

Yet during that moment the potential information coming into it is very large. Each neuron reacts to different combinations of its inputs and sends out this new information to many places, meaning all its synapses. It is meaningless to consider one neuron in isolation; we have to consider the combined effect of many neurons.

What one neuron tells another is limited to how exited it is, yet there can be additional information in the pattern. As a neuron sends chemicals down its axon, in some cases these may convey additional information, but the rate of this transport is too slow to convey fast information. The receiving (target) neuron doesn't know where the signals came from. This explains, in part, why we do not know exactly where our perceptions and thoughts are taking place in our brains. There are no neurons whose firing symbolizes this information.

Clusters and Circuits

Neuromodulation, the firing of cells in synchronicity, is not confined to the cellular level, or neighboring clusters of neurons – it occurs at every level of brain functioning. Think of a drug or alcohol altering one or more neurotransmitters or their receptors; it is easy to observe how human behavior, an obvious order of organization, is altered in the presence of such drugs.

The cerebral cortex consists of two separate sheets of nerve cells, one on each side of the head. The sheets vary somewhat in thickness, typically between 2-5 millimeters thick. This constitutes the so-called grey matter. It is primarily made up of neurons, although there are many accessory cells, called glial cells. There are about 100,000 neurons under each square millimeter of cortex. Some connections between neurons are local -- the axon is a fraction of a millimeter to a few millimeters -- but others leave the cortex and travel some distance before entering another part of the cortex or before going elsewhere. These longer axons are often covered by an "insulating" material called myelin, which enables the signal to travel faster and gives the tissue a somewhat glistening white appearance, hence its name, white matter. About 40 per cent of our brain is made of white matter – that is, these longer connections. The most common type of neuron in the neocortex is called a pyramidal cell, because its body is pyramid-shaped, leading to a large apical dendrite. Other neurons such as stellate neurons have branches in all directions; they have been so named because they "resemble" a star.

Neurons, in their resting state, when not much is happening, send impulses at a relatively slow rate, typically between 1-5 Hertz. When talking about neurons in the cortex, I distinguish several types of impulses; two of them, the "echo" signals and the "handshake" signals have two modalities: the resting state, that maintains communication between specific areas, and the active state, which activates related areas. The echo signals serve to help direct the traffic of incoming signals to various parts of the cortex. The handshake signals activate other relevant parts of the cortex. This activity keeps the neurons "alert" and ready to fire. When neurons receive excitatory signals, they become excited and fire at rates typically between 50-100 hertz or more. In the excited state firing can reach rates of 500 Hertz for short periods.[9] If a neuron receives an excess of inhibitory signals, its output of impulses may be slowed down to less than the "echoing"

[9] Richard M. Restack, *Receptors.*

or "handshaking" rate. But the impulses are always of one type; there can be no "negative" impulses.

Neural impulses from the senses are sent to the thalamus. These sensory impulses are relayed to the cortex from here. These relayed sensory signals are what I call "mirror" signals. Any signals generated to produce an action are what I call "command" signals, the true output of the brain.

A circuit is a group of neurons that are linked together by synaptic connections. A system is a complex circuit that performs some specific functions, like seeing or hearing, or remembering, or detecting and responding to danger. The brain formulates categories and uses clusters of neurons,[10] generally in a vertical-cylinder configuration, to represent these. Some clusters, such as the visual systems extend about 10 centimeters square, and within such systems there are multiple maps, which can compress half of a sensory world, one for each eye, into one-centimeter square of cortex. Within each map are distributed many networks or circuits, each contained in about a cubic millimeter of tangled neurons. These neurons stretch over various distances, though many are contained in 0.1 cubic millimeters. The synaptic connections between them are a hundred times smaller. Molecules at least ten thousand times smaller than the synapses, control all this. And last, some of these form structures, such as membranes (and channels through membranes), and others move as messengers through membranes.[11]

Synaptic interactions between two types of neurons, called projection neurons and interneurons, are keys to understanding how circuits and systems function. Projection neurons have relatively long axons that extend out of the area in which their cell bodies are located. In a hierarchical circuit, their main job is to turn on the next projection cell in the hierarchy as well as reaching out to other circuits that need to be activated. Projection neurons are the ones responsible for sending echo and handshake signals some distance. As soon as the sensory-mirrored signals reach the cortex, the cortex broadcasts patterns, the handshakes, and in this way, objects and events are represented.

Interneurons send their short axons to nearby neurons, often projection neurons, and are involved in information processing within a given level of a hierarchical circuit. One of their main jobs is to regulate the flow of synaptic signals by controlling the activity of projection neurons; inhibitory interneurons release a transmitter from their synapses that decreases the likelihood that the postsynaptic cell will fire an action potential. These neurons play an important role in counter balancing the excitatory activity of projection cells.

Projection neurons tend to be idle in the absence of inputs from other projection cells. They are, however, firing in their echo or handshake (background) mode. It should be noted that the handshake signals should be considered whether they are part of feedforward or a feedback signals. Even though in both cases they are activating associated neurons, in former case they are reflecting incoming signals (they are representing what is going on), and in the latter case are activating expected outcomes.

Inhibitory interneurons, though, are often tonically active, which means they are firing all the time. Part of the reason that projection cells are inactive when not being stimulated is that they receive tonic inhibition from interneurons. As a result, when excitatory inputs try to turn on a projection neuron, pre-existing inhibition of the

[10] Joseph, LeDoux, *Synaptic Self.*
[11] Francis Crick, *The Astonishing Hypothesis.*

projection cell has to be overcome. The balance between excitatory and inhibitory inputs to a neuron determines whether it will fire.

The amount of inhibition affecting a neuron can change from moment to moment, depending on other factors. For example, when projection cells in one area of a hierarchical circuit send enough convergent inputs at about the same time to activate projection cells in the next area, the level of inhibition in the second area usually goes up as well. This happens because the excitatory inputs in an area often activate interneurons as well as projection neurons. The momentary increase in excitatory inputs to interneurons leads to a momentary increase in their inhibitory behavior, which in turn produces a momentary inhibition of the projection neurons. So called elicited inhibition contrasts with tonic inhibition. Because rapidly changing states of excitation and inhibition direct the flow of signals through the brain, it's easy to see how a breakdown in the flow of impulses could lead to a neural gridlock.[12]

Also, glial cells can join via gap junctions to form additional networks (syncytium). Gap junctions are essential to astrocytic signaling and it is estimated that more than 50,000 gap junction channels interconnect each astrocyte to its neural neighbors. Through release of Ca+2, a glial syncytium can regulate simultaneous neurotransmission in the synapses enveloped by the astrocyte,[13] and thus assist a group of neighboring neurons to fire synchronously.

Imagine a circuit consisting of two projection neurons, A and B, linked together in series. When A is active, B fires. If the job of the circuit were to make B fire as often as possible as long as A is active, these two neurons are sufficient to do the job. But suppose its job instead is to take a barrage of action potentials in A and turn them into fewer action potentials in B, something that actually occurs quite often in the brain. This could be achieved by giving neuron B an inhibitory playmate (I). This local circuit neuron, like B, receives the output of A and then connects to B. So when A fires, it turns on B and I, and each produce an output. The output of B helps turn on the next cell in the circuit, while the output of I turns B off. As a result, B now produces fewer action potentials when A fires it. If we put more excitatory cells with A to drive B, and time the arrival just so, the tonic inhibition can be overcome. B can now be continuously activated. But being stuck in a fast firing mode is not good for neurons, which can be damaged or even destroyed by unchecked excitation. Each burst of excitation thus needs to be countered with another round of inhibition. This is where elicited inhibition, like that described above, comes in. When an excitatory surge overcomes tonic inhibition, elicited inhibition can rein in the excitation, resetting the circuit and preparing it for new inputs. There are many possible variations of this.

The job of a projection neuron is to turn on the next circuit or the next projection neuron in the circuit. Projection cells thus need to use a neurotransmitter that has two properties. The transmitter first must be able to act quickly at postsynaptic sites – otherwise we could not keep up with rapidly changing events. And it must also be able to change the electrical state of the postsynaptic neuron in such a way that the occurrence of an action potential is more likely to occur. Glutamate fulfills both requirements, and is the main neurotransmitter of projection neurons.

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[12] Joseph LeDoux, *Synaptic Self.*

[13] Cotrina, M.L., Gao, Q., Lin, J.H., & Nedergaard, M. (2001). *Expression and function of astrocytic gap junctions in aging. Brain Research, 901, 55-61.*

Glutamate has two roles. First it serves as a neurotransmitter in the brain. Second, it plays a major part in basic life-sustaining metabolic processes that go on continuously in the body. It is the building block of peptides and proteins. It also is used to produce GABA (gamma-aminobutyric acid). In the brain, it also helps detoxify ammonia, which is a natural by-product of certain chemical reactions.[14]

The precursors of glutamate are glucose and sometimes pyruvate to make the protein alfa-ketoglutarate, which in the presence of the enzyme glutaminase produces glutamate. Also, glutamate can be made from glutamine using the same enzyme. Glutamate in turn is used in the synthesis of GABA in the presence of glutamic acid decarboxylase and the presence of the cofactor pyridoxal phosphate.

The reuptake of GABA is accomplished by removal of GABA from the synapse by GABA transporters (GATs) located in neurons and glial cells. There are four known GATs (GAT-1, GAT-2, GAT-3 and BGT-1). They are often found in GABAergic neurons, thus allowing for collected GABA to once again be concentrated into synaptic vesicles for release. They require the presence of Na+ and Cl- as co-transporters. Eventually GABA is degraded into succinate by the mitochondrial enzymes: GABA aminotransferase and succinic semialdehyde dehydrogenase.

In contrast, inhibitory neurons, especially inhibitory interneurons, often release GABA. In contrast to glutamate, GABA reduces the likelihood of an action potential being generated in the postsynaptic cell.

The inside of the neuron is more negatively charged than the fluid outside when the neuron is at rest. When glutamate binds to the postsynaptic receptors it allows positively charged ions to enter the cell. In contrast, when GABA receptors are occupied, the inside of the cell becomes more negative because negative ions are allowed to pass the membrane. Whether an action potential occurs depends on the relation between glutamate and GABA and other neurotransmitters.

Glutamate receptors tend to be located out on the dendrites, whereas GABA receptors tend to be found on the cell body or on the part of the dendrites closer to the cell body. GABA can extinguish excitation coming down a dendrite and headed for the cell body.

Modulators are neurotransmitters in the sense that they provide a chemical link between the site from which they are released and the location of the receptors upon which they act. In contrast to glutamate and GABA, modulators are less directly involved in the transfer of information from point to point in the hierarchical circuits. Modulators have slower and longer lasting effects. The main classes of modulators are: peptides, amines and hormones. Each can have excitatory or inhibitory effects, depending on the specifics of their participation in each circuit.

Neuropeptides and their receptors are located in far flung areas, sometimes inches apart. Much of the information moving around the brain is kept in order not by synaptic connections but by the specificity of receptors. Miles Herkenhma has estimated that less than 2 percent of neuronal communication actually occurs at the synapses. The way in which peptides circulate through the body, finding their targets in regions far more distant, makes the brain resemble the endocrine system, whose hormones can travel through the entire body.[15] The nature of peptides makes them ideal to communicate

[14] Joseph LeDoux, *Synaptic Self*.
[15] Candace Pert, *Molecules of Emotion*, 1997.

between different systems: the nervous system, the endocrine system and the immune system.

New peptide-containing groups of neuronal cells in the brain called nuclei, the sources of brain-to-body and body-to-brain hookups, are now being elaborated. Ed Blalock from the University of Texas has found immune cells that make endorphins. In his studies Blalock noticed that interferons, peptides that are made by lymphocytes, sometimes mimicked the activity of hormones. He found that lymphocytes also secreted mood-altering brain peptide endorphin, as well as ACTH, a stress hormone, previously thought to be produced only by the pituitary gland. This is an example of how a particular chemical produced by the immune system can be used to communicate between the endocrine system and the nervous system.

Another example is interleukin-1 (IL-1), a polypeptide hormone produced mainly by macrophages in the immune system, and is one of fifty or so identified peptides that mediate the inflammatory reactions caused by injury, trauma or a an activated immune system. In a sequence, IL-1 causes fever, activates the T cells, induces sleep and puts the body in a healing state, allowing it to mobilize its energy reserves to fight pathogenic intruders with maximum efficiency. IL-1 receptors are found in the hypothalamus (long recognized as having a role in fever), in the cortex and higher brain centers (mainly on glial cells and the tough membranes around the brain. Numerous, perhaps all, of the peptides of the immune system can be produced by the brain under some circumstances, and can act on receptors in the brain. A two-way highway of communication can be established via immunopeptides and neuropeptides. This suggests that neuropeptides are also found in the immune and endocrine system, forming a psychoimmunoendocrine network.[16]

Hormones are typically released from bodily glands, like the adrenal, pituitary, or sex glands, into the bloodstream where they travel to the brain and other parts of the body. In the brain they can act as modulators by altering the efficacy of glutamate or GABA transmission by binding to specific receptors. The most common are cortisol, released from the adrenal gland during stress; and the sex hormones, testosterone and estrogen. Because hormones reach the brain through the bloodstream, they can influence many regions simultaneously. However, since only certain areas, and only certain circuits in those areas, possess the relevant receptors, considerable specificity can be achieved by hormonal modulation.

After a neurotransmitter molecule has done its job, in some cases it is recycled – taken back by the axon of the terminal of the first neuron for future use. This is known as reuptake. In other cases it is degraded in the synapse and the waste materials are flushed out by the cerebrospinal fluid, then to the blood, and then the urine. If these process of clearing the neurotransmitter fail (reuptake ceases or degradation stops or both), suddenly a lot more neurotransmitter remains in the synapse, giving a stronger signal to the target neuron than usual. Thus the proper disposal of these messengers is integral to normal neuronal communications.[17]

Occasionally two neurons communicate electrically. For this to happen, their membranes have to fuse in such a way as to allow direct flow of electricity from one to the other. These points are called fusion gaps. In the hippocampus, recent studies have

[16] Ibid.
[17] Robert M. Sapolzky, *Why Zebras Don't Get Ulcers.*

shown, a gap junction electrically couples GABA cells. Consequently, when a GABA cell is activated, excitation can spread between them in such a way as to activate many of the interconnected cells at once. The cells then fire together, in synchrony, and thereby can regulate activity of projection cells throughout the region.[18]

It has been conclusively shown there is neurogenesis (the birth of new neurons as well as synaptogenesis (the creation of new synapses between existing neurons). Synaptogenesis is a common phenomenon, especially early in life, and probably continues up until the moment of death. Synapses are changed every time our brains store an experience[19] or a memory. New connections formed by activity are not entirely created anew, but rather are added to preexisting connections.

Neurons can communicate at different rates and using different neurotransmitters. Recent studies have shown that oscillatory processes at the level of one neuron or a group of neurons in the subthalamic nucleus and the external globus pallidus, which are part of the basal ganglia, produce autonomous oscillations, which underlie tonic activity and are important in synaptic integration. This provides further support for the view that both pattern and rate of neuronal activity encode information.[20]

When a stimulus is presented repeatedly, the exact time of neuronal spikes occur jitters from one trial to the next (relative to the stimulus onset), while the average number of spikes varies less. That is, the first time around, the neuron fires 12 spikes above and beyond its "spontaneous" rate in the 200 msec interval following the stimulus presentation, while the following three presentations evokes 11, 14, and 15 spikes, respectively. Such widespread observations support the *firing rate* view of coding: the assumption that what is relevant is a continuously varying firing rate, obtained by averaging the spiking response over many repetitions of the stimulus presentation. A firing rate code assumes a population of neurons that all express more or less the same features, making this coding strategy expensive in terms of neurons, yet robust to damage.

However, much data suggests that there is more to information coding than firing rates. Also important for coding strategies are oscillations, and synchronization, and probably what is termed, ultra-sparse temporal coding. While individual neurons can generate in excess of 100 spikes within one or two seconds, a cell in the hippocampus might signal with a handful of spikes. Such meager firing can be easily reconciled with the conventional view of rate coding unless the rate is computed over large ensembles of neurons. In other networks an appropriate stimulus triggers a brief burst of activity, say one to four spikes within 10 msec or so. For the following seconds, the neuron is quiet, with no "spontaneous" firing at all. The observed specificity can be amazing, with the cell contributing a single note to the ongoing music and then falling silent.[21]

The Cortex

[18] Ibid.
[19] Ibid.
[20] Mark D. Bevan, Peter J. Magill, David Terman, J.Paul Bolan, Charles J. Wilson, *Move to the Rhythm: Oscillations In The Subthalamic Nucelus-External Globus Pallidus Network.*
[21] Christof Koch, *The Quest for Consciousness.*

The cerebral cortex is a thin layer about 2 millimeters thick and sits atop a mass of white matter. On average there are 148,000 neurons in each square millimeter. This 2-millimeter layer is arranged in six special layers. However, neurons with similar activities tend to be arrayed in vertical cylinders called cortical columns. Minicolumns are about 30 micrometers in diameter, encompassing about one hundred neurons, whereas macrocolumns are in the range of 0.4-1.0 millimeters. Columns have been named blobs, stripes, and barrels and are considered by some to be cortical modules, but cortical cluster would be a more appropriate term.[22] It is at this level, the level of columns, that complex memories are stored. The cortex (in humans) is the repository of a huge memory bank.

Primarily made of neurons, the nervous system is composed of: a) a series of large centers of nerve-matter called collectively, the cerebro-spinal centers; b) small centers, termed ganglia; c) nerves connected either with the cerebro-spinal axis or the ganglia; and d) certain modifications of the peripheral terminations of the nerves forming the organs of the external senses.

The nervous system can be divided into three parts: the spinal cord, the brain stem (at the top of the spinal cord), and the forebrain above that. The nervous system receives information only from the various transducers in the body. A transducer turns a chemical or physical influence, such as light, sound or pressure, into an electrochemical signal.

The cortex sometimes referred to as gray matter is composed primarily of the bodies of neurons and derives its name from its color. The gray matter is generally arranged in six layers; from the surface inwards: (I) a thin layer of white substance with very few cells consists mostly of axons running parallel to the surface; (II) a layer of gray substance; (III) a second layer of white substance; (IV) a second gray layer with stellar neurons; (V) a third white layer with pyramidal neurons and a class of extra-big pyramid-shaped neurons; and (VI) a third gray layer with several types of unique neurons.[23] Layers II and III are similar with many pyramidal neurons.

The columns are arranged perpendicular to the layers. The layers within each column are connected through axons with many synapses along the way. In general, but not always, neurons in a column tend to become active together for the same stimulus.

The somatic sensory cortical areas are part of the cortex. The cortex has six principal cell layers. Thalamic neurons that project to the cortex (mirroring signals) generally do so to layer IV. This is the input layer of the cortex. Neurons in layer IV distribute this incoming information to neurons in other layers, mostly layers II and III, which cause neurons in layers V and VI to become active. Layers II, III, V, and VI are the output layers of the cortex. Pyramidal neurons in these layers project to other cortical areas as well as subcortical structures. Layer I does not contain many neurons, mostly dendrites of neurons located in deeper layers and elsewhere.

For the most part, neural impulses travel horizontally in layer I and vertically in layers II through VI. Roughly ninety percent of the synapses in neurons within a column come from places outside the column, in some cases from the opposite hemisphere.

There are slight variations in the layers in different areas of the cortex, but the six layers are found in approximately 95% of the cortex. The remaining 5%, termed the allocortex, is morphologically distinct, and is involved in olfaction comprising the

[22] William H. Calvin, Handbook of Brain Theory and Neural networks, Cortical *Columns, Modules, and Hebbian Cell Assemblies*
[23] Henry Gray, *Gray's Anatomy.*

olfactory bulb and some aspects of learning and memory, primarily in the hippocampal formation, parts of the occipital lobe and the dentate convolution.

The cortex has three kinds of efferent projections from the output layers, mediated by three separate classes of pyramidal neurons: corticortical association, callosal, and descending projections. The efferent projection neurons with different targets are located in different layers and their impulses have slightly different functions: (a) Corticocortical Association neurons are predominantly in layers II and III and project to areas on the same hemisphere; used for handshake signals; (b) Callosal neurons are also in layers II and III, but they project their axon to the contralateral cortex via the corpus callosum; also used for handshakes, but to the opposite hemisphere; (c) Descending projection neurons are separate classes of projection neurons used for echo and command signals whose axons descend to (1) the striatum (the caudate nucleus and the putamen receive echoes and commands), (2) the thalamus (receives echoes), (3) the brain stem (receives commands), and (4) the spinal cord (also receives commands). Descending projection neurons that terminate in the striatum, brain stem, and spinal cord are found in layer V (used for echoes and commands), whereas those projecting to the thalamus are located in layer VI[24] (used for echoes) and branch to the first order nuclei and the reticular nucleus. Studies have also shown some projection neurons from layer V terminate in the thalamus without branching to the reticular nucleus.[25] These are also used for echo signals, but are coordinating the mirroring of the signal to additional cortical areas.

There are slight variations in the cortex, as expected, according to functionality. The prefrontal association cortex and the primary motor cortex present a much thicker layer III than the parietal-temporal-occipital association cortex and even more so then the primary visual cortex, with layers I and II of similar thickness. In contrast, layer IV, the input layer, is thickest in the visual primary cortex, less so in the parietal-temporal-occipital association cortex and the prefrontal cortex, and thinnest in the primary motor cortex, reflecting the amount of input signals in each region. As expected, vision requires the largest input. Area V, which sends signals to the striatum, brain stem and spinal chord, as expected, is thickest in the primary motor cortex, sending motor commands; less thick in the parietal-temporal-occipital association cortex; then the prefrontal association cortex; and thinnest in the primary visual cortex. Layer VI, which send signals to the thalamus, is thickest in the parietal-temporal-occipital association cortex, reflecting the high density of echo signals required to coordinate the myriad input sensory signals. Layer six is approximately the same thickness in the other regions.[26]

Another way of looking at the cytoarchitecture of the cortex divides it into four layers. First, we encounter the molecular layer. This is equivalent to layers I and II. In this layer the neurons are polygonal, triangular or fusiform in shape. Each polygonal neuron gives off some four or five dendrites, while its axon may arise directly from the cell or from one of its dendrites. The triangular neurons give off two or three dendrites, from one of which the axon arises. The fusiform neurons are placed with their long axes parallel to the surface, each end prolonged into a dendrite. Their axons, two or three in

[24] John H. Martin, *Neuroanatomy,*
[25] Guillery RW. *Anatomical evidence concerning role of the thalamus in corticortical communication: a brief review.* J Anat 1995 Dec;187(Pt 3):583-92.
[26] John H. Martin, *Neuroanatomy.*

number, arise from the dendrites, and like them, take a horizontal course. The distribution of the axons and dendrites of all three sets of neurons is limited to the molecular level.

The second and third layers are known as the layer of the small and the layer of the large pyramidal neurons, respectively. As the name implies, the difference resides in the size of the neurons. These two layers are equivalent to layers II, III and IV. The body of each neuron is pyramidal in shape, its base being directed to the deeper part of the brain. The axon-cylinder projects from the base of the neuron and passes into the central white substance, giving off collaterals in its course. It is distributed as a projection, commissural or association fibre. Both the apical and basal parts of the cell give off dendrites. The apical dendrites end up in the molecular level.

The fourth layer is called the layer of the polymorphous neurons, and these neurons, as the name implies, are very irregular in shape, the commonest varieties being of a spindle, star, oval or triangular shape. Their dendrites are directed outward, toward, but do not reach the molecular level; their axons pass into the subjacent white matter. This is equivalent to layers V and VI.

There are two other kinds of neurons, but their axons pass in the opposite direction of the pyramidal and polymorphous cells, among which they lie. They are the cells of Golgi, the axons of which do not become medullated, but divide immediately after their origin into a large number of branches directed toward the surface of the cortex; and the cells of Martinotti, chiefly found in the polymorphous layer. Their dendrites are short, and may have an ascending or descending course, while their axons pass out into the molecular layer (I and II) and form an extensive horizontal arborization.

The nerve fibres fill up a large part of the intervals between the neurons. They may be medullated or non-medullated, the latter comprising the axons of the smallest pyramidal cells and the cells of Golgi. The fibres may be either transverse (tangential or horizontal) or vertical (radial). The transverse fibres run parallel to the surface, intersecting the vertical fibres at a right angle. They consist of several strata, of which the following are the most important: (1) a stratum of white fibres, equivalent to the first layer of white matter on top of the molecular level (layer I); (2) the second white layer that runs through the layer of large pyramidal neurons (layer III); (3) the third white layer, which runs between the layer of large pyramidal neurons and the polymorphous neurons (layer V).

The white matter consists of medullated fibres, varying in size and arranged in bundles, separated by neuroglia. They are primarily axons and their myelin coating is what gives it its distinctive white color and name.

In summary, layer IV is the input layer to the cortex, where the mirror signals from the thalamus arrive; layer I distributes information horizontally through handshake signals; layers II and III are processing layers where handshakes activate other related areas; and layer V and VI are the output layers: from layer V, command and echo signals go to the brain stem, spinal cord and striatum; from layer VI, echoes go to the thalamus to help direct incoming signals and automatize responses. The cells of Golgi and Martinotti serve as inhibitory feedback signals from the input (IV) and output (V and VI) layers back to the processing layers (I, II and III). The cells of Golgi have extensive transverse arborizations. The cells of Martinotti are equivalent to inverted pyramidal neurons. The inhibitory impulses from the cells of Golgi and Martinotti serve to quiet the processing layers once the input has been received and once the output layers have fired. In this way,

both the input and output affect the processing, which in turn further affects the output. The change in output of layer VI affects the input from the thalamus because the echoes are changing. In this way, the sensory impulses are quickly and efficiently mirrored to all relevant cortical areas. Later we will see in more detail the hierarchical structure of the flow of neural impulses.

Brief Brain Anatomy

There are cavities in the brain that are filled with cerebrospinal fluid called ventricles. The cerebrospinal fluid contains all the chemicals needed by the cells that make up the nervous system. This fluid is a clear secretion originating deep within the brain and acts as a shock absorber for the brain and spinal cord. It also provides support, as the brain is buoyant and floats within the cerebrospinal fluid.

The brain is that portion of the cerebro-spinal axis that is contained in the cavity of the cranium. For purposes of description the brain has been divided into five parts: (1) the two cerebral hemispheres, (2) the inter-brain, (3) the mid-brain, (4) the hindbrain, made of the pons Varolii and cerebellum, and (5) the medulla oblongata.

The brain is divided into two hemispheres. They are composed of an outer stratum of gray matter, called the cortical substance (generally referred as cortex). It presents a number of creases, termed fissures and sulci, which separate the surface into irregular eminences, named convolutions or gyri. The fissures are of large size, few in number and nearly constant in their arrangement. The sulci are more numerous, superficial depressions of the gray matter, which is folded inward and only indents the white substance. The sulci are fairly constant in their arrangement, and have received names indicative of their position and direction. They vary slightly from individual to individual and are similar, without being identical, on the two sides of the brain.

Fissures divide the brain's surface and these divisions are known as the frontal, parietal, occipital and temporal lobes.[27]

Each hemisphere is a distinct half, and each has four major components: cortex, hippocampal formation, amygdala, and basal ganglia. The portion of the basal ganglia that has the most complex shape is called the striatum. The internal capsule splits two components of the striatum, the caudate nucleus and the putamen. The putamen, together with the globus pallidus, is termed the lenticular nucleus.

The internal capsule is a two-way path for information from the thalamus to the cortex and from the cortex to the subcortical structures.[28] Also known as the corona radiata, it is the pathway for the mirror and echo signals. The echo signals arrive from the cortex to the thalamus and help direct the flow of signals from the senses to the cortex. The mirror signals are the sensory signals relayed to the cortex by the thalamus.

The inter-brain is the region of the third ventricle, and comprises the parts developed from the second cerebral vesicle, together with that portion of the first vesicle that is not concerned with the formation of the cerebral hemispheres. It is connected above and in front with the cerebral hemispheres; behind, with the mid-brain.

[27] Henry Gray, *Gray's Anatomy*.
[28] John H. Martin, *Neuroanatomy*.

The two hemispheres are connected by the Corpus Callosum, which is a thick stratum of transversely directed nerve fibers, by which almost every part of one hemisphere is connected with the corresponding part of the other. The fibers of this body when they pass through it radiate in various directions, to terminate at the gray matter of the cortex.

The corpus striatum has received its name from the striped appearance that its section presents, a result of diverging white fibers mixed with the gray matter, which forms the greater part of its substance. The larger portion of this body is embedded in the white substance of the hemisphere and is known as the lenticular nucleus. The other part is known as the caudate nucleus.

The mid-brain is the constricted portion of the brain that connects to the pons Varolii with the inter-brain and hemispheres. It is developed from the third cerebral vesicle. In front and above, it is continuous with the inter-brain; below, with the pons.

The thalami are two large oblong masses, situated on either side of the third ventricle. They are composed mainly of gray matter, but their free surfaces are coated with a thin layer of white nervous matter separating them from each other. They present outer and under surfaces, which are blended with contiguous parts of the brain, and upper, inner and posterior surfaces, which are not. This gray matter is arranged in two masses, the outer and inner nuclei.[29] There are many inter-thalamic connections between these surfaces, as well as numerous thalamic-cortical, and cortico-thalamic connections.

The thalamus is intimately connected with the following structures: (1) a relay for the greater number of fibres of the tegmentum; (2) the pulvinar, which receives many of the fibres of the optic tract; (3) the frontal, occipital, temporal and parietal lobes; (4) the corpus striatum: the projections to the caudate nucleus leave the external surface; those for the lenticular nucleus leave the inferior aspect of the thalamus; (5) the corpus albicans through the bundle of Vicq d'Azyr.[30] The thalami are one of the main keys to understanding the brain's functions. They are the main relay station of signals and automatic switches to activate and deactivate different brain structures.

The pineal gland is a small reddish gray body, placed immediately above and behind the posterior commissure and between the anterior corpora quadrigemina, on which it rests.

The tegmentum is that portion of the mid-brain which is superior to the substantia nigra. It consists of longitudinally directed strands of white fibres that are separated from each other by transversely arched fibers. There is also a considerable quantity of gray matter.

The substantia nigra is a layer of deeply pigmented gray matter which separates the crusta from the tegmentum.

The hindbrain comprises those parts developed from the fourth cerebral vesicle; namely, the pons, the cerebellum and the upper half of the fourth ventricle.

The cerebellum consists of three lobes, a median and two laterals. It is contained in the inferior occipital fossae, and is situated beneath the occipital lobes.

The medulla oblongata is the lowest division of the brain, and is continuous with the spinal cord. It is developed from the fifth cerebral vesicle, the cavity of which forms the lower half of the fourth ventricle. It extends from the pons Varolii to a plane passing

[29] Henry Gray, *Gray's Anatomy.*
[30] Ibid.

transversely just below the decussation of the pyramids, at which level the spinal cord, commences.[31]

Neurons in the basal nucleus of Meynert contain acetylcholine and project laterally to the cortex and medially to the cingulate gyrus. The cholinergic projection to the hippocampus and adjoining regions originate from the medial septal and the nucleus of the diagonal band.

The dopaminergic neurons are mostly located in the midbrain, in the substantia nigra and the ventral tegmental area. The major targets are the striatum and the frontal lobes.

There are numerous brain stem nuclei with noradrenergic neurons. However, the locus ceruleus has the most widespread projections. Based on these connections, they play an important role in the response of the brain to stressful stimuli, particularly those that evoke fear.

The raphe nuclei consist of numerous distinct groups of brain stem neurons located close to the midline. They use serotonin as a neurotransmitter. The raphe nuclei from the rostral pons and midbrain give rise to ascending projections to the thalamus, the cerebellum, and the cortex. Projections from the raphe nuclei in the medulla target other brain stem regions and the spinal cord.

The importance of these connections and neurotransmitters will become apparent later.

2
Neural Networks

Several simple examples of neural networks illustrate some interesting and potential ways that neurons can achieve the symbolic representation of a concept. These, of course are gross simplifications. I draw for this small section on the book *Apprentices of Wonder, Inside the Neural network Revolution* by William F. Allman.

Neural networks have been simulated on computers in an attempt to understand how neurons can work together in the brain. One of the simplest types of neural nets is called a perceptron. They have one layer of modifiable connections between their input and output connections.

Suppose that you want to build a machine that can select what drink to serve depending on what food is being offered. If we had four inputs, we could consider, in binary form, steak to be 1010, fish could be 0101, pizza then 1100, and peanut butter 0011. The output could be, correspondingly, red wine 1100, white wine 0011, beer 1001 and milk 0110. By introducing a threshold in some connections, making it more biological-like, which in some cases could be receiving a signal from two neurons, it is straightforward to see that by playing with the connections you could easily produce the desired result when you are presented with a certain input. This type of network can only hold a few patterns and make some simple associations. More sophisticated networks have been created by adding to this simple design. There are nets with many more neurons, with neurons that can fire in more ways (several values like 1, 2, 3 or +1 and -1), or connections with changing values that make the threshold higher or lower. These

[31] Ibid.

networks can have an associative memory – that is, they can take a partial input and fill out the rest of the output pattern.

As networks become more and more complex, it becomes harder and harder to determine the values for the connections, so ways were found to make the connections adjust by themselves. In other words, the nets would have to learn. This brings to mind the varying strengths between synapses that are associated with the NMDA channel and the Calcium ions mentioned earlier. Simplistically, in artificial nets, you turn on the desired input and output; then the connections between neurons are adjusted. If a pair of neurons contributes to a partially desirable output, it is strengthened. With these simple trial and error adjustments (learning as we coach it) the neural net can be trained to recognize patterns and make generalizations. Minsky and Papert convincingly demonstrated that these types of networks are fundamentally incapable of performing many tasks; consequently, they were abandoned as not being of much interest.

When another layer of neurons is added between the input and the output layers, many more interesting things can occur. An interesting example is the Little Red Riding Hood network. On one side you have as input: Big Ears, Big Eyes, Big Teeth, Kindly, Wrinkled, Handsome. On the other side, you have as output: Run away, Scream, Look for woodcutter, Kiss on cheek, Approach, Offer food to, Ask for help. You connect every input with every output, but the strength of the connection is weighted according to the degree of relation between desired output and input. For example, Big Teeth and Kiss on cheek would be connected very mildly, and Wrinkled and Offer food to would be connected strongly. The desired output could be easily programmed in a two-layer perceptron.

We could build a neural network with three hidden neurons between input and output. For argument's sake, we'll call these three "units" Wolf, Grandma and Woodcutter. If we now make the connections with the appropriate weights between input and Wolf, Grandma and Woodcutter, and in turn then make the appropriately weighted connections between these three and the output, we will have less connections, but more importantly we have a representation of the outside world. The Wolf unit is most active when the input is big ears, eyes and teeth. The Grandma unit is most active with big eyes, a kindly manner and wrinkled skin. The Woodcutter unit is most active for Handsome, kindly with big ears.

This ability to form representations of something gives neural nets with hidden units tremendous power. The hidden units allow for more complex types of computation but also allow for a representation of high-level concepts that are needed for complex tasks. They can represent meaning. The problem is determining which the important concepts are and wiring the network to use them. In the Little Red Riding Hood network, the concepts of Granny, Bad Wolf and Woodcutter and how to wire the net are fairly obvious. But for more complicated tasks there are no immediately apparent solutions. Much less is it obvious how to wire hundreds or even thousands of connections in large multilayerd networks.[32]

There is another small group of neural networks called auto-associative memories. These are also built of simple "neurons" that connect to each other and fire when they reach a certain threshold. They are, however, connected differently, using lots of feedback. Instead of only passing information forward, as in the back propagation

[32] William F. Allman, *Apprentices of Wonder*.

network just described, auto-associative memories fed the output of each neuron back into the input. This feedback loop leads to some interesting features. When a pattern of activity is imposed on the artificial neurons, they form a memory pattern. The auto-associative network associated patterns with themselves, hence the term auto-associative memory. To retrieve a pattern stored in such a memory, you must first provide the pattern you wish to retrieve.

Yet, an important property is that you don't have to have the entire pattern you want to retrieve in order to retrieve it. You only need a part of the pattern, or even a some-what messed-up pattern. The auto associative memory can retrieve the correct pattern, as it was originally stored even though it is presented with a messy version of it.

Unlike most other neural networks, an auto-associative memory can be designed to store sequences of patterns, or temporal patterns. This feature is accomplished by adding a time delay to the feedback. With this delay, you can present an auto-associative memory with a sequence of patterns, similar to a melody, and it can remember the sequence.[33]

3
The Magic, A Brief Overview

In this chapter I present a brief overview of the complexities and elemental functions of the brain. The basis for a neuropsychological model that can serve to guide future research and help improve therapeutic approaches will be laid out

Basically, the brain constantly receives internal signals from the body and external signals from the environment through the senses. It interprets these signals and produces the right responses or behaviors for the continued *existence of the organism in a state of optimal well-being, and optimizes the ability to reproduce* and pass on its genes. At first glance, the brain seems to achieve this as if by magic, imbued by some higher intelligence. A careful analysis, however, reveals an amazingly ingenious solution of self-organization towards maximizing adaptability.

The brain exists inside and as part of the body; it is not independent of it. The brain is intimately connected to the body. It has evolved to serve the whole organism as a system that manages the well being of the body and coordinates the most appropriate responses to the ever-changing environment. The brain achieves this by continuously monitoring chemical signals in the blood and the electrochemical signals received from all the senses and interior brain and body impulses.

It all begins with neurons signaling one another. The nervous system is organized into two anatomically separate but functionally interdependent systems: the peripheral and the central nervous system. The peripheral nervous system is divided into somatic and autonomic divisions. The somatic division contains the sensory neurons that innervate the skin, muscles and joints. This division also contains the axons of motor neurons that innervate skeletal muscle, although the cell bodies of the motor neurons lie

[33] Jeff Hawkins, *On Intelligence.*

within the central nervous system. The autonomic division contains the neurons that innervate glands and the smooth muscle of the viscera and blood vessels. This division, with its separate sympathetic, parasympathetic, and enteric subdivisions regulates body functions.[34]

The neural impulses travel from all parts in the body to the spinal cord and up to the mid brain and from there to the thalamus. The thalamus relays the signals to the cortex with the assistance of echo signals. The cortex is an expanded memory system. Through the clever use of memory, the storage of patterns, the brain achieves many of the functions it performs. There are different body impulses relayed to the cortex and they can be divided into three main categories: muscle-skeletal, tactile and homeostatic.

The homeostatic impulses relate to the entire internal house keeping functions necessary for the well being of the organism. These are related to keeping track of the body state: the signals relating to blood pressure and temperature, tension in the arteries, heart beat, concentration of sugar and water in the blood, the state of the organs and so on. The autonomic system coordinates these homoeostatic functions to maintain the organism in optimal condition. The autonomic system will closely regulate heartbeat, breathing, sweating, digesting and all functions necessary to supply all the organs and their cells with all the chemicals needed for a healthy existence.

The autonomic system uses, in addition to acetylcholine and norepinephrine, all of the known peptides, distributed in subtly different intricate patterns all the way down both sides of the spinal cord.[35]

I call the proprioceptive (muscle-skeletal) and tactile signals the somatosensory impulses, as they are relayed by the thalamus to the somatosensory regions of the brain's cortex.

The tactile impulses from the surface of the skin include vibrations, the hot and cold, and pressure signals. These impulses are relayed to areas adjacent to the primary somatosensory area.

Our senses -- eyes, ears, taste, smell, proprioceptive, and tactile -- continuously give us information of the outside world. Let's call all this information the sensory impulses. We can differentiate them by calling them visual, auditory, gustatory, olfactory, proprioceptive and tactile impulses, respectively. Each sense (except smell whose pathways are direct to the cortex) has its own pathways to send information to the thalamus, which in turn relays the signals to specialized areas in the cortex.

The basic premise is that the brain achieves many of its different functions using similar architectures and electro-chemistries: all neurons are always firing impulses known as background signals. The cortex is an expanded memory system that aids the other structures of the brain. This assumption is based on the fact that the cortex is remarkably uniform in appearance and structure. Regions of the cortex can vary slightly in thickness, cell density, proportion of types of neurons, number of synapses or length of projections, but still maintain a similar cytoarchitecture of six layers with the same cell types and connections throughout. The neural activity for seeing, hearing, thinking or remembering must be similar, if not identical.

The background neuronal signals can be of various types. The quiet state of the neuron is basically announcing that since there is no change, there is nothing new to

[34] John H. Martin, *Neuroanatomy*.
[35] Candace B. Pert, *Molecules of Emotion*, 1997.

convey. This quiet state sends signals of two types: echo and handshake signals. The echo signals primarily go from the cortex to the thalamus and the striatum, and the handshake signals go from one area in the cortex to another, from one hierarchy to another and back. The background signals serve to maintain certain connections ready to be activated and to assist the flow of signals. The echo and handshake signals have two states: (1) the quiet state maintains the connections, and (2) the excited state, which activates related circuits.

As soon as there is some change, the neuron is said to have become excited and sends a signal. The signals in the ascending pathway of the corticospinal tract carry the somatosensory signals relating to tactile sensations of the skin, hot and cold, and pressure, as well as signals relating the position of all body parts. The sensory signals are relayed to the thalamus. The basal ganglia sit atop the midbrain at the top of the spinal cord, at the center of the brain. The basal ganglia consist of several interconnected structures: the thalamus, the putamen, the globulus pallidus, the caudate nucleus and the amygdala.

Conversely, the basal ganglia, particularly the thalamus, are continuously receiving echoes from the cortex. The thalamus is primarily responsible for determining the nature of the incoming signal by finding a best match with the signals it is receiving from the cortex. The cortex is basically a hugely expanded memory system. In this way the cortex assists the thalamus in relaying the signals to the appropriate areas in the cortex. I have called the relayed signals mirror signals for two reasons: a) the incoming signals, instead of being reflected as a mirror image are relayed forward to the cortex retaining the same information, much as a reflection in a mirror does; think of a mirror that transmits through it the image it captured instead of reflecting it. And b) the incoming signals, when matched to an echo, are reflected back (relayed) to where the echo originated.

The basal ganglia using the signals from the senses will create a map of the extrapersonal space and create a continuum with the map of the intrapersonal space, thus allowing the body to move successfully through the environment. In a secondary manner, the brain will interpret what all the objects of the outside world are, as well as their significance, if any.

In a parallel and simultaneous process, the brain, as it receives outside stimuli, will attempt to produce emotions corresponding to the stimuli in such a way that there is a continuous balance between the internal emotional landscape and the external ever-changing world. In so doing, as emotions shift constantly, the brain changes its mode of functioning and quickly activates the related memories and experiences. This in turn will guide the organism to find the optimum solutions to the challenges and opportunities presented according to genetically wired and learned responses.

The limbic system is made up of the basal ganglia, the hippocampus, the hypothalamus, the pituitary gland, the pineal gland, the fornix, the mammillary body and the cingulate gyrus. The limbic system, essentially following instructions from the thalamus, will orchestrate the chemical changes that govern emotions and will integrate the information from the different senses with the somatosensory information. The caudate nucleus performs the switching that will turn on certain memories and modes of thinking associated with a particular emotion and vice versa.

The signals going to the brain stem and forming a descending pathway in the corticospinal tract carry commands that will reach the motor neurons.

The echo signals primarily serve the purpose of assisting to coordinate the traffic of incoming signals. The echoes are a collection of signals (memories) that help the thalamus determine the nature of the incoming signal and where it needs to be relayed. The echo signals also serve as thalamic emotional triggers when emotional competent stimuli are matched by the thalamus, initiating automatic emotional responses without further cortical processing of signals.

When neurons send impulses from the cortex to other areas in the cortex, or the opposite hemisphere, I call these impulses handshakes. The handshake signals are primarily inquiries, a search for relevant information pertaining to the incoming signals: "Do you have something related to what I'm looking for?" If the answers is, "yes," a handshake is established, a connection activated. A hand goes out, so to speak, and when it finds a receptive hand, a handshake is established, a signal is sent back. This is equivalent to thinking that if A fires and B is firing also, the connection is strengthened with coincidental firing.

The handshakes also activate memories of what is expected to happen next, as these possibilities are also associated to the incoming stimulus. These potential expectations in turn send their own echoes, and if matched at the thalamus, generate a new set of handshakes. Forward handshakes mirror what is happening and feedback handshakes advertise what is expected. The forward signals alter the feedback signals and vice-versa.

The echoes and handshakes can carry a tag. Tags are used as addresses to relay the received signal to other areas in the cortex or to send another echo to the thalamus requesting it to relay the pertinent signal. The tags can also help coordinate the timing of the impulses and help the thalamus refer signals in time.

The sensory impulses are interpreted thanks to the echoes, handshakes and mirror signals, which ultimately will produce commands to action and thinking.

The thalamus sits at the center of the brain continuously receiving echo signals from the neurons in the cortex. When the thalamus finds a match between incoming sensory signals or body signals with a particular echo from the cortex, it relays it to the area where the echo originated, or if the tag indicates so, it relays it to the new address as well. These relayed impulses are what I call mirror signals. It is an elegant solution to quickly relay incoming signals to all the appropriate areas. Also, when an emotional competent stimulus (ECS) is matched to an echo representing the ECS, the thalamus automatically triggers the emotion without further processing of the stimulus. Further processing of the stimulus will reinforce or dampen the initial emotional response.

Pavlovian conditioning is another good example of how an echo matched to an incoming stimulus, automatically produces a response.

To support my views, I present some evidence presented by R.W. Guillery. Guillery's research suggests there are two types of thalamic nuclei, depending on the afferent fibers they receive from ascending pathways or descending from the cortex. First order nuclei receive their primary afferent signals from the ascending pathways and corticothalamic afferents from layer VI, which also send signals to the thalamic reticular nucleus. The second, higher order nuclei receive most of their primary afferents from the pyramidal cells in cortical layer V. However, these corticothalamic projections don't branch out to the thalamic reticular nucleus. Guillery proposes that these latter

projections are largely concerned with transmitting information about the output of one cortical area to another cortical area.[36]

The impulses coming from layers V and VI are echo signals, originating from areas that were activated by handshakes and are instrumental in aiding the thalamus internally to mirror incoming signals to more cortical areas. The impulses from layer VI are mostly concerned on matching echoes to incoming stimuli and so just help mirror (relay) the incoming signals to the cortex. The echoes from layer V have a hierarchical trace, and have to do with directing the original signal to a higher area in order to resolve ambiguity, or to impose an already identified situation on the lower (hierarchically speaking) cortical areas.

When the signal reaches (is interpreted by matching a pattern of signals) an area (the one that sent the echo) it makes the appropriate connections to other areas using handshakes through projection neurons and so activates other relevant areas of the cortex. These signals travel straight forward to adjacent areas, or can use the U-shaped fibers to go to farther away regions in the cortex. The tag "remembers" what other areas in the cortex need the information. Mirror signals can also have a tag, either from the original echo or added by the thalamus. This tag in turn would be interpreted by the region in the cortex receiving it to pass the signal to other relevant regions in the cortex by means of a particular handshake. Handshakes with tags can also inform an area to get in touch with the thalamus with the appropriate echo, so the original signal can also be mirrored there. The handshake can also "instruct" to relay the signal to another area.

Some cortical areas are organized in a hierarchical manner, with up to a dozen levels or more, each one subordinate to the one above it. However, as we will see in detail later, there also exist extensive feedback signals and shortcuts.

The thalamus also tags the signals it relays in a sequential manner in the order they were received; it refers the signals.[37] Think of indexing them in a correct temporal order, independent of when they were initially received or perceived (interpreted) in the cortex. The brain will construct an event using the referred tags to insure that all stimuli are presented, sequentially in time, in the correct order.

In large brains the cortex is basically divided into two hemispheres, each with an anterior and posterior half separated by the central sulcus. The posterior half is where the sensory input signals arrive: vision, hearing, tactile and proprioceptive. The larger the cortex the more finely can signals be interpreted. The anterior half contains the motor cortex, responsible for moving the body and is concerned with planning and behavior. The larger the cortex the array of more complex movements and behaviors become possible.

First, I will present an overview of how the brain constructs various maps of the body in order to control movement. At all times (under normal conditions) the brain will create a physical representation of our body. This physical representation will contain all the information necessary to control every muscle. This map corresponds with what is called the Primary Motor Area.

The somatosensory area creates a spatial body map relating to all parts of the body. The heat and cold sensors have their own body maps in adjacent areas of the

[36] Guillery RW. *Anatomical evidence concerning role of the thalamus in corticortical communication: a brief review.* J Anat 1995 Dec;187(Pt 3):583-92.
[37] William H. Calvin, *The Cerebral Symphony*.

cortex. The somatosensory impulses will enable the brain to keep track of where all our body parts are, as well as relaying all tactile sensations being sent by the skin as it interacts with the environment. The sensation of each body part is akin to a memory of it, and when accompanied by the corresponding somatosensory signals, the brain experiences the body part as real.

The brain creates, using all the homeostatic signals, a map representing the Body State. This map, as its name implies, will quickly inform the brain in what state (emotionally and otherwise) the body is.

When I refer to maps or areas in the cortex, I emphasize, these maps are slightly variable from individual to individual, and can even vary in an individual over time. These variations can be relative to size or location, but they are more or less present in roughly the same places in most individuals.

I start with body control, not only because it is one of the most studied and perhaps better understood functions of the brain, but because it illustrates the interrelatedness of all the brain areas, particularly the various cortical areas. The brain uses movement for multiple purposes: for locomotion; for speech, and through prosody, singing; through hand and body signals, for communication; and, through facial expression, gestures and body posture, for emotional expression.

All the nerve impulses generated in the brain and going to the muscles are called the motor impulses. These signals differ from the handshakes and echoes; they are command signals, and produce a contraction or relaxation of the muscles. All the commands controlling the body movements are generated in the primary motor cortex, aided by the somatosensory area, the supplementary motor cortex and the pre-motor cortex. These two latter areas correspond to the memory systems for movement; between them, they remember the correct sequences of muscle contractions to achieve complex movements. Most of the cortex is an expanded memory system. Not surprisingly, the primary somatosensory cortex and the primary motor cortex lie side by side. Connections (communications) between these two areas are, as expected, extensive.

The nervous system and more specifically the brain, construct representations of our body and store sequences of motions using memory systems. In this way, automatic control and certain types of movement are easily activated. The somatosensory signals from different parts of the body reach the brain continuously; when they are perceived, they feel like my arm or my foot is there. Likewise, the brain uses expanded memory systems to interpret signals from the environment relayed by our senses. When these memory systems are applied to signals that are processed in real time, the illusion of hearing or seeing is felt. This feeling is different than remembering or recalling a stored memory, where the memory itself is distinguished by the fact that a real sensory signal is not present.

The brain creates an illusion of our bodies to control its movement and navigate through the environment. The brain creates the illusion of seeing “what is out there”. The master magician, the brain, creates a feeling for it all: of what we hear “coming from there” or what “out there sounds like”. To protect our bodies from bad food, it will produce the illusion of “tastes yucky”. To ensure that we reproduce, it will create the most fabulous illusion of all, “Oh, I’m so in love!” Ultimately, the brain is an organ that helps maintain the illusion of self to protect the integrity of the body.

Second, I will present a brief overview of the visual system and of some of its similarities with the motor system. The visual system, which provides spatial information without necessarily interpreting what is out there, and the motor system, which controls the body through the motor map, together create a unified map of the extra and intrapersonal space. In this way, the organism relates itself to space and navigates through the environment.

In a hierarchical structure, more and more information will be extracted from the visual signals in each specialized area. In a parallel way, signals will be diverted to various areas to extract different kinds of information. This hierarchical and parallel structure will allow the brain to ultimately store memories that will distinguish patterns and detect ever more rich and useful information from the multiplicity of raw signals that are being processed.

As the cortex got larger over evolutionary time, it was able to store more memories about the world and make more predictions. The complexity of those memories and predictions also increased.[38]

To understand the visual and motor systems better, I will introduce the notion of various memory systems. Memories are built and stored slowly through experience in the cortex. Memories are a basic part of the sensory systems that help interpret the sensory signals better. This also holds true for the interpretation of signals originating from within our bodies and brains. Memories include experiences, procedures and sequences that are necessary to interpret the incoming signals according to past experience.

All these brain regions, also, in a hierarchical and parallel manner, will activate other regions that store more information (memories) to interpret the original signal as well as memories of associated expectations. Once the signal is interpreted and a response is determined to be required, the cortex will send these signals back to the basal ganglia so the basal ganglia can relay the commands to the muscles or activate or deactivate the different thought and emotional (chemical) responses required.

Behavior and prediction are two sides of the same coin. Although the cortex can make predictions, these can only be accurate if it knows what behaviors are being performed.

The motor system in the frontal lobes is also hierarchically organized. The lowest area, M1 sends projections to the spinal cord and directly drives muscles. Higher areas send motor commands to M1. The hierarchy of the motor areas and the hierarchies of sensory areas are similar, however, we need to think of signals moving down the hierarchy of the motor areas, whereas, in the sensory areas signals move upwards. Yet, we must keep in mind that through feedback information flows both ways. What we call feedback in sensory areas is the output of motor regions.[39] In other words, what is equivalent to motor commands, in the sensory areas becomes a concise output or interpretation, i.e., loud red sports car. It is extremely important to understand that information not only flows upwards in the brain's hierarchical structure, but actually has more projections going downwards.

The attentional systems evolved to deal with the unexpected. When the thalamus matches a stimulus with an echo, it relays the signal to the cortex. Handshakes activate expected memories associated to the stimuli. These in turn generate echoes. The echo that

[38] Jeff Hawkins, *On Intelligence.*
[39] Ibid.

is matched to the next pattern of stimuli is relayed to the cortex and becomes the starting point to generate the new handshakes that activate the next expected pattern. When the thalamus cannot make a match between expected echoes and stimuli, an unexpected event is detected and the attentional systems are automatically focused on these stimuli.

The hippocampus is a brain structure that assists in storing memories. In a general level the hippocampus will be activated by novel events. In order to do this, novel stimuli must reach the highest level of the memory hierarchy. By definition this is what makes it novel. When a stimulus cannot be interpreted (a pattern matched) by various hierarchical areas of the cortex, it continues moving up the hierarchy until it eventually reaches the hippocampus. The hippocampus is the highest level. This is where new and novel memories are created.

At the most primitive level the hippocampus will create a spatial context to store spatial memories. The spatial memories will assist in locating various places: hiding spots, drinking ponds, nesting places, feeding grounds, safe havens, even sexually conducive environments. At a more advanced level, the hippocampus will create an emotional and social context to store memories with an emotional and social significance. Once the memory is created, it will be stored in the cortex. When the organism is exposed to a part of the context of a memory, the brain activates the whole context through our sensory signals and their handshake signals and the memory is recalled. In this way, important places and events are easily remembered.

The basal ganglia, also, will sort out all sensory stimuli using this architecture and determine which ones to store and in which of the different memory regions according to their common characteristics with previously stored memories. In this way, the basal ganglia add memories and improve future responses by facilitating the retrieval of these experiences for future use.

Even though we don’t know exactly, in minute detail, how the brain can store the idea of a chair (an image of a chair, the word “chair”, the concept of a chair, the category of objects that are chairs, the function of a chair, the green chair, my chair, that chair over there, a little chair, the tall chair, the leg of a chair, the armrest of the chair, the action of sitting, comfort), whatever it turns out to be, the brain uses memories to produce all the amazing things that it does.

Perhaps there are small variations. That different types of neurons use different arrangements or groupings of neurons use different neurotransmitters or frequencies, this is all that we have. But the principles are basically the same. It is in this sense that we still don’t know exactly how neurons represent objects or words or actions or feel emotions. However, we do know that certain regions, and they vary slightly from individual to individual and even in an individual through time, are activated when the brain is performing certain functions. It is in this sense that I speak of areas in the cortex. These specific sites use more glucose, send out higher frequencies, and are more easily detectable when performing specific functions. We must remember that functional imaging, the pictures of brains, are static pictures of a dynamic process. Even though we can see where in the brain some tasks occur, we cannot easily show brain activity changes through time.

Memories are shared by different senses and used by the brain to extract more information in less time. Cognition and perception are a function of memory. In a very simplified way: memories that are used by the visual system to interpret the visual field

will store memories of sights, and these will aid in producing imagination, visual imagery, and our nightly visions as we dream. The areas that are used by the brain to interpret auditory signals will produce memories of patterns of sounds, and with these, the brain will construct words with meanings and eventually speech. While mixing memories of sounds with emotions, the brain produces music and humming; using memories of speech and music produces singing; memories of movements mixed with emotions and music produce dance.

The memory systems that are a part of the motor system, the visual and the hearing systems, are interconnected and occasionally shared. As more and more powerful memory systems evolved, these were co-opted to do other functions. In a simplified way, imagining and manipulation of objects in our mind is an exadaptation of our visual system; thinking in words is an extension of the memory systems evolved for hearing.

Awareness is a minimum use of our senses to keep us oriented in space and time. When certain stimuli reach the thalamus, reflecting changes in the body or environment, it will shift from awareness to attention. Attention is the way the brain focuses the senses to interpret a stimulus more clearly. Attention activates relevant cortical areas to the stimulus. Attention is serial, meaning that it focuses one object at the time, then another. In addition, attention blocks all other stimuli not pertinent to the stimulus it is focusing on. Attention constructs the present. Attention can be thought of as remembering the now. Remembering is a reconstruction of the past, or conversely, paying attention to the past.

Attention can be directed to the outside environment through control of the senses, or it can be focused internally, using the memory systems of the senses. Attention is central to separate what is important from the trivial, so that the organism won't be overwhelmed by the myriad routine signals that are being processed simultaneously. The brain has a tendency to automatize as much as possible in order to free itself to help the organism deal with the world's opportunities and threats.

Attention helps store memories; attention to the past (recall) retrieves memories. Both functions are a construction process based on previous memories and experience. Attention constructs the present and reconstructs the past. Most of the stimuli that are perceived by the senses will not be stored as memories, precisely because they aren't important; emotions confer importance to memories. Otherwise we would remember every single detail of every second of our lives and become paralyzed by this burden of memories.

Emotions are slightly different chemical states of the body that help guide the organism to find the best responses according to experience. Each emotion is a particular map of the Body State and produces specific chemical changes in the body. When the brain detects an emotion, it is interpreted as a specific feeling; each emotion (or body state) produces a slightly different feeling: pangs, lightheadedness, gnawing, gut reactions, clammy hands. Each feeling is associated with specific memories and modes of thinking. It is an ingenious solution of natural selection that brings to the forefront the particular responses associated with the emotion, to find, in a quick and dirty manner, the best options according to past experience.

When the cortex settles into a real (as opposed to an imagined) response, the basal ganglia will coordinate the necessary actions (movements or implementation of more thoughts and emotions), i.e., talking back and getting excited. When the cortex settles

into an imagined response (in this same case) as a better alternative, you think (in terms of “voices” in your head, instead of talking back) and perhaps try to hide your excitement as best as possible. The difference, in neurological terms, between imagining something and doing something is only in sending the signal to the basal ganglia and brain stem to act or not. In the cortex, real or imagined activities present the same neurological activity in the same areas. To see my son and to imagine my son, activate the same regions in my cortex, and both also produce the same emotions.

Memories are “filed” away according to context and emotional responses. In the future, memories will be activated by emotions and contexts. The memories related to strong emotions evoke emotions, just as emotions evoke the memories associated with them. The caudate nucleus is at the center of this activity and coordinates thoughts and emotions. This is regulated by the limbic system by releasing the appropriate chemicals into the bloodstream. Emotions are a natural way to activate certain modes of thinking. In this manner, experience and the previous related thoughts and memories are brought to bear immediately on the problem that is producing the emotional response. Likewise, intellectual activity might elicit a related emotional response. This is a re-enforcing strategy to deal effectively with situations that might be similar enough to elicit the same emotional response.

When a signal fulfills the characteristics that are pre-wired genetically or have been learned and which are capable of producing an emotion, it is called an emotional competent stimulus (ECS). An echo with a tag representing the emotional competent stimulus (ECS) is stored in the cortex, and as soon as the thalamus detects a match between incoming ECS and the respective echo, it will activate the proper emotion, even before the incoming signal is further processed in the cortex.

These states produce two main changes in the brain: memories related to the particular emotion are activated; and the feeling produces an arousal, which in turn will bring attention to bear on the ECS. The feeling and attention are in direct proportion to the intensity of the emotion. In this way, feelings help find the appropriate responses to stimuli in the environment or social context in the most efficient way, according to genetics and modified by experience. As examples of genetically pre-wired stimuli we can mention a healthy fear of heights or a startle response to a loud nearby noise. As a learned response we might say, “Keep away from those good looking girls at the crap table”.

As a good example of these primary emotions we have fear and anger. If the cortex, after further processing, determines that the signal was a false alarm, it will send a signal to the basal ganglia to immediately dampen the emotion.

The activation of an emotion produces a series of chemical changes in the body and the brain that speed up the appropriate responses to produce the correct behaviors. The caudate nucleus is the brain structure that activates related memories and modes of thinking when a particular emotion is detected; it can also trigger an emotion when particular memories or modes of thinking are activated for other reasons. The caudate nucleus is a two-way relay station. This is a quick and direct system that brings to the forefront all memories (and experiences) relating to a particular emotion, and in this way, present the best possible reaction to the stimulus. All (or most all) other thoughts and memories will be inaccessible, as they have proven (through experience and evolution) to be irrelevant to the stimulus.

When specialized areas of the cortex perceive a complex combination of patterns representing the complex social or environmental situations, accordingly they will signal the limbic system to initiate the electrical and chemical changes that will induce the proper emotional reaction. As examples of this we have anxiety, guilt, frustration or falling in love. These secondary types of emotions are longer lived and are more slowly activated than the primary ones.

Particular neural circuits are established between the basal ganglia and the cortex and back for different emotions and other mental processes. Strengthened (or weakened) by experience, these loops become activated more or less automatically. When the normal functioning of these loops is disturbed, the consequences can be devastating and even fatal.

The cerebral cortex is greatly expanded in human beings compared to other mammals. This expansion is responsible for storing significantly more memories as well as more types of memories. As a consequence the brain can identify and interpret in a much more refined way the stimuli that reach it. As you go down the evolutionary ladder, and find less and less cortex in the brain, the echoing, handshaking and mirroring become less until there are practically none in the reptilian brain. At this level, the limbic system is automatically, in a genetically pre-wired manner, responding to the environment's stimuli. The reptilian brain is capable of doing almost everything the mammalian brain can do except that learned behavior is practically non-existent and experience is passed on by natural selection of pre-wired responses. While emotions are not felt, chemical changes in the body and brain generate different responses. Thoughts aren't emitted to sift through alternative courses of action. Still, the reptile is aware, attends to specific stimuli and responds accordingly.

The act of dreaming is part of the process of cataloging and storing of recent memories according to emotional association and context. The strongest emotional associations are produced early in life and will serve as a comparative base. Each emotion will come into play as individuals develop according to their experiences. Each emotion will slowly accumulate more and more memories associated with it as each is experienced repeatedly, adding to the repertoire of responses that are successful or desirable and subtracting from the ones that made the outcome worse.

The brain can communicate with itself and other brains through the "added uses", or exadaptations (to use Stephen Jay Gould's term) of the memory systems that evolved to coordinate the motor system and interpret the incoming signals of the senses. The brain produces emotionally charged displays through gestures and body postures that can be identified by others. The brain can produce symbolic language using hand or head movements. The brain uses these added memories to produce information systems to communicate and to plan future responses and to remember our pasts. The means of communication or languages that the brain evolved are an exadaptation of the senses: of our vision (visual imagery and imagination), of our hearing (speech and spoken thought), and our body movements (emotional expressions and body language as well as body and hand signals).

When emotions are triggered, there is one circuit in the brain that tends to restore a neutral calm. Due to the enormous amount of neurons and complexity of their interconnections, the ideal neutral calm is never achieved. However, this slight wandering around or near the neutral calm is equivalent to potentially generating, in the subtlest

way, the whole gamut of emotions. When the brain is in this optimal adaptive state, because it can generate the most possible varied emotions, positive and negative, which in turn allow access to the greatest possible memories and therefore more responses, the brain perceives this state as a sense of self. The illusion of the self is the brain's measure of adaptability. The stronger the sense of self the greater the range of reactions.

All these different systems are continuously interacting and being synchronized by the thalamus at the center of the brain. They cannot be considered in isolation. The sum is greater that the parts. When one or several of these circuits or systems malfunction, the emotional and behavioral responses vary from slightly amusing to terrifyingly depressive, from amazingly psychotic to lethal.

In the following chapters we will see in more detail how each one of these functions is achieved, and how they synergistically work together.

Starting in chapter fifteen we will take a quick overlook at some of the malfunctions of the brain.

4
The Phantom Body

We normally take our bodies for granted. We don't think much about them. They are there, and in general they do what we want them to. But how we actually feel and control our bodies is complex. By looking at simple acts, say smiling, or abnormal situations, such as when one suffers a stroke or looses a limb, we can begin to understand the complex processes that govern our movements.

In this section I will build on ideas put forth by V.S. Ramachandran in his book *Phantoms in the Brain*.

The Phantom Body

When a person suffers a stroke in the right motor cortex -- the specialized brain region that orchestrates movements on the left side of the body – problems crop up on the left side. Many stroke victims are paralyzed on the right or the left side of their bodies, depending on what side the brain injury occurred. When these patients yawn, they stretch out both arms spontaneously. Much to their amazement, their paralyzed limb comes to life. It does so because a different brain loop is involved in yawning, and that brain loop controls the arm movement – this loop is closely linked to the respiratory centers in the brain stem.[40] These movements are reflexive; they are motions that differ from voluntary muscle movements and are regulated by circuits that don't involve the primary motor cortex.

There are complicated circuits that perform different tasks. Facial muscles control facial expressions more than movement as well as assisting in speech articulation. The oculomotor muscles center the eye on relevant stimuli. Hand muscles used to drink from a cup perform very different tasks than the leg or back muscles when carrying a heavy object.

[40] V.S. Ramachandran, *Phantoms in the Brain.*

For motor control there are projections from the primary motor cortex and the primary somatosensory cortex to the Putamen. These come primarily from layer V.[41] The Putamen also receives inputs from the Substantia Nigra in the brain stem. The Putamen, in turn sends signals to the Globus Pallidus External and Globus Pallidus Internal, known as the short loop or direct path. The direct path is excitatory in nature (D1 receptors, excitatory). The Globus Pallidus External also sends signals to the Subthalamic Nucleus, which in turn returns signals to the Globus Pallidus Internal, known as the long loop or indirect pathway. The indirect pathway inhibits movement (D2—inhibitory-- receptors in the putamen). The Globus Pallidus Internal sends signals to the motor nuclei in the brain stem (part of the actual motor commands), the Ventral Anterior Nucleus and the Ventro-lateral Nucleus of the Thalamus. The Thalamus then sends signals back to the Primary Motor Cortex, the Supplementary Motor Area and the Premotor Cortex.[42] These latter areas are all interconnected; in this way several loops are closed. The circuit of the direct path, from the striatum to the output nuclei (globus pallidus internal, ventral pallidum and substantia nigra pars reticulata) and then to the thalamus and brain stem promotes the production of movements. The basal ganglia receive input from the entire cortex (plus the thalamus and brainstem[43]), however only the frontal lobes are receiving output from the basal ganglia through the thalamus.[44]

These circuits of the basal ganglia are creating, updating and integrating a spatial map of the body, integrates it with a spatial map of the environment (visual map), and as such assists the cortex in controlling movement. We will see later how the attentional systems aid in this complex integration of external and internal space.

What happens at the cortical level is essentially this: the premotor cortex and the supplementary motor cortex (with the stored memories of complex movements) orchestrate the sequence of muscle contractions to perform a particular movement, and then signal the motor cortex to activate, in a sequential manner, each muscle as required to perform the movement.

Most animals rely largely on older parts of the brain for generating body movements. In contrast, the human cortex usurped most of the motor control from the rest of the brain. If the motor cortex of a rat is damaged, the rat may not have noticeable deficits. Damage of the motor cortex of a human leads to paralysis.

The somatic division of the peripheral nervous system contains the sensory neurons that innervate the muscles and joints as well as the axons of the neurons that are carrying the motor commands. The bodies of these neurons are part of the central nervous system. The largest and most important descending tract, the corticospinal tract is composed of over 1 million fibers. Fibers arise from neurons in layer V in the precentral gyrus (area 4), premotor area (6), postcentral gyrus (areas 1, 2 and 3), and adjacent parietal cortex (area 5). Only a small part of the corticospinal tract originates from the large pyramidal cortical neurons, the Betz cells in each hemisphere (area 4). Yet, most of the large fibers (5-10 times thicker) originate here. The corticospinal tract fibers arise from neurons arranged in strips of different sizes. Their axons converge in the corona radiata, enter the internal capsule, and form the crus cerebri in the midbrain. In the

[41] Francis Crick, *The Astonishing Hypothesis*.
[42] Jacob L. Driesen, Ph. D, http//www.*driesen.com*/
[43] Eric Kandel, James Schwartz, Thomas Jessell, *Principles of Neural Science.* Fourth Edition. 2000.
[44] John H. Martin, *Neuroanatomy*.

medulla they form the pyramids. At the junction of the medulla and spinal cord, 75-90% of the fibers decussate forming the large lateral corticospinal tract. The uncrossed fibers form the small anterior corticospinal tract and the small anterolateral corticospinal tract.[45]

The brain stem motor pathways engage in relatively automatic control, such as rapid postural adjustments and correction of misdirected movements. These motor pathways synapse directly to motor neurons and interneurons (inhibitory) that in turn synapse on motor neurons.

The motor neurons and interneurons travel down the spinal cord to the particular muscles they control. For the head and facial muscles, the motor neurons and interneurons are located in the cranial nerve motor nuclei and the reticular formation, respectively.

The cerebellum and basal ganglia do not contain neurons that project directly to motor neurons. Nevertheless these structures have a powerful regulatory influence over motor actions. They act indirectly in controlling motor behavior through their effects on the descending brain stem pathways and via the thalamocortical pathways. When the cerebellum is damaged, movements that were smooth and steered accurately become uncoordinated and erratic.

The cerebellum receives information from virtually all other components of the limbic and extraocular systems, from the spinal cord and brain stem, and from most of the sensory systems. The cerebellum is in a position to compare intended to actual movements, and make the necessary corrections. The cerebellum provides major input to the brain stem and cortical pathways for limb, trunk and eye movement control.

The cerebellum also receives signals from the parietal association cortex (area 40) and the limbic association cortex. These areas help in the planning of movements – for example, by allowing an individual's motivation state to influence when and where he or she moves. The cerebellum also serves non-motor functions, as cerebellar damage can produce impairments in language, decision-making and affect.[46]

The persistence of sensation in limbs long after amputation is a well-known phenomenon. After Lord Nelson lost his right arm during an unsuccessful attack on Santa Cruz de Tenerife, he experienced compelling phantom limb pains, including the unmistakable sensation of fingers digging into his phantom limb. The emergence of these ghostly sensations in his missing limb led the sea lord to proclaim that his phantom was "direct evidence for the existence of the soul". For if an arm can exist after it is removed, why can't a whole person survive physical annihilation of the body? It is proof, Lord Nelson claimed, for the existence of the spirit long after it has cast off its attire.[47]

But how can we explain phantom limbs?

The body is normally mapped to the primary motor cortex (area 4 and 6) and the somatosensory cortex (areas 1, 2 and 3). The primary motor cortex is located just in front of the central fissure that separates the frontal and parietal lobes. The supplementary motor area is anterior and adjacent to the primary motor cortex, and the premotor cortex is located below the supplementary motor cortex and anterior of the primary motor cortex. The primary somatosensory cortex is posterior to the central fissure, running

[45] J. Stephen Huff, et al, *Spinal Cord, Topographical and Functional Anatomy.*
[46] John H. Martin, *Neuroanatomy.*
[47] V.S. Ramachandran, Phantoms of the Brain.

alongside the primary motor cortex. There are rich connections between all these regions, especially between the primary motor cortex and the primary somatosensory cortex.

Each part of the body is represented disproportionately to its size, in proportion to the number of neurons in each body part. For example, the hands and arms use more space than the torso and legs. I suspect that soccer players, because of practice in their use of their legs and feet to control the ball, might be a different case.

The face is represented in an area about as big as the hand. If we follow the strip of the somatosensory cortex from the top of the brain down, starting on the inside medial fold of the hemisphere, we find first the genitals, then above it the feet; now as you turn onto the outside surface of the hemisphere, the map of the trunk follows, then, neck, shoulder, and arm, trailed by the hand, with the fingers receiving a disproportionate area, especially the thumb; next follows the head from the top down, meaning forehead first, then eyes, nose, and lips, disproportionately represented, ending with the chin; and last, the thorax and voice box (the pharynx). These disproportionate representations in area are due to the fact that the lips and fingers, for example, are much more sensitive to touch and are capable of very fine discrimination.

For the most part, the map is orderly though upside down: The foot is represented at the top and the outstretched arm is at the bottom. Upon closer examination, the map is not entirely continuous. The face is not near the neck, where it should be, but is below the hand, and the genitals instead of being between the thighs, are located next to the foot.[48]

Touching any part of the body, produces firing of the respective cells in the somatosensory cortex. Conversely, if you stimulate electrically any part of the motor cortex (which is mapped similarly), the corresponding body part will move.

These body maps on the cortex of the brain can be changed with experience. The maps present at birth can be modified to some extent as adults.

When you lose an arm, the arm stops sending signals to the arm area in the brain. When no signals are received, the neighboring areas, in this case the face area, invade the territory that used to be the hand. Now, when we stimulate the face, the area corresponding to the missing arm, fires away. Of course, when we do this, the face area also fires.

When Dr. Ramachandran worked with a young patient that had lost his left arm just above the elbow, he complained of itching and painful sensations in his phantom fingers. Dr. Ramachandran took a Q-tip and stroked various parts of the patient's body. Eventually, when Dr. Ramachandran swabbed his cheek, he found a complete map of the patient's phantom hand – on his face! There was a direct perceptual correlate of the remapping of the body. The patient felt his fingers and cheek stroked simultaneously.

After checking the patient's whole body, his chest, right shoulder, right leg or lower back, a second, beautifully laid out map of his missing hand was located – tucked onto his left upper arm a few inches above the line of amputation. Stroking the skin surface there evoked precisely localized sensations of touching the individual fingers.

Input from the hand area was lost after the amputation, and consequently, the sensory fibers originating from the face – which normally activate only the face area – now invaded the "silent" territory of the hand and began to activate cells there. Also, the missing hand area has connections to neighboring areas (the arm and face regions), and in the absence of its original inputs will seek new ones to activate these dormant

[48] Carl Sagan, The Dragons of Eden.

connections. The invasion of the hand cortex also results from sensory fibers that normally innervate the brain region above the hand cortex (fibers originating in the upper arm and shoulder), which are also relayed by proximity to the hand area that is now silent. So now, touching the upper arm also evokes sensations in the phantom hand.

The first direct demonstration that such large-scale remapping occurs in adult humans was demonstrated with magnetoencephalography (MEG), which measures changes in the magnetic field of the scalp.

Not only does Ramachandran's patient experience his phantom arm, he experienced the feeling of being able to move his phantom arm voluntarily and change its posture. When we think of sensations arising from the skin, we usually think of touch. But, in fact, there are other distinct neural pathways that mediate the sensations of warmth, cold and pain that also originate on the skin. These sensations have their own target areas or maps in the brain, but the paths used by them are interlaced with each other in complicated ways.

When a drop of warm water was placed on the patient's face, he immediately reported that his phantom hand had felt distinctly warm. As a mechanism to explain this, it is probable, Dr. Ramachandran proposes, that there is tremendous redundancy of connections in the normal adult brain, but that most of them are non-functional. Thus even in healthy brains there might be sensory inputs from the face to the hand map area. If so, this hidden input remains ordinarily inhibited by the sensory fibers arriving from the hand. When the hand is removed, this silent input originating from the face is unmasked and allowed to express itself so that touching the face now activates the hand area and leads to sensations of a phantom hand. He also proposes that this reorganization could involve a sprouting of new connections.[49] This is now known as brain plasticity.

The body maps are largely stable through life, but occasionally, they are rearranged in such a way that stimulation to the face ends up in two areas: the hand map and the face map, fooling the patient into thinking his hand is still there.

There is another mechanism to explain the phantom limb phenomenon; there are connections between the hand map and the face map (because they are adjacent) that are ordinarily inactive, but in the absence of signals from the hand, the hand map "looks" for other inputs. In so doing, the inputs from neighboring areas that were "silent" become the new inputs, fooling the hand area to believe the hand is still there. Handshake signals from and to other areas relating to the hand (i.e., the area that feels warm and cold or the area that knows how to use tools) are still active and also help create the illusion of the hand!

There is a third set of connections that help create the illusion of the phantom limb. When you decide to move your hand (the real hand), the chain of events leading to its movement originates in the frontal lobes, especially in the motor cortex. It has been determined that the motor cortex is concerned mainly with simple movements like wiggling your finger or smacking your lips. The supplementary motor area is in charge of more complex skills, such as waving good-by. It oversees passing the specific instructions in the proper sequence of the required movement to the motor cortex. Lastly these signals will travel down the spinal cord to the appropriate muscles on the opposite side of the body, allowing for the specific movement to take place.

[49] V.S. Ramachandran, Phantoms in the Brain

Every time a signal is sent from the supplementary motor area to the motor cortex, it goes to the muscles and they move. Identical copies of these signals are sent to the cerebellum and the parietal lobes. Once these signals are sent to the muscle, a feedback loop is set in motion. As the muscles execute the movement, signals from the spindles and joints are sent back to the brain, informing the parietal lobes and the cerebellum that, "yes," the movement is being properly executed.[50] There are also connections in the motor (down) pathway and the upcoming sensory pathway in the spinal cord. The movement-directing neurons descending from the brain to the spinal cord have little branches to the ascending sensory pathways, serving to adjust sensory bias to communicate an expected sensory input from the about-to-be-ordered movement (the so called efference copy) for comparison purposes. [51] In this way confirmation that the signal is on its way before it reaches the muscle closes the loop quicker.

These two structures help to compare your intention with the actual performance and modify the motor commands as needed. Thus, intentions are transformed into smoothly coordinated movements. This allows the brain to anticipate (by remembering what follows next) the movements before they are executed as well as confirming that the command for the real movement is on its way. This is an elegant, timesaving, engineering solution.

When a phantom limb is instructed to move, these signals are also sent to the cerebellum and parietal lobes. Using the synaptic communication in the spinal cord, the downward neuron with the motor command informs the upward sensory neuron, that the motor command is on its way to the muscle before it reaches the muscle and the motion is executed.[52] These connections are still intact after the loss or amputation of the phantom. This short feedback pathway in the spinal cord between motor instructions and sensory signals of the missing limb, combine with the sensory information from the face and upper arm, through remapping to create the phantom hand, then converge with the motor command to the missing hand to produce a vibrant, dynamic image of the phantom hand – an image that is updated, by the continuous signal of the efference copy, as the phantom moves. This helps create the very realistic illusion of movement in the phantom limb. In the case of movement of the real hand, also, the impulses from the joint, ligaments and spindles of the arm are being fed back.[53] The phantom arm doesn't receive these signals, but through this spinal feedback pathway and the invasion of the existent signals from the face and arm, the phantom movement is felt as real.

The memory of the arm, coupled with real somatosensory impulses from other neighboring areas, as well as the feedback loops of motor commands, trick the brain into feeling the arm. Feeling is equivalent to experiencing the present, which the brain does using memories to interpret sensory signals. The difference between remembering and constructing the present is remembering, accompanied by sensory signals. This is equivalent to feeling the present.

[50] V.S. Ramachandran, *Phantoms in the Brain.*
[51] William H. Galvin, *The Cerebral Symphony*.
[52] Ibid.
[53] V.S. Ramachandran, *Phantoms of the Brain*

In the case of a paralyzed limb, the signal to move is sent, but vision confirms that there is no motion. As the signal is sent out again many times, the visual feedback confirms no movement – and a learned paralysis is stamped into the brain's circuitry.[54]

In cases where the patient felt the phantom limb paralyzed, with the use of mirrors to reflect the real hand to fool the brain into "seeing" the phantom hand, some patients have learned to un-paralyze their phantoms. By seeing their phantom limb (using the mirror-image of the real limb), and then, by synchronously moving both, movement is restored to the paralyzed phantom. In a few cases, however, the phantom limb disappeared in part or completely. This suggests that when the parietal lobe is presented with conflicting signals – visual feedback relaying movement while the phantom muscles and joints are confirming the arm is not moving – the brain resolves the paradox – there really is no movement of the arm, it must be a visual illusion, and therefore the phantom doesn't exist.

A woman who lost her left leg below the knee developed a phantom limb. She reported that every time she had sex she experienced strange sensations in her phantom foot. Not surprisingly, the genitals' map is next to the foot map. Another man who lost his leg below the knee reported actually experiencing his orgasms in his phantom foot. He reported that orgasms are much more intense and bigger because they are no longer confined to the genitals, they include his foot. He actually enjoyed sex much more after the amputation! One third of women who have had a radical mastectomy reported tingling, erotic sensations in their phantom nipples when their earlobes were stimulated.

It has been reported that people born without arms experience phantom limbs. They feel that their phantom arms and hands gesticulate and move about, that they even point at objects.

When being fitted for prosthetics, one girl born without arms reported that her phantom arms were about six inches shorter than her prosthetic arms and her phantom fingers didn't reach into her artificial fingers. When this girl walks her phantom arms don't swing like normal arms; they stay frozen at her side. But when she talks, her phantoms limbs gesticulate and move as she does so.

This is not so baffling because the brain region responsible for smooth, coordinated arm swinging when we walk is different than the one that controls gesturing. Gesturing has to do with communicating. Perhaps, in this case, the "memory" of arm swinging is never learned. But the neural circuitry, the "memory" for gesticulation, activated during speech might be genetically specified[55] establishing handshakes between speech centers and motor movement areas. It is probable that this circuitry antedates, evolutionarily, spoken language -- symbolic language (gesticulating and hand signaling) evolving before speech.

What this proves is that at least part of the circuitry to create a body image is laid down by genes and is not strictly dependent on motor and tactile experience.

Most people with phantom arms can voluntarily move their phantoms and reach out and grab objects, point, wave good-by, shake hands or even write. Some people report what is known as a telescoped phantom hand. This condition feels as if the hand were attached to the stump with no arm in between. However, if a teacup is placed two feet away they can try and reach it, as if the phantom was no longer attached to the stump

[54] Ibid.
[55] Ibid.

and was zooming out to grab the cup. When asked to reach out for a cup, and the cup is yanked away at the exact moment they are reaching for it and trying to grab it with their telescoped fingers, they report experiencing pain in their phantom fingers as if it had actually been yanked out of the phantom hand. Real pain in illusory fingers; this must mean a connection between pain, vision and phantom limbs.[56] A connection between vision and motor coordination is not too surprising. After all, vision is used continuously to allow us to move through the world around us.

About one third of phantom limb patients report that they can't move their phantoms in any way. These phantoms limbs are paralyzed, sometimes frozen in odd positions. It turns out that when the limbs had been paralyzed before the amputation, the phantoms were also paralyzed, as if the "memory" of the limb before the amputation carried over. In most cases when pain in a phantom limb is reported, similarly, there was pain before the loss or amputation of the limb and a memory of the pain is etched onto the phantom.[57]

Ernst Mach, who was right handed and suffered a stroke in the left hemisphere, reported, "The vivid dreams which I had of playing the piano and writing, accompanied by astonishment at the ease with which I wrote and played, and followed by bitter disappointment on awakening. Motor hallucinations also occurred. I often thought I felt my paralyzed hand opening and shutting, and at the same time the movement seemed hampered as if by a loose, stiff glove."[58]

Pain is one of the most poorly understood of all sensory experiences. Pain in a phantom limb is a source of great frustration to anyone who experiences it. Occasionally, one especially enigmatic complaint is that the phantom hand curls up into a tight, white-knuckled fist, fingers digging painfully into the palm. With the use of the mirror box, the patient positions his or her real hand to superimpose its reflection over the phantom hand, and after making a fist with the normal hand, tries to unclench both hands simultaneously. About half the patients report, some even on the first try, that the phantom hand opened, lessening the pain immediately.

Consider what happens in your brain when a motor command is sent from the premotor and motor cortex to make a fist. Once the hand is clenched, feedback signals from the muscles and joints in your hand are sent back through the spinal cord to the brain saying, "Slow down, enough. More pressure and it could hurt." This proprioreceptive feedback applies brakes, automatically with great speed and precision. When the limb is missing, the feedback isn't possible and the brain continues to send the signal, Clench More. Motor output is amplified even further (to a level that far exceeds anything you or I would ever experience) and the "sense of effort" may itself be experienced as pain. The mirror works by providing visual feedback, taking the place of the proprioreceptive feedback, and the hand can be unclenched. The brain creates a map of the body using the internal proprioreceptive signals. The normal integration as a continuous unit of the extrapersonal space, created by vision, with the intrapersonal space, created by the somatosensory system, explains the power of seeing the phantom move.

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[56] Ibid.
[57] Ibid.
[58] Chris McManus, *Right Hand Left Hand.*

But why the sensation of nails digging into the palm? There is a memory link in the brain between the motor command to clench and the unmistakable sensation of "nails digging", so you can readily summon the image in your mind. Yet, even though you can imagine vividly the nails digging, you don't actually feel the sensation and say, "Ouch, that hurts." The reason is that the real skin on the real palm is reporting that there is no pain. In the case of a phantom hand, there are no signals countermanding to forbid those stored pain memories.[59]

It seems extraordinary that you could use a visual illusion to eliminate pain, but bear in mind that pain is an illusion – constructed in your brain like any other sensory experience. Using one illusion to erase another doesn't seem very surprising after all.

All this helps us understand what is going on in the brains of patients with phantoms and gives us hints as to how we might help alleviate their pain and discomfort. But there is a deeper message here: Our own body is a phantom, one that our brain has temporarily constructed purely for convenience.[60] This phantom, an illusion created by the brain, allows the brain to control the body movements.

A comprehensive map of the internal space is created by the somatosensory areas and updated by the output of the basal ganglia through the thalamus and is perceived by the brain as our body. This loop is known as the skeletomotor loop: efferents from the cortex (somatic sensory, primary motor, and lateral premotor area) to the putamen, to the globus pallidus internal and the substantia nigra pars reticulata to the thalamic nuclei (ventral anterior and ventral lateral) projecting back to the cortex (supplementary motor area).[61]

To demonstrate the malleability of your own body illusion try the following experiment; it works on about half the people that try it. Sit in a chair blindfolded. Ask someone to sit in another chair in front of you, facing in the same direction. Ask another person (Joe) to guide your right index finger to the sitting person's nose. With Joe repeatedly tapping her nose with your hand in a random sequence like a Morse code, and simultaneously tapping your own nose with your left index with the same rhythm and timing. The tapping of both noses should be in perfect synchrony.

After thirty or forty seconds, with luck, you will develop the uncanny illusion that you are touching your nose out there or that your nose has been dislocated and stretched out almost three feet in front of your face. The more random and unpredictable the tapping, the more striking the illusion will be. The brain notices that the tapping of your right index finger is perfectly synchronized with the taps felt on your nose. How likely is it that this would happen naturally? The coincidence is too great; therefore my finger must be tapping my nose. The brain also knows that my hand is extended two feet away from my face. The paradox is resolved: it follows that my nose must also be out there, two feet away.[62] For the brain this illusion is just as difficult (or easy) to create as your nose is in the middle of your face.

The feeling of our body is very flexible. The use of tools, such as a shovel, can be used as an extension of the body for reaching out, grasping and digging. Humans can easily extend their perception of their body to include a car while driving it, or even a

[59] V.S. Ramachandran, *Phantoms of the Brain*.
[60] Ibid.
[61] John Martin, *Neuroanatomy*.
[62] V.S. Ramachandran, *Phantoms of the Brain*.

whole jetliner, as good pilots do. In contrast, horses do not extend their bodies to include a rider to change their movements to avoid obstacles that will impinge on the rider. They do however change their balance when they carry the extra weight of the rider.

A memory of each complicated movement has to be stored and activated at the appropriate time. Many movements can't be figured out in advance and therefore need many hours of practice to be able to repeat consistently. Practice, after all, makes perfect. The computations involved in coordinating all the muscles of the body to achieve a particular movement, like running, for example, cannot be done in real time. To place one foot in front of the other, to coordinate the arms and head and torso to maintain balance -- these sequences have to be memorized, and with small variations from the cerebellum can be managed in real time.

The supplementary motor cortex also has a body map, and unlike the motor cortex where the left hemisphere controls the right body and the right hemisphere controls the left body, the left supplementary motor cortex controls both sides of the body to a much greater extent than the right supplementary area. This area connects to the motor cortex and the spinal cord. It has as many connections to the spinal cord as the motor cortex has. It also has extensive connections to and from the parietal lobe (information about body image and spatial matters) and to the ventral thalamus (it is another major component of the movement-control system), which the motor cortex doesn't have.

When you imagine moving your fingers, the supplementary motor area becomes active, just as if you moved your fingers. It is remembering the movement, so to speak. When you actually move your fingers, the motor cortex becomes active also. The supplementary cortex is thus receiving signals from various parts: from the thalamus of where the body parts are, as well as receiving signals from the somatosensory areas; from the parietal lobes it receives signals of the body image and spatial orientation, and from the prefrontal connections, impulses that help get sequences of movements in the right order for the motor cortex to execute.

The echo signals from the somatosensory, supplementary motor, the parietal (which in turn is also receiving signals from the visual system) and the anterior prefrontal lobe are continuously streaming to the thalamus waiting for signals from the body indicating a change (no signal, means no change), and as soon as a proprioceptive signal is received and matched (by the thalamus) to an echo, it is relayed (mirrored) to the appropriate cortex area. This last receiving area in turn activates all the relevant areas in the cortex by sending handshake signals that have the function of anticipating (remembering) the next movement. These areas in turn send an echo, and the echo that is matched, will direct the next set of handshakes. In this way the handshakes move up the hierarchy, eventually, reaching the highest level of the motor cortex. Thus, the motor cortex issues, in a seemingly effortless manner, the command signals in the right sequence for whatever movements are needed.

There are two types of thalamic nuclei, depending on the afferent fibers they receive from ascending pathways or descending from the cortex. First order nuclei receive their primary afferent signals from the ascending pathways and corticothalamic afferents from layer VI, which also send signals to the thalamic reticular nucleus. The second, higher order nuclei receive most of their primary afferents from the pyramidal

cells in cortical layer V. However, these corticothalamic projections don't branch out to the thalamic reticular nucleus.[63]

First order nuclei of the thalamus match echoes to incoming sensory signals and mirror the signals to layer IV, the input layer of the appropriate sensory areas. Excitation in layer IV causes neurons in the same column in layer II and III to become excited, which activate neurons in layers V and VI. The cortex process signals in a hierarchical manner by sending forward and feed back handshakes (information). Converging forward handshakes from lower areas arrive in layer IV, which activate layers II and III in the same area, which project axons to the higher level areas. Thus information flows up the hierarchy. But information also flows down the hierarchy through feedback handshakes. Layer VI neurons project to layer I in the area hierarchically below. In layer I the axons spread horizontally, thus information flowing down hierarchically from one column has the potential to activate many columns in areas below it. Neurons from layers II, III and V have dendrites in layer I, so they can become active by the feedback running through layer I. Neurons in layers II, III and V can excite neurons in layer VI, which in turn project to layer I of the next level below.

Synapses close to the cell body have a stronger influence on whether a neuron will generate a pulse compared to synapses further away. However, the cast majority of synapses are not close to the body. As a general rule, forward handshakes (neural impulses) moving up the cortical hierarchy are transferred via synapses close to the cell body, which increase the certainty that they will pass from area to area. Also as a general rule, feedback handshakes, flowing down the hierarchy, do so via synapses far from the cell body. Cells in layers II, III and V send dendrites into layer I and form many synapses there.[64] But layer I is a mass of synapses receiving input from the higher cortical areas and input from mirrored signals from the thalamus originated by layer V echoes. These signals propagate over a large amount of columns in a local area. So even though these synapses are far from layer II, III and V neurons, the multiple inputs amplify the effect. We also have to keep in mind that in some cases the feedback projections vastly outnumber the forward projections, which indicate that feedback is just as important or more. In this way the forward and feedback handshakes have more or less the same certainty of being sent up and down respectively.

The neurons in layer V project to the second order nuclei, which in turn project back to layer I. Thus the echoes coming from layer V assist in directing the mirroring of signals to layer I. When the sensory signals are mirrored to layer IV, handshakes are immediately sent through layers II and III to the next level above. When the signals are mirrored to layer I, it reinforces the signals from layer VI from the next higher level. There is a delayed feedback here that Jeff Hawkins proposes is similar to auto-associative memories that learn sequences.

This is a simplification but it helps to understand how the motor system works: The motor command to extend the right arm to pick-up a cup is at the highest level. The neurons in layer VI send an echo to the thalamus and a signal to layer I of the next lower level. In this case, the beginning of the motor sequence. The neurons in layer V of the next lower level send an echo to the thalamus, which mirrors the signal to layer I and

[63] Guillery RW. *Anatomical evidence concerning role of the thalamus in corticortical communication: a brief review.* J Anat 1995 Dec;187(Pt 3):583-92.
[64] Jeff Hawkins, *On Intelligence.*

reinforces the signal from the higher level from layer VI. This causes layer V to fire a command to initiate the movement. Layer VI sends a signal to layer I in the next level (or the next sequence), and in a cascade of signals moving through the entire sequence the arm is extended, the palm opens and the fingers grasp the cup with the right amount of pressure. The memory of the movement is stored in the hierarchical connections that activate the right sequence of muscle contractions and relaxations.

In order to free the brain for other activities, the brain excels at automatizing sequences of movements by storing them in memory, particularly if they are part of habits or routines. The sequences of movements are activated through handshakes, which are an integral part of the memory of a movement. For example, walking or the action of hammering a nail, or getting dressed. To change how you do these activities requires attention.

The primary motor cortex differs from that of sensory areas in the other lobes. Whereas the sensory areas have a thick layer IV (mostly input from the thalamus) and a thin layer V (where descending projections originate to the brain stem, spinal cord and striatum, and the thalamus), the primary motor has a thin layer IV and a thick layer V. The thalamic terminations, in the motor areas, have a wider laminar distribution than sensory areas.[65] This architecture is suggestive of high echo rates to the thalamus, to help coordinate distribution of incoming proprioceptive and somatosensory signals, and high command rates to the brain stem and spinal cord for movement, after the striatum integrates visual spatial information with the body map. There is a one to one map of body to the cortex, and as a consequence less mirror signals are required to control the body compared to sensing the body and the spatial relations of its parts.

The Main Switching and Relay Station

The thalamus is such an important structure regarding brain functioning that it is appropriate to review some of its characteristics in detail. The thalamus is located in the mid portion of the diencephalon in the center of the brain in both hemispheres. It is shaped in the form of an egg with the slender part pointing backwards. Each egg-shaped thalamus is roughly anatomically divided into three by bands of myelinated axons, called the internal lamina. The frontal part is called the anterior nucleus. The internal side is known as the medial nucleus. The lateral section is further divided into the ventral anterior nucleus, ventral lateral nucleus, lateral posterior nucleus, ventral posterior nucleus and the pulvinar nucleus, with the lateral dorsal nucleus, as the name implies on the dorsal-lateral part of the thalamus. Internally we find the arcuate nucleus and, projecting out the back, the medial geniculate nucleus and the lateral nucleus. A thin sheet surrounding the thalamus, the reticular nucleus is inhibitory in nature. The reticular nucleus input is cortical and thalamic, and its output is intrathalamic. The cortical inputs are the echo signals that help orchestrate the traffic of incoming signals to the thalamus. The thalamic inputs are the sensory signals reaching the thalamus. The output is the result of the matches between signals and echoes and directs intrathalamic activity to mirror the signals to appropriate cortical areas.

[65] John H. Martin, *Neuroanatomy*.

In neuroscience, resonance refers to the ability of neurons to respond selectively to inputs at preferred frequencies, and amplifying currents serve to synchronize patterns of circuit activities.[66] In general, when the corticothalamic echoes from layer VI arrive at the reticular nucleus, and their frequencies match certain frequencies of the intrathalamic stimulus, I say a match is made. The corticothalamic and intrathalamic frequencies resonate (when they match), amplifying in this layer and initiate rhythms that will produce oscillations, which in turn activate certain circuits. In other words, the signal is mirrored to layer IV. When the echoes arrive from layer V the signal is mirrored to layer 1 where it can activate larger areas. Some of these circuits are intrathalamic, and others are thalamocortical.

In chaos theory, stochastic resonance refers to the presence of vibration or noise that keeps a system in motion and tracking an overall course of least resistance, pushing out, rather than getting stuck in small grooves or "minimas," allowing the system to "wander" about a point. Stochastic resonance has been demonstrated in neural networks. An individual trigger system may be able to detect very weak non-stationary signals [the echoes] using stochastic resonance.[67] This is another possible mechanism for echoes to direct signal traffic, or to trigger the thalamus's automatic emotional responses.

In the majority of cases, the two thalami are connected by a mass of neurons known as the massa intermedia. Postmortem studies show that the massa intermedia was absent in 22% of females and 32% of males. Among individuals with massa intermedia, the structure was an average 53 % larger in women than in men. The anterior commissure, which connects the two temporal lobes, is on average 12 % larger in females than in males.[68]

The thalamus is the main gateway to the cortex. The cortex is where the major processing of sensory signals is done in order to extract the most information from the world and from the internal state of the body.

The nuclei of the thalamus can be functionally subdivided into relay nuclei, subcortical nuclei and intralaminar nuclei. The functional divisions can be further subdivided based on the efferent projections. These mostly go to the cerebral cortex and also receive reciprocal connections from the cortical areas that they project to. These afferent projections outnumber the efferent projections.[69] There are also efferent projections to discrete regions of the cortex (focal projections) as well as fibers that connect to very broad regions of the cortex (diffuse projections). This demonstrates the higher rate of echo signals required to coordinate the distribution of mirror signals.

All sensory information (except olfactory) arrives at the thalamus. The thalamus is continuously receiving a stream of signals from the body and the skin, as well as visual, hearing and tasting inputs. The thalamus is also continuously receiving a cascade of signals from different areas of the cortex. These signals are the echoes of the cortex.

The cortical echoes, according to their specific handshakes and nature, help the reticular nucleus, the subcortical and intralaminar nuclei determine where to relay the incoming sensory signals. The thalamic nuclei are matching incoming signals to echo

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[66] Allan N. Schore, *Affect Dysregulation.*
[67] F. Moss and K. Wiesenfeld, *Nonstationary Stochastic Resonance in Single Neuron-like Systems.* 1995.
[68] Allen LS, Gorki RA, *Sexual Dimorphism of the Anterior Commissure and Massa Intermedia of the Human Brain.*
[69] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

signals, and when a match is found, the signal is mirrored (relayed) to the area that originated the echo. These are the mirror signals, reflecting (relaying) the nature of the sensory signals to the appropriate cortical areas. The echoes can carry tags, and the purpose of the tags is to help the thalamic nuclei determine if the signal should be mirrored to other areas as well. Accordingly, the sensory signals will be relayed to broader regions of the cortex, primarily through diffuse projections originating in the intralaminar, dorsomedial, dorsal tier, pulvinar and lateral posterior nuclei. In this way, broad areas are activated to process the incoming signal further. It is an elegant, efficient system that automatically (according to genetically and learned routines) distributes the incoming signals to the different memory systems that can identify and extract the maximum information from the raw sensory inputs.

Depending on the channel and nature of the incoming sensory information and the echoes from the cortex, different parts of the thalamus coordinate different activities: vision, hearing, movement control, triggering of emotional responses and so on.

The efferent projections of the intralaminar nuclei to the cortex are regulating levels of cortical activity. There are afferent and efferent fibers to and from the frontal and parietal cortex. There are afferent fibers from the reticular formation and efferent fibers to the basal ganglia.

When the thalamus matches an incoming signal to an echo that represents an ECS (emotionally competent stimulus), the thalamic nuclei will initiate the emotional response, as well as relay the signal to the appropriate areas in the cortex for further processing. This is a quick and direct way of activating the primary emotions even before the signal is further processed, as the responses to the environment, particularly threats or danger, require immediate action.

The thalamus also sends (relays or mirrors) the sensory signals to the appropriate cortical areas low in the hierarchy. The lower the hierarchy, the more specific is the neural response, i.e., reacting to lines, colors, shades, boundaries or movement. As the signals are relayed higher up, more specific concepts can be interpreted, and a broader view seen. Eventually there is an area that will interpret that face is my mother's, and eventually, my mother is approaching me with a tray of cookies becomes possible.

When numbers are used to denote areas of the cortex, Brodmann's numbering is used. These areas can vary slightly in function and from individual to individual. These divisions are based primarily on cytoarchitecture of the cortex, such as size and shapes of neurons in the different laminae and their packing densities. Yet, research on different functions of the cortex has shown that different functional areas have slightly different cytoarchitectures.[70] Within certain areas, i.e., area V1 (area 18), even though it is an area dedicated to vision, there are many very small areas that respond to specific sensory signals.

The dorsomedial nucleus is responsible for emotional (and motivational) responses to sensory stimuli with afferent and efferent fibers to the prefrontal (areas 8, 9, 10, 11, 44, 45 and 46) and orbital cortices (areas 10, 11 and 47), as well as afferent fibers from the olfactory cortex and parts of the limbic system, and efferent fibers to the hypothalamus.

The pulvinar and lateral posterior nuclei are the largest of the thalamic nuclei. They handle visual and language processing signals with afferent and efferent fibers to

[70] John H. Martin, *Neuroanatomy.*

and from the parietal (areas 5, 7, 4, 39 and 40), temporal (area 38) and occipital (areas 18, 19 and 37) lobes.

The anterior and lateral dorsal nuclei also handle emotional responses to sensory stimuli with afferent fibers from the limbic system, the hippocampus (LD) and the cingulate gyrus (anterior nucleus), and with efferent fibers to the cingulate girus (areas 23, 24, 29 and 32). The anterior nucleus serves as a limbic relay.

The ventral anterior and ventral lateral nuclei regulate execution of motor programs. There are afferent and efferent fibers to and from the supplementary cortex (VA), the premotor cortex and the cerebellum (VL), as well as afferent fibers from the globus pallidus. The ventral lateral nucleus and the basal ganglia control movement.

The ventral posterior nucleus regulates incoming sensory information from the body and skin with afferent fibers from the ascending somatosensory pathways and efferent fibers to the somatosensory cortex. The ventral posterior nucleus receives signals from the trunk and limbs and the ventral medial receives signals from the head, neck and face.

The medial geniculate nucleus serves as the auditory relay and the lateral geniculate nucleus serves as the visual relay.

The lateral dorsal, the anterior nucleus and all the ventral nuclei have focal projections to the cortex; the lateral dorsal to the associative areas (7 and 31) and the attentional system (area 40). The anterior nucleus and ventral nuclei project to the premotor and primary motor areas (4 and 6) and the primary somatosensory region (areas 1, 2 and 3).[71]

The thalamus sends signals to the supplementary and primary motor cortex, and the primary somatosensory and primary motor cortex send signals to the putamen. As mentioned, there are extensive connections from the cortex to the corpus striatum.[72] The corpus striatum is in turn made up of the caudate nucleus and the putamen and globus pallidus. These cortical signals are compared to signals coming from the substantia nigra and passed on to the globus pallidus external and the globus pallidus internal, which through a feedback loop through the subthalamic nucleus sends the final instructions to the motor nuclei in the brain stem and from there to the actual muscles performing the movement sequence.

The putamen also receives visual information from the occipital lobes in a similar circuit and integrates this spatial information to help coordinate movement. Of particular interest are the extensive efferent fibers from the visual cortex (frontal eye field and the supplementary eye field) to the caudate (body), projecting to the Globus Pallidus internal and the substantia nigra pars reticulata. From here the information goes to the thalamus (ventral anterior and medial dorsal) and then on to the cortex (frontal eye and supplementary eye fields). This circuit is known as the oculomotor loop.[73] It shares some neural pathways with the skeletomotor loop.

There is also a pathway from the cortex to the cerebellum and back to the thalamus and so to the cortex.[74] This suggests an architecture whose function is to use these circuits to integrate the spatial map of the body with the visual spatial map of the

[71] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.
[72] Francis Crick, *The Astonishing Hypothesis.*
[73] John H. Martin, *Neuroanatomy*.
[74] Francis Crick, *The Astonishing Hypothesis.*

outside world, which is constantly updated by the visual system. In this way, the brain produces one continuous, integrated map of the extrapersonal with the intrapersonal space, the skin being the boundary between the two spaces, so necessary for controlling movement through the environment.

The thalamus relays all sensory information to the cortex, which processes the signals further. For this purpose, the cortex evolved ever-greater memory systems that allow more complicated processing of sensory signals. Each sensory modality evolved its own memory systems, and at some point these evolved into tools that the brain uses for other purposes. When the brain perceives the activation of these memory systems for purposes other than the processing of sensory signals, the perception feels like thinking in different modalities, like imagining or "talking in our heads" or remembering.

The memory systems of vision evolved into imagination and manipulation of objects in our mind's eye. The memories that aid in interpreting sounds evolved into producing words and speech, and this in turn feels like thinking through voices in our heads. Speech became a major source of communication between one brain and another. Using body movements -- hand symbols, gestures and body postures -- the brain evolved other means of communicating with other brains. Probably, all these forms of communication evolved simultaneously and reinforced each other.

Each different area in the cortex specializes in interpreting different aspects of the signals, and relaying them to other parts of the cortex for further processing. It is a hierarchical process, where one area responds to vertical lines, or movement and passes this information upward. The higher areas feedback information to the lower areas. There are sideway connections as well. These relays, upwards, sideways and back are the handshake signals that activate the different areas that ultimately will interpret a specific object.

In a serial and parallel manner, more and more information is extracted and ultimately concepts like, "The red Corvette is approaching fast down the street under the trees and I better get out of the way before I get killed," become possible, thanks to the incredible visual and semantic memory systems that can easily discern concepts like red, car, speed, approach, tree, impact, pain, hurt and so on.

Our senses help us navigate through the world to find food and sex, to help us avoid predators and danger. If this were not so, we could not move across a room or we would crash into obstacles. Consider the visual information in relation to modifying body movements as you run through the forest, avoiding tripping on stones, hitting your head on low branches, not falling into a crevasse, and making sure that a lion doesn't get too close. This integration of the outside world with our body should not be surprising; think of the complicated coordination of eye and body movements needed to catch something or throw a spear to kill an animal.

The thalamus directs attention when small changes in the environment or the body are detected, particularly visual attention, by automatically controlling eye, head and neck movements. In this way visual attention focuses on what is relevant of the extrapersonal space, and through its connections to the putamen and globus pallidus, which are also receiving body signals from the substantia nigra, adjusts the body movements as necessary.

The visual spatial information has to be relayed to the three motor areas and somatosensory region through the basal ganglia and thalamus. This information is also

sent to the cerebellum and parietal lobes, which are monitoring and correcting the intended movements. It also has to be relayed to the frontal lobes, which are involved in determining where and why we are moving next. It is at this point that attention comes into play.

There are two more input-output loops through the basal ganglia. They are called the prefrontal cortex, or association loop and the limbic loop. The prefrontal loop involves projections from the cortex (posterior parietal, middle and inferior temporal lobe, and the prefrontal and premotor) to the caudate (head) to the substantia nigra pars reticulata and the globus pallidus internal, with efferents to the thalami (ventral anterior and medial dorsal – same as the oculomotor loop) and feeding back to the cortex. The limbic loop with efferents from the cortex (medial and lateral temporal lobes and anterior cingulate girus) and the hippocampal formation to the ventral striatum, with projections to the ventral pallidum, the globus pallidus internal and the substantia nigra pars reticulata.[75] This architecture suggests a complicated emotional integration affecting volition to determine willful movements of the body (intrapersonal space) through the world (extrapersonal space).

Once the brain controlled movement, it's uses quickly evolved beyond "simple" locomotion to communication with other brains -- using gestures, body postures and facial expressions to convey information about internal states.

Movement As Communication
Social & Emotional Phantoms

Consider the simple act of smiling. When you see a loved one, you smile; but what happens when she aims a camera at you and asks you to smile? Most people produce a grimace instead of the natural expression. Paradoxically, an act that you perform effortlessly many times a day becomes difficult when someone asks you to do it. The reason these two kinds of smiles differ is because different brain regions handle them, and only one of them has a specialized "smile circuit". A spontaneous smile is produced by the basal ganglia, clusters of cells located next to the thalamus. A smile is an emotional response, orchestrated by the brain structures responsible for generating emotions. When you see a loved one, the image of his face reaches the emotional centers or limbic system and is relayed to the basal ganglia, which in turn orchestrates the sequences of facial muscle activity needed to produce a smile. When this loop is activated by the correct stimulus, your smile is genuine. Everything happens in a fraction of a second without the thinking parts of the cortex ever being involved. An echo matched a pleasant stimulus, and a smile was emotionally activated automatically.

Consider what happens when someone asks us to smile. The verbal instruction is received by the higher thinking centers in the brain, including the auditory cortex and language centers. From there it is relayed to the motor cortex, which specializes in producing voluntary movements. Despite the apparent simplicity, smiling involves the careful coordination of dozens of tiny muscles in the appropriate sequence. As far as the motor cortex (which isn't specialized for smiling) is concerned, this is as complex a feat as returning Pete Sampras's serve with a top-spin-down-the-line shot with no tennis

[75] John H. Martin, *Neuroanatomy.*

lessons. Consequently, the attempt fails totally. Your smile is forced and looks like a frozen grimace.[76]

There are some reflexive gestures, for example the gustofacial reflex, where sweet tastes evoke a smile, bitter tastes produce a look of disgust and sticking out the tongue, while sour taste produces a pursing of the lips. Different tastes produce fixed and stereotyped expressions,[77] as newborn babies easily confirm. This reflex is controlled in the lower brainstem and is hardwired, not learned.

Some movements are used as expressions of, and are closely linked to emotions. Consequently they are orchestrated by the limbic system that controls emotions. It is important, particularly from a social functioning view, that emotions be communicated to others, and this is accomplished by gestures and body postures. Facial expressions are universal across cultures and some are even universal across species. Think of aggression and the baring of teeth. Perhaps a small variation of the baring of teeth evolved into a smile,[78] as a signal that we are friend and not foe. It is relatively easy to read expressions of disgust, shame or fear, for example.

The memories of our body movements and face gestures generated by reflexes, feelings or by voluntary action are a part and parcel of our everyday existence. As such, we need to consider communication with hand gestures, body postures and facial expressions as an integral and basic form of language that the brain uses to communicate our internal state to others. As a good (and highly evolved) example of this, we have pantomime and dance.[79] There is a natural, close relationship between our emotions that produce characteristic facial expressions and body language across many cultures, i.e., anger, sadness, joy, disgust and surprise.

Other species have also evolved body languages to communicate with each other. Horses have an extensive language that involves ears, mouth, eyes, body posture and orientation. A pair of forward ears shows interest in something in front. Forward ears with head high denote interest in something in front but far off. Forward ears with head held low indicate interest in something up close, near the ground. Split ears, one forward, one backward, signifies interest in something in front, but also concern for something in the rear. Ears pinned back on the neck, reflect anger. Switching the tail, when not clearing insects, shows discontent.

Genetics imparts much of the language, but a lone horse's communication is dull, less defined. Horses raised in a wild herd display a purer form of equine language.

The key ingredient in the equine language is the positioning of the body and its direction of travel. The attitude of the body relative to the long axis of the spine and the short axis is their vocabulary.

Men can communicate with horses using their language. Keeping the mouth closed invites the horse's discomfort. Opening it slightly is fine. Opening a fist on the side of the body away from the horse draws the horse in, while opening a fist close to the horse, draws it away. Hands above the head, with fingers splayed, provokes panic (perhaps a trigger of primordial fear of cat's claws). Locking the eyes on different body parts can alter the direction and pace of movement of a horse, even from a distance.

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[76] V.S. Ramachandran, *Phantoms in the Brain.*
[77] Richard E. Cystowic, *The Man Who Tasted Shapes.*
[78] V.S. Ramachandran, *Phantom in the Brain.*
[79] Galaburda, Kosslyn, and Christen, *The Languages of the Brain.*

When a horse squares up and faces another, it means, “Keep away.” When a horse paces with his nose close to the ground, it is asking for a chance to end its isolation. If the horse presents the long axis of the body, offering the vulnerable areas, it is asking for forgiveness. When a horse throws his nose out in a circular motion, it means, “I’m sorry. It just happened.” A licking and chewing action is a sign of penitence and a sign of trust. More than a hundred signs have been identified in the equine language.

Deer have a similar language to horses, except that deer are more sensitive to orientation and body movements.[80]

The best example of evolving specialized areas in the cortex for specific purposes is the cortical area of Broca (area 44 and 45), which controls speech. It is directly connected by long tracts to area 10 and the supplementary motor area (6).[81] This area serves as a transducer of thoughts to spoken words, of thoughts transformed into carefully controlled movements of tongue, mouth, vocal chords and larynx, coordinated all with air exhalations.

What can be more real than our own bodies? However, we have seen that our bodies are illusory, careful creations of our brains, maps of our body that allow the brain to control it in order to navigate through the environment and help communicate our internal state to others. For social animals, communicating our emotions is very important. It is not surprising that we use our bodies to do so. The body we experience is essentially a phantom that feels and corresponds to our experience of us in contact with the environment and others. It is a continuously updated illusion that relies on the most recent memories of our body and its changes in relation to its parts as well as in relation to the world around us.

5
Vision: What You See, Might Be.

Eyesight seems to be the most marvelous of our senses. The fact that we can see has even been used as proof that God exists. Some have proposed seriously that something as complex as sight had to be designed by a higher power, it just could not have evolved naturally. One of the more famous analogies is that of the blind watchmaker. But the truth is that vision has evolved in different ways at various times. Vertebrates evolved a pair of eyes; most insects, pairs of multiple eyes.

Elegant experiments have been carried out to record the neural responses at various stages of transmission in all the senses including the somatomotor systems. The essential finding, alike in all sensory systems, is that the neural activity directly evoked by the stimulus is observed in bursts of input-driven action potentials that serve to select a pattern of activity to be created in and by that sensory cortex to which the stimulus is directed. The pattern generated is not a “representation” of the stimulus but is instead a briefly sustained neural discharge that constitutes the significance and value of the stimulus. Such patterns depend on past learning that has been embedded in the modified

[80] Monty Roberts. *The Man Who Listens to Horses.*
[81] Jean Talairach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

synapses in cortical networks, so the patterns are unique to each individual and not specific for the stimuli by which their construction is triggered.[82]

Having said this, lets take a look at how one of the senses works. Vision is one of the most studied senses, at least in neurological terms. Vision could be thought of as three senses – motion, color, and luminance (contrast).[83] Much of what we do know is from very in-depth studies of cats' vision. Most of the ideas presented here are from Francis Crick's *The Astonishing Hypothesis*. He gives a good presentation of vision, which I am greatly summarizing, and in very small ways changing to reflect my different views.

Francis Crick starts with a simple question: How exactly does my brain work when I see? What do we mammals use our eyes for? When photons of light impinge on our eyes, the only information that can be extracted from this is how much light comes from a particular visual field, plus perhaps some information concerning its wavelength. What we really want to know is what is out there, where is it going, and what is it doing. We need to see objects, their movements and interpret some meaningful relations. Not only do we need this information to survive, to avoid predators, find food and a mating partner, but also, we need this information now.

Now means right away. It doesn't do me any good to see a tiger running towards me, if, a couple of hours after the fact I realize it was a tiger that bit my arm off. There is a very high premium to extract information as quickly as possible.

The eye and the brain must work closely together to be able to achieve all that vision does. However, the visual information provided by the eyes can be ambiguous; we are easily deceived by our visual system. Seeing is a constructive process.

What we see is not really what is there; it is what our brain interprets is there. In most cases this will indeed correspond with the characteristics of the world before us, but in some cases our interpretations may turn out to be mistaken. Our brains make the best educated guess possible according to previous experience and the limited and ambiguous information provided by the eye.

Clearly we have a "picture" in our heads of the world in front of us. Yet few people believe that we have a screen somewhere inside the brain. If we had a symbolic screen inside our heads that was a dot-to-dot representation (like a television screen) of the scene that reaches the eye, we can easily see that we would have a black and white representation of the world. By adding three dots to every dot, we would be able to add color. The cells of this symbolic screen do not produce light, but some form of electrochemical activity that symbolizes light. The problem with such an arrangement is that it couldn't perceive anything except patches of light. There is no way that these patches can be turned into the image of someone sitting in front of us.[84] There is nothing built into this kind of system that will recognize that someone is sitting there, much less that it is a woman, and even less that it is your sister. There has to be a higher order symbolic description, probably a series of higher levels.

We must keep in mind that the mammalian retinae contain more than fifty distinct cell types, each with a different function. The retinae itself begins the interpretation of the light that impinges on it. The sole output of the retinae is the 1.5 million axons of the ganglion cells that constitute the optic nerve. About 90 per cent of the fibers in the optic

[82] Walter J. Freeman, *Neurodynamic Models of Brain in Psychiatry.*
[83] Jeff Hawkins, *On Intelligence.*
[84] Frances Crick, *The Astonishing Hypotheses.*

nerve project to the Lateral Geniculate Nucleus (LGN) of the thalamus and from there on to the primary visual cortex. About a 100,000 ganglion cells project to the superior colliculus (SC) at the top of the midbrain.[85]

When the signals reach the cortex, more information is extracted. These higher-level interpretations are implicit in the pattern of light falling on the eye, but this is not enough. The brain must make these interpretations explicit. In neural terms, explicit could mean that neurons are firing in a way that symbolizes such information fairly directly. We need an explicit multilevel, symbolic interpretation of the visual scene in order to "see" it. It is hard for people to accept that what we see is a symbolic interpretation and not the "real world". We have no direct knowledge of objects in the outside world. It is an illusion produced by a very efficient system.

In order to give light meaning, to see objects, our brain must perform some basic operations: calculate their position (in relation to us and to each other), and motion, and identify certain attributes, such as shape, color and so on. Our brains have to use various clues and tricks to enable us to group together those parts of the visual field that correspond to an object.

When we see a black cat moving, we generally associate that all moving parts are moving with the same object. We don't think that we see legs, a body and a head with eyes moving in the same direction. We see a cat moving. Proximity (in this case color and movement) in space is generally interpreted by the brain as belonging to the same object. Similarity would play an analogous role. When an object is partially hidden by another object, say a dog behind a slatted fence, we tend to think that the partially hidden dog is one, and not two or more dogs. The brain quickly arrives at this logical conclusion.

When we see a border, as can be clearly seen in a line drawing, we interpret it as a figure bounded by this border. In general the brain tries to arrive at the simplest interpretation according to our experience.[86]

The photoreceptors in the eye respond to intensity of light falling on them. Suppose that a whole patch of photoreceptors is responding in the same way, because you are looking at a large, fairly uniform, smooth object. Why send all this information to the brain? It is much of the same. It is better for the retina, at the back of the eye, to process the visual information, so that the brain is told where the light intensity changes in space at the edges of the object. If there isn't any spatial change across the retina, no signal is sent. The brain infers that no signal means no change.

To some extent the brain processes different sorts of information in somewhat parallel streams. Therefore, it makes sense to study separately how we see shape, motion, color and so on, even though these processes interact somewhat.[87]

In a simplified way, to obtain color information, more than one type of photoreceptor is needed, each with a different wavelength-response curve. These curves overlap somewhat, but an incoming stream of photons of one wavelength will on average excite the different photoreceptors by different amounts. The brain uses the ratios of their excitations to decide the color. The brain is not primarily interested in the combination of reflectance and illumination but in color. It tries to extract this information by comparing the eye's response to several regions in the visual field. It manages this by using the

[85] Christian Koch, *The Quest for Consciousness.*
[86] Frances Crick, *The Astonishing Hypotheses.*
[87] Ibid.

assumption that the color of the illumination is much the same everywhere in that scene at that instant, even though it may be considerably different on other occasions.[88] That is why, even under candlelight, my wife's blue jeans still "look" blue.

When the visual signals arrive to the thalamic relay and associated structures, through the use of echoes and tags coming from the visual areas in the cortex, these signals are mirrored (relayed) to the appropriate regions in the cortex. Each different group of neurons that specializes in identifying various characteristics of the visual signals will send echoes (there will be echoes for borders, echoes for colors, echoes for movement, echoes for direction, echoes for varying slants and so on) to the thalamus, which in turn are interpreted as "mirror the signal to here", or through the use of tags, interpreted as "relay the signal to here and there as well." When the echoes are matched they activate their respective handshakes and these regions in turn, activate other higher areas in the cortex that will extract more or different information. The areas that received the handshakes, in turn, can also send an echo to the thalamus and thus receive the originally relayed signal to analyze specific properties. This starts the process of extracting information from patches of light and directing the flow of traffic to the appropriate areas.

It is obviously useful for the brain to find the edges to determine shape. It turns out that different parts of the brain respond better to fine detail, others to less detail, and still others, to coarser spatial changes. When the details change, the brain notices; different areas respond to the changes.[89]

Another problem is seeing in three dimensions. To see all objects in three dimensions is not enough. We need to see the whole scene in three dimensions in order to know what objects are closer. There are strong clues even in a two dimensional picture. The first is perspective. Another clue is occlusion – when an object nearer us hides one farther away. Another clue to distance is texture gradient. As the texture gets smaller, we interpret it is farther away. Another clue can be apparent size. When a familiar object is in our visual field, and we know its size, we can determine the size of other objects.[90]

The fact that we have two eyes, and each eye has a slightly different view of the world, also helps us extract depth information. This is called stereopsis.

The perception of motion is handled by two main processes called (somewhat inaccurately) the short-range system and the long-range system. The short-range system is believed to occur before the latter. The short-range system does not recognize objects, but merely changes in the patterns of light sensed by the retina and sent to the brain. It extracts movements without knowing what is moving. It operates automatically and is not influenced by visual attention. It is also suspected that the short-range system separates the object from the background. The short-range system controls involuntary eye movement to place the motion in the center of our visual field.

The long-range system registers movement of objects. It registers what is moving from one place to another. The long-range system engages attention. Attention will activate all the semantic memories to identify what is in the center of vision, and

[88] Ibid.
[89] Ibid.
[90] Ibid.

voluntarily control eye movement to keep the object in the center of vision by controlling neck and eye movements in a coordinated fashion.[91]

The brain uses motion in other ways. If an object has an expanding image in our visual field, the brain will interpret it as coming towards us. When we are moving through the environment, the visual scene slips past us on either side and above and below our heads. We don't see the world moving because our brain compensates and interprets correctly that we are moving.

Arousal is a general condition affecting all of one's behavior, as when you first wake up in the morning. Attention is more specific, it implies withdrawal from some things in order to deal effectively with others. One form of visual attention uses eye movement (often assisted by head movement). Because we see more clearly close to the center of our gaze, we get more information about an object if we direct our eyes on it. We get coarser information from objects that are in the periphery of our vision.[92] Eye movements range from reflex-like responses, such as directing our sight toward a sudden movement, to willed movements, i.e., I wonder what she's doing over there? All forms of attention have both reflex and willed eye movements.

An attended event is reacted to more rapidly at a lower threshold and more accurately. Attention also makes the event easier to remember.[93] One cannot attend to two different places (or objects) in the visual field. There is substantial evidence, however, that attention can be focused in space or, alternately, made more diffuse. For example, as you read these words, you attend to the words, not each separate letter. There is some agreement that attention involves a bottleneck. The idea is that early processing is largely parallel (many activities happening at the same time). Then there are one or more stages where there is a bottleneck in information processing; only one (or a few) object(s) can be dealt with at a time. This is done by temporarily filtering out the information from the unattended object, and then the attention moves fairly rapidly to the next object, and so on.[94] Attention is mostly serial.

Seeing is a complicated process. The visual system consists of one very large primary system, one secondary system, and a number of minor systems. They all receive input from some of the million or so neurons, the ganglion cells, at the back of the eye. The primary visual system connects to the visual cortex in the occipital lobe via the Lateral Geniculate Nucleus (LGN) of the thalamus. The secondary system projects to the superior colliculus at the top of the midbrain. Each eye sends signals to both sides of the brain, so that both the left and the right visual cortex are receiving information from both eyes.

Starting from the eyes, any particular ganglion cell will respond vigorously to a small spot of light turned on (or off) in one particular part of the visual field. In total darkness, a ganglion cell fires at a low, irregular rate, called its background rate. A spot of light on the retina will generally excite a group of ganglion cells, though not all to the same degree.

There are two types of ganglion cells, called on-center and off-center. Both of these in turn are divided into classes of ganglion cells: the M cells and the P cells. The M

[91] Ibid.
[92] Ibid.
[93] Daniel L. Schacter, *Searching for Memory.*
[94] Francis Crick, *The Astonishing Hypothesis*.

cells are larger than the P cells and have a thicker axon, which in turn allows them to send signals faster to the brain. They respond well to small differences in light intensity and so handle low contrast well. The P cells are more numerous and their responses are more linear (proportional to the input) than the M cells. They are more interested in fine detail, higher contrast, and especially color. There are several types of P cells, each interested in different color contrasts. Once again, the retina is not just transmitting raw information; it has started the job of processing this information and is doing so in more ways than one.

Both the M and P cells (each having on-center and off-center members) send their axons to the LGN in the thalamus, where it is relayed to the visual cortex. The retina also projects to the superior colliculus. P cells do not do so, but some M cells do, as do a number of minor, miscellaneous cell types. The lack of P-cell input means the superior colliculus is colorblind.

Thanks to the work of Hubel and Wiesel we started to a have a view of how vision works. Retinal cells exhibit excitation and inhibition when light impinges on them; when colors change, the geniculate neurons become active. The optimal stimulus for these two types of cells is a white spot on a dark background (for other cells it is the opposite, a black spot on a white background) of a certain size, but always round.[95]

Each eye projects to both sides of the brain, but it does so in such a way that the left side of the brain receives input relating only to the right half of the visual field, meaning the right half of the left eye, and the right half of the right eye. So everything we see to the right of our center of gaze goes to the left LGN on its way to the visual cortex and also to the left superior colliculus. Several tracts of nerve fibers of which the largest is the corpus callosum connect the two halves of the brain. If this is cut, the left half of the brain of that person sees the right side of the visual field and the right half only the left side. This can produce somewhat surprising results, almost as if there were two persons in one head.[96]

Evidence of the constructive process of seeing comes from patients with tiny lesions that damage just V4, the color area, or just MT, the motion area. If V4 is damaged on both sides of the brain a syndrome called color cortical blindness or achromatopsia results. Patients with cortical achromatopsia see the world in shades of gray, but have no problem reading a newspaper or recognizing people's faces or seeing direction of movement. Conversely if MT, the middle temporal area, is damaged, the patient can still read books and see colors but can't tell which direction something is moving, or how fast.[97]

Keeping in mind the columnar organization of the cortex, most neurons within a column, from top to bottom, a few millimeters in thickness, become active together. For instance, cells stacked above each other in V1 code for orientation of visual stimuli (i.e., everything that has a diagonal orientation) within a particular region of visual space, while column in area MT represent one particular direction of movement (i.e., everything that moves rightward).[98]

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[95] William H. Galvin, *The Cerebral Symphony.*
[96] Francis Crick, *The Astonishing Hypothesis.*
[97] V.S. Ramachandran, *A Brief Tour of Human Consciousness.*
[98] Chritian Koch, *The Quest for Consciousness.*

The secondary system that projects to the superior colliculus is the main visual system in lower vertebrates; in mammals, most of its functions have been taken over by the cortex. Its remaining function seems to be the control of eye movement and some aspects of visual attention. The colliculus is a three-layered structure. The upper regions receive various kinds of retinal, auditory and somatosensory inputs. The inputs are crudely mapped. The neurons in the upper region are selective for movement. Very interested in small stimuli, their response to the change of light is often very transient. These are all factors that command attention; they signal, "Look out, there is something there."

In the cortex, the messages are rearranged to make new patterns. For some of these neurons, the optimal stimulus is lines and elongated edges. When the stimulus switches from spots to lines and edges, the Geniculate cells decrease their activity, and a certain group of cells in the cortex arranges this changed output so as to sum together the activity of many input cells whose receptive fields centers were not all in the same place: indeed, they were all strung out in a line.[99]

The cortex stores memories of sequences of patterns. Through handshakes, the cortex sets up associations of patterns, which can be recalled auto-associatively. In this way groups of patterns, as they move up the hierarchy, will represent specific aspects, like color, size or movement, of an object until eventually my mother's face becomes possible. My "mother's face" in turn will send out feedback handshakes which in turn will modify how neurons react to this face as opposed to any other face. In a hierarchical structure (in the cortex higher and lower is really sideways) many lower areas provide converging sensory signals. The receiving areas send echoes to the thalamus informing of what patterns to expect next, anticipating what the incoming signals should "look" like. The higher up in the hierarchy, the more united the information from the multiple senses becomes, including the changes of the position of the body (or its parts), so the representation of the world and its inter-relationships remains constant.

The lower visual areas provide inputs that become stable representations higher up. In a few steps, letters on this printed page are represented by symbols, groups of letters represent words (objects or concepts), and in this way a visual input could be converted to and abstract thought. Every scene is composed of collections of smaller objects. There are nested structures.

There are very fast changes in V1 reflecting the changes of what impinges on the retina. The higher up, going to V2, V3 V4, to VOT or DP, from there to VIP or LIP, and up to FEF or 7b and 7a, the less the rate of change, reflecting a more stable representation, or interpretation. Until finally the hippocampus would be activated to resolve any issues that are not in memory, and initiate the establishment of a new memory.

People with a small lesion to a specific part of the cortex do not suffer an across-the-board reduction in al their cognitive capacities. Instead there is often a highly selective loss of one specific function while other functions remain intact. On example is a situation called prosopognosia or face blindness. When the fusiform gyrus in the temporal lobes is damaged on both sides of the brain, the patient cannot recognize faces. Most everything else is normal. There exists another strange situation called Capgras syndrome. In such situations, the patient is convinced (feels) that loved ones are

[99] Francis Crick, *The Astonishing Hypothesis.*

impostors. Perhaps the fusiform gyrus and all the visual areas are intact (because they can identify the person), but the connection that goes to the emotional centers (the amygdala) is not operating properly (or is severed). So in the absence of an emotional response, the brain responds to this peculiar paradox by deciding it must be an impostor.

There is no such delusion if the loved person calls on the phone, as the auditory cortex and it connections to emotional centers are operating normally. So auditory cognizance remains intact while visual cognizance has disappeared[100] (partially). The visual echoes that trigger an emotional response have been disrupted, as opposed to the auditory echoes that continue to function normally. To support the view that the neural activity of hearing and seeing is similar, and the echoes streaming to the thalamus from various cortical areas are just as similar, newborn ferrets brains' have been surgically rewired so the animals' eyes send signals to the areas of the cortex where hearing normally develops. The result is that the ferrets develop functioning visual pathways in the auditory portion of their brains. Similarly, pieces of rat visual cortex have been transplanted around the time of birth to regions where the sense of touch is usually represented. As the rat matures, the transplanted tissue processes touch rather than vision. Human's cortex is just as plastic. Adults who are born deaf process visual information in areas that normally become auditory regions. And congenitally blind adults use the occipital areas to read Braille.[101]

Hubel and Wiesel went on to show that some cortical cells prefer horizontal lines, others vertical and still others preferred various in-between angles. Different groups of neurons specialize in different tilts. Other neurons are stimulated at boundaries, such as the horizon and the sky, while other neurons prefer narrow black lines, and others narrow white lines. The cortex has a lot of variety. Neighboring neurons tend to prefer the same tilt, until suddenly there is a neighbor that prefers quite a different tilt. When a line is moved sideways, every cell in the retina, the geniculate and the (thus far) explored cortex cells would stop firing. However, there is another group that responds to small angles of orientation of around 10 to 15 degrees wide. They called these latter ones complex, as opposed to the other neurons that they called simple. The complex cells generalize.[102] The simple cells and complex cells seem to do an AND operation and an OR operation, respectively. The thalamus does some initial processing, and according to the echoes it is receiving from the cortex relays this information on to the primary visual cortex.

The inputs to the deeper regions are more various. These deep regions also connect to the brain stem onto neurons that lead to control of muscles in the eyes and neck. The deepest region is connected contralaterally, via a pathway called the intertactal commissure.

The eyes make quick movements, called saccades, about three times a second. The eye moves and stops. The stops are called fixations. For instance, each V1 neuron might fire vigorously when a line or an edge slanted thirty degrees enters the receptive field. The slanted edge has little meaning; it could be the side of a palm tree, or the side of the letter M, or a hill. With each new fixation the neurons receptive field comes to rest on a new and entirely different portion of visual space. On some fixations the cell will fire strongly, on others it will fire weakly or not at all. Thus in each saccade, many cells

[100] V.S. Ramachandran, *A Brief Tour of Human Consciousness.* 2004.
[101] Jeff Hawkins, *On Intelligence.*
[102] William H. Galvin, *The Cerebral Symphony.*

in V1 are likely to change their activity.[103] Higher up the hierarchy, other cells will fire and remain active as long as the palm tree, the letter M or a hill are in the visual field.

When viewing a face, the sequence of patterns determined by saccades is not fixed. Sometimes the fixations will follow an "eye-eye-nose-mouth" order, at other times the order might be "mouth-eye-nose-eye." The components of a face are a sequence. They are statistically related and tend to occur together in time, although the order might vary. If you perceive "face" while fixating on "nose," the likely next saccade will fixate on "eye" or "mouth."[104] The cortex certainly would not expect "pen" or "car" to appear in the next saccade.

The main neurons in the LGN produce excitation. In addition, there is a minority of GABAergic cells that produce inhibition. The LGN of the thalamus seems to be a relay; the principal cells receive input directly from the retina and mirror (send their axons) directly to the visual area (17 or V1) of the cortex. There are no other neurons in between, hence the name relay. The M and P inputs are largely kept apart, as are the inputs from the two eyes. The Macaque LGN has six layers. Two of these have large cells called magnocellular; one gets its input from the right eye, the other from the left eye. There is little interaction between the layers. Their input is mainly from the M cells. The P cells connect to the other four layers with small cells, called the parvocellular. It has been determined that the parvocellular layers carry signals relating to color, texture, shape and stereopsis, and that the magnocellular neurons specialize in movement and flicker.[105] Each layer will be responding to different echoes and therefore relaying slightly different information.

So far we have only talked about the principal excitatory cells. The inhibitory neurons fall into two main classes, those in the LGN proper and those in a thin sheet of cells called the reticular nucleus of the thalamus. This thin sheet of cells surrounds much of the thalamus. Its neurons are all inhibitory. They receive excitation from most of the axons passing to and from the cortex and they interact with each other. Their output is mapped onto the underlying part of the thalamus immediately beneath them. Here is where the main matching of stimulus to echoes is achieved and the orchestration of where and how to send the impulses begin. This is where awareness starts; this is where attention is controlled.

From the LGN there is a direct projection to the cortex, the primary visual area, called V1 or area 17. Here the density of neurons can be as high as 250,000 per square millimeter. The cortex is divided into several layers. The neurons in each layer have more interconnections with their neighbors than with other layers. The input from the LGN goes mainly into layer IV of this area, but some go to layer VI. Layer IV has several subdivisions. The inputs from the P and M layers tend to be segregated into different sublayers of layer IV (the layer of the small pyramidal and the large pyramidal neurons). Every axon branches extensively and communicates with as many as 1000 neurons, but only about twenty per cent of the spiney stellate neurons in this layer receives inputs directly form the LGN. The rest of the synapses receive inputs from somewhere else, mainly from neurons in the neighborhood. There are a series of "blobs" in the layer above and below level IV and these neurons seem to be concerned with color and brightness.

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[103] Jeff Hawkins, *On Intelligence.*
[104] Ibid.
[105] Francis Crick, *The Astonishing Hypothesis.*

Seeing is a hierarchical processing of signals. It is worthwhile to see how neural impulses are sent up and down the cortical hierarchy. I have adapted the following from Jeff Hawkins, *On Intelligence*. First lets see how forward handshakes move up the hierarchy. The initial mirroring of sensory signals from the thalamus arrives at layer IV, the main input layer. Consequently, converging inputs from lower regions always arrive at layer IV of higher areas. In passing they also from a connection with layer VI. Layer IV neurons then send projections to layers II and III within their column. When a column projects information up, sends forward handshakes, many layer II and III neurons connect to layer IV of the next higher area.

Signals flowing down the hierarchy, the feedback handshakes, take a less direct path. Layer VI cells are the downward-projecting output cells from a cortical column and project to layer I in the regions hierarchically below. Here in layer I, the axons spread over long distances in the lower cortical region. Thus signals flowing down the hierarchy from one column has the potential to activate many columns in the areas below it. There are very few cells in layer I, but neurons in layers II, III, and V have dendrites in layer I, so these cells can be excited by the feedback [handshakes] distributed all across layer I. The axons coming from layer II and III neurons form synapses in layer V as they leave the cortex and are believed to excite cells in layers V and VI. So we can say that as information flows down the hierarchy, it has a less direct route. It can branch in many directions via the spread in layer I. Feedback information starts in a layer VI neuron in the higher regions; it spreads across layer I in the lower region. Some neurons in layers II, III and V in the lower area are excited, and some of these excite layer VI cells, which project to layer I in regions hierarchically below, and so on.[106]

Specific sensory signals activate related memories through handshakes. Related memories include expectations of what will happen next. As related memories are activated some neurons in layers V and VI send echoes to the thalamus to help orchestrate the distribution of sensory signals. In the case of vision it takes several levels of processing up the hierarchy to get to these related memories, lets call them expectations or predictions. Motion, boundaries, and so on, create an expectation of what will appear in the visual field next. The echo that matches best with what actually occurs next will determine, moment by moment, which way to propagate the visual signal. In this way the various possible predictions guide what we see, and what we see trims the number of possible predictions. The feedback handshakes going to layer I assist in interpreting the small changes that a particular object goes through as it moves through our visual field. Even though an object's perspective, distance from us, or its movement or rotation changes, we still recognize the object and keep track of the specific details and changes through time.

The different visual areas should probably be further divided, according to their excitability. Essentially the neurons in V1 are interested in orientation, movement, disparity and color. V1 is a map of the opposite half of the visual field.

Close inspection of V2, the secondary visual area (area18), reveals that neurons receive input from both eyes. Their receptive fields are larger than those in V1 (17) and respond in more subtle ways. For example there are neurons that fire when presented with certain subjective contours. There appear to be several distinct streams of information flowing through V2 (area 18) that are sensitive to color, disparity and so on.

[106] Jeff Hawkins, *On Intelligence.*

A region in the fusiform gyrus contains an essential node for the perception of color; a more anterior part of this gyrus includes an essential node for face perception, with the amygdala becoming active when perceiving fearful facial expressions. In the case for faces, there are patches encoding for eyes and the nose, the gender identity of the face, its angle of gaze, its emotional expression and so on.[107]

There are many connections between V1 (17) and V2 (18) in the occipital cortex. Also area 18 connects with neighboring area 19, and area 19 connects contralaterally.[108]

The LGN neurons also receive [echoes] back pathways coming from the first visual cortex (V1). There are more axons coming back from V1 than going to it, but they tend to synapse onto those parts of the dendrites rather distant from the cell bodies of the LGN neurons.[109] V1, after extracting some information, sends more echoes and tags through these projections to help the LGN interpret where else to mirror the original signals, and there different information will be extracted. V1 will also pass on the information it processed by sending handshakes to other adjacent areas.

V1 (area17) projects to V2 (area 18) and almost as many neurons project backward. The difference is that V1 projects to layer IV, the input layer, of area V2, whereas the backward projection avoids layer IV of V1. This feedback affects the processing layers of V1.

There are inputs from the brain stem that modulate the behavior of the thalamus and especially its reticular nucleus. This means that the LGN freely transmits visual information when the animal is awake but blocks the transmission somewhat when the animal is in slow wave sleep.

There are at least thirty visual areas that are known today: some areas are known as 46, 35 and 36. Other areas are known by initials denoting their names like MT (middle temporal), VIP (Ventral intraparietal). There is much known about all these areas but the exact details of how they work together isn't yet known. For example MT (also known as V5) is a small area; it has a fairly good retinotopic map of the visual hemifield. Its neurons are strongly interested in the movement of stimuli, including its direction. The neurons have little interest in color, but they do respond to the movement of boundaries.

To give an idea of the complexity of the visual system, as you move up the hierarchy, areas known as V3 and VP (area 19, which connects to V1 and V2); then higher up PIP and V3A, moving up to MDP, MIP, PO, V4t, and V4; then DP and VOT; Then VIP, LIP, MSTd, MST1, PST, PITd and PITv; then 7b, 7a, FEF, STPp, CITd, CITv; then STPa, AITd and AITv; which go on to connect to area 36, 46, TF and TH. Then area 36 and ER, and a t the top of the hierarchy the hippocampus. Many of the areas project in both directions, connect at the same level, and can also project two, three or four levels higher.

At the top of the hierarchy, the entorhinal cortex connects in turn to area 35, 36, 46, STPa, TF, TH and the hippocampus. The hippocampus is connected to area 35, 36, TF and TH. In this way circuits are completed.[110]

If we look in more detail to the connections going from the retina to the LGN and from there to V1, to V2, V3, V3A, V4t, V4, and upwards through the visual hierarchy,

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[107] Christof Koch, *The Quest for Consciousness.*
[108] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.
[109] Francis Crick, *The Astonishing Hypothesis.*
[110] Ibid.

the hippocampus sits at the top level. From the retina to the hippocampus, depending which route is followed, there are between 6 and 14 levels. We need to keep in mind that most of these connections are in both directions. A typical neuron can reset itself in about 5 milliseconds. This would tie in nicely with the vision fusion threshold, where two flashes of light blur into one, of 20 to 30 milliseconds, with the time required to move through at least six levels in the visual hierarchy.

Visual inputs, through associative handshakes that go to the attentional areas (area 39 and 40 and 7, traditionally called associative areas) can lead to signals flowing down the motor cortex resulting in a response. The visual inputs activate related areas in the auditory and tactile memories, and in this way create a deeper understanding of what we see. The handshakes activate areas that are related to expected events, which depend on the physical movement of the body and the changes in orientation of the head or eye movements. In this elegant way, the visual field is adjusted to remain constant, instead of the ground passing below us or the sky passing above us as we move forward, or bobbing up and down as we walk.

The feedback handshakes from these other areas, tactile or auditory, as they flow back, can be interpreted as prediction signals because they are sending information related to what is expected (i.e., how the ground will feel as our feet touch it when we walk, or the sound of our footsteps.) The way the cortex achieves these predictions is analogous to how the motor cortex generates movement. Information flows through the hierarchy from high to the lower areas. Sensory signals simultaneously flow in anywhere and everywhere – and then flow back down any area of the hierarchy, leading to predictions or motor behavior. Although the motor cortex has some special attributes, it is correct to see it as just a part of one large hierarchical memory-prediction system. It's almost like another sense. Seeing, hearing, touching and acting are profoundly intertwined.[111] And, as we will see later, memories are intensely sensitive to emotional states. Consequently, there is an emotional component to what our senses interpret and what our responses are.

It has been know for many years that particularly large layer V neurons within the motor cortex (M1) make direct contact with muscles and motor regions of the spinal cord. These neurons literally make the muscles contract and relax. If you speak, type or perform any sophisticated behavior, these neurons are firing on and off in a highly coordinated way. Recently, researchers have discovered that large layer V neurons may play a role in behavior in other parts of the cortex. Large layer V neurons in the visual cortex project to part of the brain that moves de eyes (area 8). So the visual areas of the cortex, such as V2 and V4, not only process visual input, but they help determine the movement of the eyes themselves, and therefore what reaches the visual cortex. These large layer V cells are found throughout the cortex, suggesting a more widespread role in all kinds of movement.[112] More importantly, the axons of these large layer V neurons split in two. One branch goes to the thalamus sending the echoes of anticipated movements and serves to find matches with the proprioceptive signals, orchestrating the overall motor output. However, these echoes produce the mirroring of signals to layer I, activating broad areas of columns. The echoes from layer VI make the mirrored signals

[111] Jeff Hawkins, *On Intelligence.*
[112] Ibid.

go to layer IV of a single column. The anticipation of expected signals needs to be narrowed to a single solution.

Ambiguous inputs need to be resolved by activating a single column but generally several columns are activated reflecting the ambiguity. Therefore a column with strong inputs should inhibit the activity in other columns. These interneurons only affect the area surrounding a column, but many columns in an area can be active. In essence, when a signal arrives from the thalamus or from a layer below, it activates cells in layer IV. Layer IV neurons activate layer II and III neurons. Layer II and III neurons send forward handshakes to a higher level area, as well as activating layer V and VI neurons within the same column. The whole column becomes active when receiving a mirrored sensory signal or a signal from a level below. Layer II, III and V have many synapses in layer I. If these synapses are active when layer II, III and V are firing, the synapses are strengthened. When these synapses become strong enough, they can make cells in layers II, III and V fire even when layer IV cells haven't fired. Thus through handshakes in layer I, neurons learn to anticipate even before receiving signals from layer IV. When a column becomes active via layer I, it is expecting to receive a signal from layer IV from an area lower in the hierarchy. It is anticipating, it is predicting. The layer VI neuron also becomes active simultaneously and sends a signal to layer I of a lower area, reinforcing the input signal (if it arrives) into layer IV of the lower area. Only the column where the signal arrived becomes reinforced and inhibits its neighbors standing out more clearly.

Under certain conditions, half the input to layer I is driven by activity in layer V. This represents what was happening moments before. When the order of these patterns occurs consistently over time, the columns will store the sequence of patterns, and fire one after another in proper sequence. The other half of the input to layer I comes from layer VI neurons in the hierarchically higher area. This information is more stable. It represents the name of the sequence. If your columns are phonemes, then it is the spoken word you are hearing. If the columns are active with spoken words, then the impulses from above are the speech you are reciting. Thus the information in layer I represents the name of the sequence (through feedback handshakes) and the last item of the sequence (through forward handshakes). In this way, a particular column can be shared among many different sequences without getting confused. Columns learn to fire in the right context and in the correct order.

However, neurons receive and send input to many surrounding columns. Ninety percent of all synapses are from cells outside the column, and most of the synapses are not in layer I. Neurons in layers II, III and V have thousands of synapses in layer I, but also thousands of synapses in their own layers. Usually, activity in nearby columns has a strong correlation. For example if a line is moving or changing orientation in your visual field, it will activate successive columns. More often, the information needed to predict a columns activity is more widespread, thus the role layer I synapses play.

In the lower levels of the cortical hierarchy, each column's activity changes with each new sensory input. But as you go up the hierarchy, columns remain active prior to the arrival of new inputs from the lower areas. The activity of layers II and III passes on to a higher level through projections to layer IV. The activity of these cells is the input to a higher level. But that's a problem. In order for the hierarchy to work, a constant pattern during learned sequences must be relayed; the name of the sequence has to be relayed. Before learning a sequence, only the details can be relayed. The cortex needs some way

to keep the input in the next region constant during learned or memorized sequences. We need to turn off the handshakes of the layer II and III neurons when a column predicts its activity, or, alternately, to make these cells active when the column can't predict its activity. The echoes from layer V fit the later alternative. Echoes are set to match learned stimuli, otherwise there is only a direct relay of signals to the higher areas of the cortex. The echoes from layer V (represent learned stimuli) cause the thalamus to mirror the signal to layer I of the next higher cortical area. This activates neurons in layers II, III and V, which in turn make layer VI neurons fire back to layer I of the lower area reinforcing the original mirror signals to layer IV. In this way, memorized stimuli keep layers II and III sending forward handshakes to the next level and become stable.

Before learning, columns can only become active via layer IV inputs. After learning, columns can become active through memory.[113]

The classical Hebbian algorithm using auto-associative memories can learn spatial patterns and sequences of patterns. The main problem is that the memories can't handle variation well. Jeff Hawkins proposed that the cortex has gotten around this problem by stacking auto-associative memories in a hierarchy and partly by using a sophisticated columnar architecture. I have added the use of echo and mirror signals through the thalamus to make the model of the cortex more powerful. The basic components of learning are forming the classification of patterns and building sequences. These two memory components interact through forward and feedback handshakes, and with the aid of echoes to the thalamus aid in mirroring input to areas above or below the hierarchy. Once an area learns a sequence, the inputs it sends to layer IV cells in higher regions change. These layer IV cells learn to form new classifications, which in turn changes the pattern projected back to layer I in the lower area, which affects the sequences.

The basics of forming sequences are to group patterns together that are part of the same object. One way of doing this is by grouping patterns that occur simultaneously in time. As one area of the cortex builds sequences, the input to the next area changes. The input changes from representing mostly individual patterns to representing groups of patterns. The input to a region changes from notes to melodies, from letters to words, from noses to faces, and so on. Because the bottom-up inputs to a region tend to become more "object-oriented," the higher area of the cortex can now learn sequences of these higher-order objects. Where before an area built sequences of letters, it now builds sequences of words. During repetitive learning, representations of objects move down the cortical hierarchy, requiring fewer steps. Initially it requires the whole visual cortex to learn letters. But as the memories of the letters move down the hierarchy, the higher regions acquire the ability to learn complex objects like words and phrases.[114]

It is worthwhile to see in more detail how vision works through memories. At the first or second level in the visual cortical hierarchy, lets suppose a slanted line us detected. This could be interpreted as part of a nose, the side of the letter "W" or the side of a sand dune. Layer VI sends an echo to the thalamus, which mirrors the signal back to layer IV. Layer V sends and echo to the thalamus, which mirrors the signal to layer I of the next higher area.

[113] Ibid.
[114] Ibid.

At this point, the slanted line could be any of three things (could be a lot more), and consequently layers II and III send a forward handshake to the next higher level. In this case three different areas, the "nose" area, the "W" area and the "sand dune" area. Simultaneously, other aspects of the scene, let's say the "contour" area determines to forward the signal to "nose" area, the "sand dune" area, the "cliff" area, but not the "W" area. This will strengthen the "nose" and "sand dune" area. If simultaneously we add the signal from the "color" area, lets say the color of skin, this is also forwarded to the "nose" area, and perhaps the "cliff" area. The echo of layer V is mirrored to a higher level, in this case, the slanted line, or the color of skin or the contour is mirrored to the nose area. The input of the mirrored signal to layer I of the "nose" area, in addition to the forward handshake to layer IV, establish that as long as any of these inputs is present, nose is a better alternative. The feedback handshakes from layer VI to layer I of the areas below strengthen the signal even more. The result is that the slanted line, the contour and the color now stand in for "nose."

At this level, the "nose" interpretation is passed on to a higher area, the "face" area, sending a forward handshake from layers II and III to layer IV. The echo from layer V, again will have the thalamus mirror the signal to layer I. Simultaneously, other facial features, lets say "eyes" or "mouth" (if a face is present) will converge on layer IV of the "face" area, and their respective V echoes will mirror the original signal to layer I. In just three or four levels of the hierarchy, we have gone from slanted lines, contours, color, and so on to "face." The interesting thing is that as long as the "face," "nose," and or slanted line, contour and color are active, the slanted line, contour and color stand in for "face." The original sensory input now is interpreted as a more complex object. One more level up would get us to "animal faces" or "human faces" and then on to my "wife's face."

The activation of two successive cortical levels, probably takes around 15 msec. It takes about 5 msec to relay an impulse from neuron to neuron. Receive input in layer IV of lower area, activate layers II and III to send forward handshake to layer IV of higher area (about 10 msec), activate layer V to send echo to the thalamus, which mirrors it to layer I in the next level (about 15 msec), activate layer VI to send to layer I in lower level (about 10 msec). In about 15 msec three levels are activated.

The combination of the mirror signal to layer I and the input to layer IV of the higher area, activate layers II, III, V and VI (about 15-20 msec since the initial sensory signal arrived in the cortex). Another forward handshake to the next level or a feedback handshake to the level below takes another 5 msec, closing the cycle in about 25 msec. This would account neatly for the vision threshold of 20-30 msec.

It is important to keep in mind that vision accomplishes two vastly different tasks. The first one is to construct a spatial map of the external environment, primarily concerned with where all objects are in relation to the body; how close, how high, in what direction and so on. The second one is concerned with interpreting what the objects are; what for, friend or foe, food or poison, and so forth. Different circuits and areas in the cortex accomplish each of these tasks. The latter is called by some the what pathway, and the former the where pathway.[115]

The forward pathway, from the LGN to the layer VI pyramidals, seems to be weak. The back pathway, from layer VI to the LGN, has very many axons, perhaps five

[115] Christof Koch, *The Quest for Consciousness.*

to ten times as many as the forward projections from the LGN to layer IV.[116] A greater number of echoes is needed to coordinate where the thalamus mirrors the incoming signals, and is reflected by this massive back pathway from layer VI of the cortex to the LGN. There are also massive projections from layer VI to the other nuclei of the thalamus, and they work in a similar fashion.

It has been noted, in general, that projections from area "V1" to "V2" go heavily into layer IV. The reverse projection from "V2" back to "V1" usually connects strongly to layer I. The projections from the eyes to the cortex – those going heavily into layer IV of V1 – is what I call the mirrored (forward projections) signals, and those going to layer IV of V2 and the reverse projection (from V2 to V1) are the handshakes (the back projections).

The primary visual cortex (V1 or area 17) sends echoes to the thalamus from layer VI, and handshakes to the secondary visual areas (area 18 and 19) from layers II and III. Area 19 has callosal projections (contralaterally) from layers II and III, thus helping to integrate both visual fields of vision. The secondary visual areas receive these processed signals from the primary visual area along with the mirrored signals. It is thus, methodically, in a hierarchical manner, certain more complex patterns, of shapes, textures and movements, with the aid of the visual memory systems, quickly and effortlessly are assembled to recognize triangles, faces, animals, plants, and even Mary. The cortex is not computing the answer in a serial manner like a computer, but retrieving the objects from memory. The handshakes that activate all memories relative to a particular object create the rich feeling of seeing.

The rule about layer IV connections can be generalized, but there are complications. There are some important exceptions. For example, there are many cross connections between cortical areas at the same level or to one level higher or lower. In a few cases, the connections can skip levels.[117] These connections, when projecting beyond a cluster, are used to transmit handshake signals. As a general rule most connections are reciprocal, but again there are exceptions. Neurons that fire together tend to stay together.

The complex web of handshakes between all these regions and other memory systems produce the seeming effortless act of seeing. Visual awareness is the result of the brain's attempt to make sense of the information streaming in from the eyes and to express it in a compact and well-organized manner. What we see is a combination of the sensory signals and the associated handshakes to expected memories. This information is likely to be needed in several distinct places; the map of the exterior world needs to be accessible to the motor system, especially its higher planning levels, for the use of spatial relations, and to allow us to navigate through the world. The phantom-body map needs to be seamlessly integrated with the illusory, spatial representation of the external world. Visual attention, when engaged, also sends the signals to the hippocampal system (involved in the temporary storage or coding of episodic memory, as well as memorizing spatial relations). It is at this stage that the basal ganglia receive information from the occipital lobes, and makes it available to other areas of the cortex. For this purpose, various loops sharing in part the same structures, or the same thalamic nuclei, integrate the visual information with the map of the body. Using the oculomotor loop and the skeletomotor loop, which share the globus pallidus internal, the substantia nigra pars

[116] Francis Crick, *The Astonishing Hypothesis.*
[117] Ibid.

reticulata and the ventral anterior thalamic nuclei, the extrapersonal space is integrated to the intrapersonal space or body.

Vision is a hierarchical process. This view is supported by the general responses of the neurons in different areas. As we ascend the hierarchy two rough rules apply: (1) The sizes of the receptive fields increase, so that for the highest areas they often cover the whole visual hemifield and even part of the other half of the visual field (connected via the corpus callosum); and (2), the features to which neurons respond become more complex. Some neurons in V2 (area 18) respond to certain contours, while some in area MT respond in a less simple way to patterns of movement. Neurons in area MST fire in response to movements that correspond to objects moving closer, others to receding objects. Neurons in V4 respond to perceived color, rather than a particular wavelength.

V4 is an area of the cortex where a complete map of the opposite half of the visual field is found; the center of the retina is on one side and the periphery on the other side, with neurons in between specializing in intermediate areas. There are several visual maps, each doing slightly different things. Some cells in V4 like certain different degrees of convergence of the two eyes. Other V4 cells respond more to colored lights than V1 neurons. In the medial temporal MT region, the neurons respond to dumbbell shapes and cloverleaf shapes, and also respond to faces. Probably faces are made of combinations of these shapes. And then of course, there is some overlap between these different areas.

Moving to higher areas, we find neurons that respond to the front view of a face. Other neurons respond best to a face seen in profile. Neurons in another area (7a) are mainly interested in where an object is in relation to the head or the body, and much less in what it is. The inferotemporal regions (those with IT in the middle of their initials) are more concerned with what an object is.

The general pattern is that each area receives several inputs from lower areas. These lower areas have already extracted more complex features than the rather simple ones to which V1 responds. It then operates on this combination of inputs to produce more complex features, which are then passed on to higher levels. At the same time, the information flows in somewhat separate but interacting streams.

At certain levels in the hierarchy, some cells become active and stay active when entire objects appear anywhere in the visual field. In the IT area, a cell might fire robustly whenever a face is visible. As we move from the retina to the IT area, neurons change from quickly changing their rates of firing depending on if they are spatially specific or tiny-feature recognition, to constantly firing, spatially nonspecific, object recognition groups of neurons.[118]

An extreme form of explicit representation is neurons that respond to one particular object or concept, and to that object alone. Such highly specific cells are referred to as grandmother neurons, because they would become active every time you see your grandmother, but not when you see any other elderly woman. In one case, Itzhak Fried at the University of California at Los Angeles detected a “Bill Clinton” neuron. The neuron responded to 3 out of 50 images: a line drawing of U.S. President Bill Clinton, his presidential portrait, and a group photograph with him.[119]

Information also flows downward, from higher areas to lower areas. There are bundles of axons that go from IT to lower areas like V4, V2 and V1. Moreover, there are

[118] Ibid.
[119] Christian Koch, *The Quest for Consciousness.*

as many if not more feedback connections in visual cortex as there are feedforward connections.[120] The feedback handshake signals alter the feedforward signals as they indicate what and object is and also anticipate what will happen to the object in the visual field, as we move through space, or even as saccades change the focus of the eye.

Axons from layers II and III generally form synapses in layer V as they leave the cortex. Likewise, axons projecting to layer IV from lower areas of the cortex make a synapse in layer VI. So here we find an intersection where the forward and feedback handshakes converge forming a specific prediction out of the many possible. The other columns representing other potential predictions don't meet this criterion, and therefore don't fire. Neurons in layer VI will fire when this happens, and this will be interpreted as seeing or about to see something specific. The job of neurons in layer VI is to announce to lower areas that a specific representation of the world, whether true, imagined, or expected is happening.

Feedback is needed for the cortex to make predictions. Prediction requires a comparison between what is happening and what is expected to happen. What is happening flows upward and what is expected to happen flows downwards. Where the two sets intersect is what we perceive. Combining partial prediction with partial sensory input resolves ambiguity by filling in missing information and deciding between alternate possibilities.

Neurons in layer VI, in addition to sending their output to layer I of lower cortical areas, can also send their output into layer IV of their own column. When they do, the predictions become the input. In the case of vision, this is how we visualize in our "mind's eye." In the auditory regions, we "hear" voices as we think.[121]

The whole system does not operate like a one-shot, static picture. It operates by many transient, dynamic interactions, conducted at a fairly fast rate, producing a continuous dynamic representation of the world. [122]

We have to keep in mind (a figure of speech) that there is no such thing as a direct perception. We don't have a "mother" or "father" sensor. The brain is in a dark cavity in our skulls with nothing other than neural impulses streaming in through our input sensory signals. The motor cortex generates motor commands inversely as the sensory areas interpret the sensory signals, but memories of events are generated similarly to motor commands. On the sensory side a wide variety of inputs becomes a stable cell assembly that represents some abstract concept. On the motor side a stable cell assembly representing an abstract motion (hitting a tennis ball or signing your name) is carried out using many muscles and respecting a wide variety of other constraints. This symmetry should not be surprising if the cortex runs a single algorithm through out.[123]

What Francis Crick calls the Processing Postulate, which states that each level of processing is coordinated by a single thalamic region, serves to illustrate the notion that as you move down the evolutionary ladder, the thalamus must engage more and more in a genetic, automatic, switching capacity, without the aid of echoes from the cortex. In other words we should expect less learning and less experience and more genetically pre-wired behaviors, the lower we go on the evolutionary ladder.

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[120] Jeff Hawkins, *On Intelligence.*
[121] Ibid.
[122] Francis Crick, *The Astonishing Hypothesis.*
[123] Jeff Hawkins, *On Intelligence.*

In the primate visual system, the LGN is relayed mainly to V1 (the primary visual area). The other visual regions of the thalamus lie in a part called the pulvinar, which has subdivisions, some, that may consist of several sub-subdivisons. Some of these sub-subdivisions are strongly associated with the cortex at different levels. One type connects to layer IV or layer III, and another type usually projects heavily to layer I.[124]

In the model I present, the echoes from layer VI will determine where to mirror the signals (to which different areas), primarily to level IV. In turn the handshake signals will move to adjacent areas at the same level or one level up or down. In this way, level II, III and V would become activated and all levels of the column become active simultaneously. Keep in mind that level VI is echoing the thalamus. Level VI is the output, determined by the processing layers I, II and III. The output feeds back to the processing layer I of the next lower area and changes the new output according to the most recent experience.

Another brain region, the claustrum,[125] consists of a thin sheet of neurons lying next to the lower cortical layers near a part of the cortex called the “insula”. It appears to work alongside the cortex since its input comes mainly from the cortex and its output goes back to the cortex. Some, but not all the visual areas of the cortex project to one part of it.[126]

It may well be that this thin layer, the claustrum, aids in propagating and coordinating the handshake signals on a global control.

Ultimately a memory system is established to identify objects and a map is constructed to determine their orientation in space in relation to our bodies. Just like the motor system memorizes routines to walk or turn the head, the visual memory system effortlessly helps identify objects and make sense of the world in terms of patterns of inputs from all the different groups of specialized neurons and creates a map of space around us.

The anatomical connections between the visual and polysensory regions of the cortex and the hippocampal system are now well known. It is clear that visual areas V4 and MT and the inferotemporal regions do not project there directly. The visual information has to go through other cortical regions to get to the hippocampus, namely area 35, 36, TF and TH and the entorhinal cortex.[127]

There is a massive pathway from all over the cortex to the corpus callosum (which connects the two hemispheres). Interestingly, this comes from some of the pyramidal cells in layer V. These are the only neurons that project right out of the cortex. From this layer the commands go to the striatum, brain stem and spinal cord and echoes to the thalamus. From the striatum signals are sent to the motor nuclei in the brain stem (integrating visual output to the motor commands) and echoes to the ventral anterior and ventro-lateral thalamic nuclei, and from there, according to incoming somatosensory information and the echoes of the visual areas, mirrored to the various motor and premotor areas in the frontal cortex.

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[124] Francis Crick, *The Astonishing Hypothesis.*
[125] H. Sherk. (1986) The claustrum and the cerebral cortex (Chapter 13). In E.G. Jones and A. Peters, *Cerebral Cortex: Sensory-motor Areas and Aspects of Cortical Connectivity.*
[126] Francis Crick, *The Astonishing Hypothesis.*
[127] Ibid.

As was mentioned in the motor discussion, there is a pathway from the cortex to the cerebellum and back to the thalamus. The skeletomotor loop that goes from the primary motor, premotor and supplementary motor areas, to the putamen, to the globus pallidus internal and the substantia nigra pars reticulata, to the thalamus (ventral anterior and ventral lateral nuclei), and back to the cortex. Similarly, another pathway goes from the visual areas, the oculomotor loop goes from the frontal eye field and the supplementary eye field, to the caudate, to the globus pallidus internal and substantia nigra pars reticulata, to the thalamus (ventral anterior and medial dorsal nuclei) and back to the cortex.[128] It is at this level that the putamen, the caudate and the globus pallidus integrate the visual information (map of extrapersonal space) with the somatosensory map (intrapersonal space or body), creating one single map.

Most areas of the cortex, including the visual areas, participate in the creation of movement. Perception and behavior are almost the same. The layer V neurons that project to the thalamus and then to layer I also seem to have a motor function because they simultaneously project to motor areas of the old brain. Thus, the knowledge of "what just happened"—both sensory and motor is available in layer I.

Sensory perceptions are constructed from the bottom-up, and movements are performed from the top-down. As a motor command travels down the hierarchy, it gets translated into the myriad muscle contractions in the correct sequences to achieve the desired movement. This happens in both the motor cortex and the sensory cortex, blurring the distinction between the two. If region IT of the visual cortex perceives "nose," the mere act of switching to the representation for "eye" will generate a saccade necessary to make this prediction a reality. The saccade to move from nose to eye varies depending on where the face is. A close face requires a larger saccade; a more distant face requires a smaller saccade. A tilted face requires saccading at a different angle. The visual areas require knowledge of the movement of my head as I walk to compensate and maintain a constant visual field, not one bobbing up and down.

Prediction and motor behavior go hand in hand as patterns flow up and down the cortical hierarchy. Your predictions not only precede sensation, they determine sensation.[129]

What can feel more real than what we see out there? However, we have seen in a very simplified way how the brain effortlessly (seemingly) constructs a symbolic image of our environment and interprets it, not only spatially but also contextually. What we see feels real, because it is in accordance with our past experience, our memories. When the visual signals are accompanied by the brain's interpretation of them, it is experienced as seeing. Otherwise, when the brain uses memories of the visual system to imagine, the qualitative experience is quite different: it is not accompanied by sensory information. Visual memories are created in a parallel, serial, hierarchical manner using cluster of neurons. The brain creates another great illusion using the light that impinges on our eyes.

Visual imagination, the manipulation of objects in our "mind's eye" and the visual aspects of dreaming are an exadaptation of the visual memory systems employed to create a spatial map and to identify objects; these are types of thinking (visual

[128] John Martin, *Neuroanatomy.*
[129] Jeff Hawkins, *On Intelligence.*

recreations). Normally, imagination is like "seeing" with our eyes closed. But just like imagination is based on vision, imagination can affect vision.

An easy experiment of how the brain adapts vision to what it expects is to wear colored tinted glasses. At first, the world will seem redder (if the glasses were green), the sky will look purplish, and the asphalt of the road reddish. However, after a small interval, the brain will make adjustments and the pavement will appear gray and the sky blue, just as we are used to seeing. Curiously, after a while of wearing the glasses, when we take them off, the world will seem redder, and only after a while will the colors return to what we consider normal.

The subjective "corrections" of the information supplied by the sensory cortex are apparently learned. Some years ago human subjects were fitted with prism spectacles that turned the visual image upside down (Stratton, 1987; Snyder and Pronko, 1952). At first the subjects did see the world upside down. Also the subjects could not point accurately to a spot in the visual field.

However, after wearing these spectacles continuously for about a week, subjects began to be able to behave as if the image was normal. They reported not being aware of the inverted image: but, when asked, they recalled it actually was upside down! When the spectacles were removed, the subjects' visuo-motor accuracy was again briefly less accurate; it recovered within a few days.[130]

A neurological syndrome called blindsight was discovered by Larry Weiskrantz and Alan Cowey at Oxford and Ernst Poppel in Germany. It has been know for some time that damage to the visual cortex (which is part of the new [evolutionary speaking] visual pathway) on one side of the brain produces blindness on the opposite side. For example, a patient whose right visual cortex is damaged is completely blind to everything to the left of their nose (the left visual field). When the patient was shown a little spot of light in the blind region and asked what he saw, the patient reported, "Nothing." But when asked to reach out and touch the light by guessing he could accurately point to the dot he could not perceive.

The older visual pathway, the one that goes to the brain stem and superior colliculus, is still intact and serves as a backup. So even though the message from the eyes doesn't reach the visual cortex, given that the visual cortex is damaged, it takes the parallel route to the superior colliculus [this still is the main visual system in reptiles] that allows him to locate the object in space.[131] Somehow, the message (where the light is), without reaching awareness, can guide the hand movement accurately to point to the "invisible" object.

A few years ago I was reading a book on the holographic interpretation of quantum mechanics. A hologram, in a very simplified way, is produced by shining a laser beam on an object. The beam is reflected, diffracted and scattered by the object and then passes through a holographic plate. Simultaneously part of the laser beam is split off as a reference and is reflected at a specific angle by a mirror onto the holographic plate. The two laser beams interfere with each other, producing a series of dark and light bands; light bands result when the two beams are in step, when the crest of one meets the crest of the other and the trough of one meets the trough of the other; and dark bands appear where they cancel each other. These dark and light areas are called interference fringes.

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[130] Benjamin Libet. *Mind Time.*
[131] V.S. Ramachandran, *A Brief Tour of Human Consciousness.*

The image on the plate bears no resemblance to the object photographed. The plate, however, contains a detailed record of all the phase and amplitude (the frequency and the height of the crests and troughs) information present in the beam that was reflected from the object. By reversing the procedure, shining a laser beam of the same frequency at the correct angle, the interference fringes act as a diffraction grating, bending or diffracting the light to reverse the original conditions of the laser that created the hologram. As a result, an image that can be photographed is created in three dimensions.

In the interpretation of quantum mechanics from a holographic perspective, the vibration of the nothingness together with the right interference patterns makes the Universe spring to life. This is a very strange concept because the Universe is here and not here at the same time. It is here when you have the correct interference, meaning having the right senses to detect it; it is not here if you can't detect it or tune into it. Fortunately we have evolved the right senses to "see" this Universe; otherwise we could not detect anything. The Universe, or us, ultimately, could or could not be here, in a real quantum mechanics indeterminate sense.

One evening while I was pondering these strange ideas I was sitting outside trying to envision a vibration of the nothingness. Not an easy task, as I find that the brain is very uncomfortable with a blank or even attempting to stop its activity. It is easier to imagine infinity, more of the same never ending! When suddenly the quality of my vision seemed to change, gradually at first and very subtly. My normal vision seemed to be replaced slowly by thousands of pulsating dots, which changed in size, and pulsated at different frequencies. The dots seemed to be moving around each other as if they were dancing.

One of the strange effects of this was that I could see through these pulsations. The best that I can describe it is a feeling I was both seeing the objects and seeing through them. I could see through the chair, then through the tree, then through my house, then through the neighboring hill. Ultimately, I found myself staring into the infinite nothingness – a pulsating conglomerate of dancing dots. I could “see” the etherealness of our physical Universe. I was staring fascinated, trying to control what I was seeing, or better yet, what I was not seeing, slowly overcome by an indefinable fear. Perhaps, it was a fear of hallucinating, perhaps a fear of the nothingness itself. The sensation that death and nothing is the same crept into my awareness and my fear increased. I tried to bring the fear under control, and through that effort, slowly my vision returned to normal and the fear dissipated. I had no conception of how much time had elapsed.

Another curious thing that happened as a result of this experience was that for the next two months I couldn't dream in full color. My dreams came into my awareness in a black and white version of the dots. I was *seeing* in my dreams as I *saw* that dark night. I was seeing through things and seeing them at the same time. My full Technicolor vision was replaced in my dreams by representations made of dancing, pulsating dots. I still knew what I was seeing in my dream, but it was a very different kind of seeing. Thinking of quantum mechanics and trying to imagine the nothingness had been able to intrude in my way of dreaming and it had momentarily altered my vision. It was as if in a strange way my thinking resonated with my visual system and altered my perception of how and what I saw; especially in my dreams. But if the brain can create the illusion of seeing, why not see with a different illusion?

6
Memories: We Are What We Remember.

Sight and movement are based on memory systems, so we now turn our attention to our memory systems in order to understand them better.

The words “feels more real” and “feels uniquely ours,” that we use so liberally indicate that the brain’s sensory systems are focusing (paying attention) on specific stimuli: in the case of vision, external stimuli; in the case of imagining or remembering, internal stimuli.

Visual memories aid sight, help interpret what is out there, and produce a spatial map of the environment. Motor memories, along with a proprioreceptor map of the body, coordinate movement through space.

In general, memories with shared characteristics are helpful to interpret better the information coming from the senses or the body into the brain. The cortex in Homo sapiens is mostly an expanded memory system. The various memory systems of each sense are shared by associations established through handshakes signals. This allows memories to be activated by perception of a partial or even a distorted sequence of patterns. The feel of a pencil in my hand, goes along with what a pencil looks like, as well as the uses I can put a pencil to: writing, drawing, scribbling or as a letter opener. The memory of the pencil in my fingers is different than the memory of holding my pencil in between my teeth, and the sensory signals arriving at the cortex arrive in various different places, but I am able to maintain the memory of the pencil independently of where the sensory signal arrived. Memories are stored in hierarchies, starting with simpler sequences of patterns. For example, skin, nose, eye, face, my wife’s face.

In addition, the brain has evolved organized regions to specialize in categories of memories or procedures, e.g., a memory of faces, a memory of plants, a memory of tools and procedures to use them, a memory of animals, spatial memories, movement procedures, and so on.

These expanded memory systems allow for ever more refined distinctions of objects to be interpreted as well as storing more complex memories by categories, context and emotional association.

The memory systems used by the different senses to extract the most information from the world around us are shared, as this information needs to be integrated into a coherent whole. And our increased memory systems have been (evolutionarily speaking) co-opted for further tasks. The cortex is a complex associative memory system. The handshake signals maintain these associations. Each functional area is waiting vigilantly for familiar sensory inputs. This is achieved by the echo signals streaming continuously to the thalamus. The mere sound of a familiar voice is enough to activate everything related to the owner of the voice. The sight of a friend unavoidably activates memories related to her.

Hearing-memories used by the brain to interpret the information from our ears is used to make sense of speech sounds, building from sounds into words, and in turn gives words a syntactical and grammatical meaning, and eventually “think” (using these voices) in terms of a “voice in our head”. Actually, several voices or ideas are

continuously going on inside my head. The hearing memories of language, integrated to the appropriate motor memories, control speech.

A child or a man can speak a word with different accents, or in a song, but at a certain levels this doesn't matter. A word is a word. When the word is heard, the word will issue feedback signals that activate the relationships to this word. In this way, understanding is generated.

Furthermore, the same visual memories that help us interpret what is in our visual field allow us to "see" in our "mind's eye" and to imagine as well as manipulate objects in space and "turn them in our heads".

In this way, thoughts and memories are associated by handshakes. Sensory signals are associated (by echoes) to themselves and by handshakes to what normally follows next. This would explain the predictive power of memories. Anticipating the future is like recall; it is "remembering" the future.

Most of the ideas pertaining to memory presented in this section are borrowed from Daniel Schacter's excellent book *Searching for Memory*.

And as he explains, you tend to think of memories as something belonging to you, as a guide to your past. Rather, they are an expanded filing system that extracts more information from your senses though your emotions. Your emotions make your memories feel uniquely yours, quite distinct from everybody else's. You feel this way because our memories are rooted in the ongoing series of episodes and incidents that constitute our daily lives. Your subjective sense of remembering the past is such a familiar and frequent part of your life that you may fail to see any need to examine it.

As you think back, you may feel as though you are focusing on images, sounds and emotions that are slumbering somewhere in your memory. As innocent and as plausible as this seems, it is fundamentally misleading. Our experience of remembering an event does, naturally, partly depend on information about the event that has been stored in our brains. However, there are other contributors to the subjective sense of remembering. To appreciate memory's fragile power, we need to understand them.

Every time you start to drive your car, you are calling on knowledge and skills acquired earlier, but you do not feel you are reliving your past. These uses of the past call on two of the brain's major memory systems: semantic memory, which contains conceptual and factual knowledge, and procedural memory, which allows us to learn skills an acquire habits. But there is something special about the subjective experience of explicitly remembering past incidents that separates it from other uses of memory, like storing and retrieving information. In order to be "experienced" as memory, the information must be recalled in the context of a particular time and place and with some emotional reference to oneself as a participant in the episode. Remembering, for the rememberer, is a mental time travel, a sort of reliving of something that happened in the past.[132]

Jeff Hawkins conceived of a thought experiment. He calls it the altered door. Every one of us goes through our front door when we arrive home. We reach out, turn the knob, walk in and shut it behind us. It is all a habit, like driving a car. Suppose that someone, while you were away, changes something about the front door. It could be anything, change the latch, the knob, the placement of the knob, the weight of the door, or simply make the hinges squeaky or paint it a different color. This time, when you

[132] Daniel L. Schacter, *Searching for Memory*.

attempt to open the door, you will quickly detect that something is different, either that the location of the knob is different, or the color is changed, or if it feels heavier when you push with the wrong amount of force.

There is only one way to interpret your reaction to the altered door: your brain makes low-level sensory predictions about what it expects to see, hear, feel at every moment, and it does so in parallel. All areas of the cortex are simultaneously trying to predict what their next experience will be. Visual areas make predictions about edges, shapes, objects, locations and motions. Auditory areas make predictions about tones, direction to source, and patterns of sound. Somatosensory areas make predictions about touch, texture, contour, and temperature.[133]

The sensory signal (sight or sound or touch) of something familiar (our door, our house) will be matched by the thalamus to the echo of the memory of that something. This initiates a cascade of handshakes to activate everything relevant to the stimulus, which include the memories of what is expected to happen next.

Prediction means that neurons become active in advance of actually receiving sensory input. When they receive the handshakes activated by the initial stimulus, they activate an echo, which will make it easier to match with the incoming expected signal. The various possible future scenarios that have been encountered (that are stored in memory) are all activated. When one of them is matched, this in turn will activate the next possible scenarios, eliminating the possibility of the other previous ones.

As you approach the door, your cortex is forming a slew of predictions based on past experience. As you reach out, it will predict what you will feel on your fingers, when you will feel the door, and at what angle your joints will be when you actually touch the door. It will predict how much resistance the door offers when you push it open. When all predictions are met, you are not even aware what your cortex did. But if your expectations about the door are violated, the error will cause you to take notice. Correct predictions result in understanding. Incorrect predictions result in confusion and prompt you to pay attention.[134]

When you remember something, do you see yourself in the scene? Or do you see the scene through your eyes, as if you were looking outward, so that you yourself are not an object in the scene? These two modes of remembering are referred to as field and observer memories, respectively. The majority of memories can be classified as field memories, but a significant minority (more than forty per cent) can probably be classified as observer memories. We tend to see ourselves as actors in the older memories, whereas we tend to re-experience more recent memories from the original perspective.

People experience more field memories when focusing on feelings and experience, more observer memories when focusing on objective circumstances. This means that an important part of your recollective experience – whether or not you see yourself as a participant in a remembered event – is, to a large extent, constructed or invented at the time of recall. The way you remember an event depends on your purposes and goals at the time of recall. This observation suggests that the emotional intensity of a memory is determined, in part, by the way in which you go about remembering the

[133] Jeff Hawkins, *On Intelligence.*
[134] Ibid.

episode. And the emotions that you attribute to the past may sometimes arise from the way in which you set out to retrieve a memory in the present.[135]

In this context, there is a memory of the feeling of the emotion, which in itself turns on a complete set of memories relating to that particular emotion.[136] This is coordinated by the caudate nucleus. It detects specific signals from the amygdala, the orbital frontal cortex, the anterior cingulate gyrus and the lateral prefrontal cortex and activates the related thoughts and experiences indirectly by signaling to the thalamus through the basal ganglia outputs.[137] To find out more about the difference between emotions and feelings, you need to read ahead. For now suffice it to say that feelings are how the brain interprets emotions, and these in turn represent specific body states.

When you recall past events, you can perceive two slightly different subjective experiences, referred to as "remembering" and "knowing" the past. Several studies have shown that recall of visual information about a physical setting or context of an event is crucial to having a "remember" experience. Visual images tend to make us feel that we are remembering a real event. Part of the reason is that some of the same brain regions are involved in both: visual imagery (imagining) and visual perception (seeing). If we rely on these areas to perceive the external world, it should not be surprising that when we use them to create visual images, they might feel like a residue of actual, past events. This has an important implication: creating visual images may lead us to believe that we are remembering an event even when the incident never happened.[138]

Though it is clearly important, visual re-experiencing is probably not the sole basis of the subjective sense of remembering. We are also likely to feel we are remembering something from the past when we can recall associations, ideas and feelings that occurred to us during the initial episode.

On the other hand, if we are distracted or preoccupied as an event unfolds, we may have great difficulty remembering details, even though we might have a general memory of it. Knowing but not remembering can be embarrassing in a social situation; you forget that you met someone or her name. When attention is divided, it generally leads to "I know this" instead of "I remember that."

The experience of "just knowing" is related to another experience we are all acquainted with: the sense that a bit of information is on the "tip of our tongue". It seems that the tip-of-the-tongue experience arises in part because we can retrieve some of the desired information but not enough to produce a full recall.[139]

Scientists agree that the brain does not operate like a video camera or a copying machine. Then what aspects of reality do remain in memory once an episode has concluded?

Memory is linked to emotions and learning, and the brain structures and interconnections that perform this are grouped in the limbic system encircling the diencephalon on the medial brain surface and thus are at the border between subcortical nuclei and the cerebral cortex.

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[135] Daniel L. Schacter, *Searching for Memory.*
[136] Antonio Damasio, *The Feeling of What Happens.*
[137] Jeffrey M. Schwartz, *The Mind and the Brain.*
[138] Daniel L. Schacter, *Searching for Memory.*
[139] Ibid.

The basic circuits for emotion, learning and memory are different from the sensory and motor systems. The different sensory and motor systems are structurally and functionally independent regions that are interconnected at the highest levels of processing. This functional independence makes sense. For example, although perceptions are enriched when information from various modalities combined, you can nevertheless identify a ball by touch alone or a dog by the sound of a bark. In contrast circuits for emotions, learning and memory are highly integrated from the start. This reflects the fact that emotions depend on the concurrent analysis of diverse sensory information and actions, and therefore are highly integrated behaviors.

Just as drugs can affect what we remember, neuropeptides can act as ligands to shape our memories as we are forming them.[140] The neuropeptides are an integral part of an emotion, and in this way shape memories, which later can be activated by the same emotion. In other words, the presence of the specific neuropeptides is a part of the memory. A memory triggers an emotion. In this way, the neurons that become activated by a friend's face, remain excited as long as the face is anywhere in the visual field, regardless of its size, position, orientation, scale or facial expression. This concept is also particularly helpful to understand the phenomenon known as dissociated states of learning and state-dependent recall. The hippocampus, which is instrumental in learning and remembering, is a nodal point for neuropeptides receptors, containing virtually all of them. The neuropeptides acting as internal ligands will help establish echoes and handshakes to assist in later recall.

Each emotional state generates various neuropeptides ligands, which are part of the mechanism that activates a particular neural circuit.

Two key subcortical structures, the hippocampal formation and the amygdala, form distinct neural circuits that mediate the two major limbic system functions: learning and memory, and emotions.

The hippocampal formation and amygdala receive their major inputs from the limbic association area (area 10, 11, 32, 25, 24, 23, 31, 29, 30, 34, 35, 36 and 38). These cortical areas receive highly processed information from various cortical association areas and higher order sensory areas.[141]

Studying patterns of spared and impaired functions that are the result of specific brain damage have been used to infer the structure of the brain. We infer the functional and neural separability of a circuit assumed as necessary for the performance of a task if it can be damaged independently of other processes.

This logic can be extended to differences in performance for types of stimuli. For example, the selective deficit (inability) to recognize faces may be used to infer the existence of special circuits to process faces. However, this observation does not unequivocally support the inference of a distinct circuit for processing faces. It could be that faces differ from other objects not in terms of a processing circuit but in the levels of processing complexity, and probably a combination of both. There are many areas that have been used to infer distinct processing mechanisms. The dissociation of processing words versus objects indicates the existence of two distinct circuits, one related to hearing and the other to the visual.

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[140] Candace Pert, *Molecules of Emotion*, 1997.
[141] John. H Martin, *Neuroanatomy.*

The general idea that memories are built from fragments of experience can help understand key aspects of the rememberer's recollective experience, as well as memory distortions and other effects of implicit memory.[142] What we believe about ourselves is largely determined by what we remember about our pasts.

Schacter tells the story of a man who had suffered a stroke that damaged the left thalamus could not move his right arm and had difficulty speaking. Most frighteningly he had no specific memories of his past and was uncertain about his identity. Weeks later he could still not recognize his own paintings; he could not recall the subject of the book that he had been writing. Though he could recognize and name his wife and children, he couldn't remember anything about them. He was shown photographs of himself at art exhibitions, but professed no memory for any of it. The city he lived in seemed entirely unfamiliar. He could not recall any specific events from his life. He was suffering from retrograde amnesia, in which people have problems remembering experiences that occurred prior to the stroke, head injury, or some other physiological or psychological trauma. He also had poor memory for ongoing, day-to-day experiences, anterograde amnesia. As his amnesia continued for months, his sense of well being evaporated. He felt depressed, hopeless about his amnesia to the point that he could find no inspiration to paint again, because as he said, "he had no more self to express."

About a year later, he was undergoing a procedure to implant a pacemaker. As he was lying quietly on the operating table, he felt some discomfort as the surgeon prepared his chest for the pacemaker. Then in a stunning instant, he clearly remembered that he had experienced a virtually identical situation some twenty-five years earlier when he had undergone another operation. Soon his head was filled with memories of his past life. His memories, at first chaotic, soon rearranged themselves into a sensible chronology. As he sorted through all this and made sense of it, he eventually came to feel like the self that had existed before the stroke. It is extraordinary for someone to lose his entire personal past and then recover it all in an instant. Not all of the patient's memory problems evaporated – he continued to have great difficulty remembering ongoing events – but he had his past back, and with it a sense of self.[143] And with a sense of self, his depression lifted.

Storage-Retrieval: A Contextual and Emotional Filing System

An encoding process is a procedure for transforming something we see, hear, think, or feel into a memory. Encoding involves paying attention to ongoing events and has a major impact on subsequent memories of them. How things were encoded will determine how they are later recalled. The echoes and tags generated by a memory in the cortex will be matched to future stimuli and accordingly will trigger a recall. Important or novel events are remembered better than routine or common occurrences.[144] However, events that have many relations and thus establish many handshakes are more easily remembered than events that have very few other associations.

Research has shown that short-term memories last for only seconds. These temporary records are called working memory. This specialized system is not localized. It holds small amounts of information for a brief time that allows you to do something in

[142] Daniel L. Schacter, *Searching For Memory.*
[143] Ibid.
[144] Ibid.

the immediate future, like dialing a phone number. If you are distracted (not paying attention) for even a moment, you will need to consult the phone book again. And you will probably not be able to remember this number in a few moments or ever again.[145] There are momentary, short-lasting handshakes established between different areas of the cortex as attention focuses on these bits of information to allow us to act upon them. The triple cortico-thalamic and thalamico-cortical projections to area 40, together with adjacent area 39 in the parietal lobes, with their rich connections to visual areas 18 and 19 and auditory integration areas 22 and 42,[146] indicate that area 40 is instrumental for attention and coordinating short-term memories.

There is one particular circuit that could conceivably be involved in very short-term memory. This is the circuit from the thalamus to the type of pyramidal neuron in cortical layer VI, which sends signals back to the same part of the thalamus. Both these thalamic and cortical neurons have very few axon collaterals that spread sideways, so they probably interact rather little with their neighbors.[147] At the very least, we can clearly see the loop associated with echoes to the thalamus and the mirroring of signals to the cortex. This activated loop is transient and could represent the short-term memory or short-term relay of sensory signals.

Memories are stored in a form that captures relationships, not the details of the moment. What makes a face recognizable are its relative dimensions, relative colors, and relative proportions. Spatial intervals between features define a face just as pitch intervals between the notes of a song define a melody. When the cortex sees, feels, or hears something, it takes the detailed specific input and recalls the stable representation. The changing signals are compared to an invariant form that is stored in memory.[148] So regardless of the changes in orientation, lighting conditions or point of view, my wife's face remains my wife's face. This trick is performed by the thalamus matching echoes to incoming signals, and automatically triggering an emotional response. Once the face is identified, those neurons remain active. The chemistry of the emotion aids in stabilizing the memory.

Long-term memories depend on a different network of brain structures than working memory. People with damage to the inner part of the temporal lobes in the center of the brain have no difficulty retaining a string of digits for several seconds, yet have great difficulty forming and remembering enduring memories.[149]

Other people with damage to a specific part of the parietal lobe (parts of area 39 and 22) on the cortical surface can form long-term memories, but cannot hold and repeat a string of digits. They lack a specific part of working memory, known as the phonological loop (connections to the auditory integration centers known as area 22) that most of us rely on when we need to hold a small amount of linguistic information for several seconds. This phonological loop, established momentarily by handshakes, enables us to remember (pay attention) to a stimulus for a short time.

To establish a durable memory, incoming information must be encoded much more thoroughly or deeply by associating it meaningfully with knowledge that already

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[145] Ibid.
[146] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.
[147] T. Tombol (1984) *Layer VI cells.* In: A. Peters and E.G. Jones, *Cerebral Cortex*, vol 1.
[148] Jeff Hawkins, *On Intelligence.*
[149] Daniel L. Schacter, *Searching for Memory*.

exists in memory. In other words, extensive handshakes must be established between many of the characteristics of an object or event. Attention to shared characteristics with previous memories will allow a quicker and more extensive series of handshakes to be established, and facilitates tying into the previous existing sets of handshakes. Mirroring incoming stimulus according to echoes that are similar will activate these. It is a highly efficient system to add memories and tie them into the old ones.

When we engage in deep, elaborative encoding of an event, we are more likely to remember that event well; when we engage in shallow, superficial encoding, we will later remember that incident less well. Deep encoding produces more handshakes and more areas will send echoes than superficial encoding, and in this way the chances of finding a match are increased, and retrieval is more likely.

In our everyday lives, memory is a natural, automatic byproduct of the manner in which we think about an unfolding episode. If we want to improve our chances of remembering an incident or learning a new fact, we need to make sure that we carry out elaborative encoding by reflecting on the information and relating it to other things we already know.

What we already know shapes what we select and encode; things that are meaningful to us spontaneously elicit the kind of elaborations that promote later recall. Our memory systems are built so we are likely to remember what is most important to us.[150] What elicits emotions is important. Think of having gone to the last family reunion where one hundred relatives showed up. You can probably name the one hundred people from memory because of all the deep associations to each one of your relatives: uncles, cousins, brothers, spouses, and their children. However, if you went to a reunion with a hundred strangers and you were introduced to all of them, you most probably would have difficulty naming even a few of the people that you met with any accuracy.

A core cognitive act, like visual imagery mnemonics – creating an image and linking it to a mental location – is a form of deep elaborative encoding. As an example, chess masters exhibit phenomenal memory for the locations of chess pieces on a board. A chess master after just five-second exposures to a board from an actual game could remember the locations of nearly all the pieces. However, when the masters were shown a board of randomly arranged pieces that did not represent a meaningful game situation, they could remember no more than any novice. Studies of experts in various fields have established it takes about ten years to build the knowledge base necessary for the highly refined, powerful and elaborate encoding that enables them to pick out key information efficiently and to imbue it with meaning by integrating it with pre-existing knowledge.

Expert knowledge requires the setting of vast memory banks that will quickly and quietly process a lot of stimuli. This knowledge will produce a set of related echoes in the cortex. Once these echoes are established they will automatically trigger subtle emotional responses to matching stimuli. These emotional responses will serve as a guide to behavior or to intuitive knowledge, what is called knowing with a sixth sense. Thus art experts “know” (by having a gut feeling) what is good art or even when they see a forgery. In this manner experts know the answer without knowing exactly why. First impressions and snap judgements are also a manifestation of the echo-triggers-emotion mechanism. The emotional component is what makes these experiences more salient.

[150] Ibid.

Thomas Hoving has talked to what he describes as fakebusters. They agree that how they get to the truth of a work of art is an extraordinarily imprecise process. Hoving describes their subjective description of the echoes triggering emotions; he says they feel, "a kind of mental rush, a flurry of visual facts flooding their mind." One described the experience as if his eyes and senses were a flock of hummingbirds popping in and out of dozens of way stations. Within minutes, sometimes seconds, he registered hosts of things that seem to call out, 'Watch out!'" The art historian Bernard Berenson, in a court case, referring to a fake, could only say that his stomach felt wrong, or he had a curious ringing in his ears, or momentarily got depressed. In another occasion, he felt woozy and off balance.[151]

A good artist has the ability, through his art, to activate many echoes (good and/or bad) and thus will create a feeling in the observer. The more echoes that are matched, the stronger the feeling, as more echoes trigger subtle emotions. Another way of looking at this is that an artist attempts to generate more matches in as many visual areas as possible with a painting or a sculpture than could be achieved with natural visual scenes.

Cognitive, imaginative, and decision-making processes all can proceed outside awareness. This shows how subtle or varied the emotional responses triggered by echoes can be. The same holds true when decisions have to be made under pressure and without complete information, as might be the case of experienced soldiers in the battlefield, or nurses, stockbrokers, firefighters, policemen or doctors in the ER. A set of particular stimuli that has been repeatedly encountered will set echoes in the cortex and will guide responses (triggering emotions according to past experience). These echoes become ghostly representations of ECS. This is part of the reason why first impressions of experts are different; the echoes stored in their cortex can "see" what most of us can't. This is not to imply that when people are performing outside their areas of passion and experience their reactions are wrong; they are merely shallower.

Transient synaptic changes have been discovered in the hippocampus. When an axonal spike arrives at a synapse, it alters it almost instantaneously, so that its synaptic strength is increased. A quick sequence of spikes produces a greater increase in synaptic strength. This increase then decays in complicated ways, with decay times ranging from fractions of a second to a minute or so. These time frames are similar to short-term or working memories. There is also evidence that transient synaptic changes occur in the cortex. These appear to be due mainly to alterations on the input side of a synapse (the presynaptic side). Since the changes are solely presynaptic, that is, they do not depend on what is happening on the postsynaptic side, they are unlikely to be Hebbian (strengthening of synapses for learning or memory).[152] Since the signals are coming from the cortex, these changes are probably due to the echoes, which in turn generated mirrors from the hippocampus to the cortex, and through the mirrors, strengthened the echoes themselves with a feedback loop.

When something unusual or highly distinctive occurs – like a loud jolting sound – the brain emits an especially large event-related potential, or ERPS, known as the P300. The P300 is a bump in the electrical waveform that occurs about one third of a second after a person is exposed to an external stimulus. As you might expect, a larger P300 tends to be associated with greater subsequent recall.

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[151] Malcolm Gladwell, *Blink.*

[152]For further review see: R.S. Zucker (1989). Short-term synaptic plasticity, *Ann Rev Neurosc 12:13-31.*

Encoding of novel events involves the hippocampus. The hippocampus is tucked away deep in the inner or medial parts of the temporal lobes. Research has shown that brain-injured patients with damage to the hippocampus can produce a severe loss of memory for recent experiences. The hippocampus is one of several anatomically related structures that play an important role in explicit remembering.[153]

In general, the cortex interprets stimuli by using memories, and matching echoes to stimuli. As the stimulus is passed up the hierarchical areas of the cortex, the handshakes activate expected patterns that in turn generate new echoes, which when matched, confirm the expectation by mirroring the signal to the area that generated the echo. However, if the lower levels cannot interpret something, the stimulus rises up the hierarchy until an area "knows" how to interpret the stimulus. When events (in other words, patterns) occur that aren't anticipated, the signals are relayed up the hierarchy until an area can make sense of them. If lower regions fail to predict expected patterns, this is considered an error and they pass the signal higher up. This is repeated until an area anticipates a pattern.[154] Ultimately, the hippocampus is activated in the presence of novel stimuli. The hippocampus lies at the highest level of the cortical hierarchy. The hippocampus stores the new memory, and slowly transfers it to the cortex for later recall.

The hippocampal response to a novel event is activated when stimuli and echoes from the cortex don't match. The hippocampus then alerts the thalamus, which automatically signal the frontal lobes (regions 9 and 10) and activates area 40 – we recognize this process as paying attention. Attention will produce a series of handshakes to many other regions in the cortex to find similarities with the present stimulus. In the absence of a match (then it must be novel), the hippocampus is activated to search for other similarities or alternate contexts, sending its own impulses hoping to find more echoes from the frontal lobe activation and start the encoding process. Once attention is on the stimulus, another network may come on line, involving the left frontal inferior lobe, which in turn makes a wealth of semantic associations (area 40 to 39) and knowledge available if needed. In this way the necessary associations between past experiences and the novel stimulus help encode in a manner that will increase the probability of being able to recall the new stimulus. As a consequence, novel events are much easier to remember than specific events that have been encountered many times repeatedly.

An engram is defined as transient or enduring changes in our brains that result from encoding an experience. The brain records an event by strengthening the connections (establishing handshakes) between groups of neurons that participate in encoding the experience. Handshakes will quickly activate all the relevant connections. In the future, when a new stimulus is matched to an echo signal of any of these differing regions, the whole network (engram) will be activated. A typical incident in our lives consists of numerous sights, sounds, actions, smells and words. Different areas of the brain analyze these varied aspects of an event. As a result, neurons in the different regions become more strongly connected to one another. This new pattern of connections

[153] Daniel L. Schacter, *Searching for Memory*.
[154] Jeff Hawkins, *On Intelligence.*

constitutes the brain's record of the event: the engram.[155] Jeff Hawkins would refer to this as invariant representations.[156]

As you read these words, there are thousands, maybe millions, of echoes and handshakes (parts of engrams in some form) in your brain. These patterns of connections have the potential to enter awareness, to contribute to explicit remembering when an echo signal is matched and activates the engram (memory); but as long as the echoes aren't matched, these engrams lie dormant, waiting for the right echo to be activated by the stimulus. Only a fraction of the original event need be present in order to trigger recall of the entire episode.

A similar, idea to the engram, but more complete, is proposed by W.J. Freeman of the Dept. of Molecular and Cell Biology at UC Berkeley. He proposes that the past combines with the present to interpret the sensory signals. While the raw sensory data, after being received in the cortex, are deleted – attenuated by spatial filtering, the sensory cortices broadcast spatial patterns (send handshakes). The signals overlap in the medial temporal lobe (area 21) combining to form multi-sensory percepts. The handshakes are used to interpret the stimulus according to stored memories as the extrapersonal spatial information of the signals is added by passage through the hippocampus and thus is integrated into recent memory.[157] At this point the signals are available to awareness.

Each handshake pattern resembles a black and white picture, in having a common carrier wave (like light) that is modulated in amplitude (light and dark). Each pattern holds briefly and dissolves, making way for the next pattern. Neuron populations create each pattern as a "wave packet," resembling the transformation of a gas into a liquid, action potentials, like water molecules in steam, condensing into scintillating disks in the cortex about the size of a toenail.[158]

According to chaos theory, stabilization of reverberating circuits allows for the organization of a network that can amplify minor fluctuations over cycles of iteration and influence a system's trajectory. Even though this reexcitational activity pushes the system into a different state, it also facilitates the creation of a path (memory) trace (engram), which is part of an attractor. Attractors, as the name implies, are part of the properties of a system that under certain conditions, inevitably "attracts" the system towards that state. If the end state is always slightly different, it is called a strange attractor. The attractor is a pattern toward which all nearby patterns converge. Attractors might be thought of as either memories or as concepts held by neural circuits. From this perspective, once a part of the network is activated it tends towards the attractor (e.g., it activates the engram).

Another way of thinking about memories could be modeled after a hologram. A hologram, in a very simplified way, is produced by shining a laser beam on an object. The beam is reflected, diffracted and scattered by the object and then passes through a holographic plate. Simultaneously part of the laser beam is split off as a reference and is reflected at a specific angle by a mirror onto the holographic plate. The image on the plate bears no resemblance to the object photographed. The plate, however, contains a detailed record of all the phase and amplitude (the frequency and the height of the crests and troughs) information present in the beam that was reflected from the object. By

[155] Ibid.
[156] Jeff Hawkins, *On Intelligence.*
[157] Walter Freeman, *Neurodynamic Models of the Brain in Psychiatry.*
[158] Ibid.

reversing the procedure, shining a laser beam of the same frequency at the correct angle, the interference fringes act as a diffraction grating, bending or diffracting the light to reverse the original conditions of the laser that created the hologram.

One interesting feature of a hologram is that if you cut the plate in half, the intensity of the image is cut in half, but the whole image is still represented. If you further cut it, the image fades more the more you cut it. The curious part is that a small piece of the holographic plate retains the information of the whole, but it will yield a washed out image; the smaller the fraction of the holographic plate the more washed out. Another interesting thing is that the same plate can be used to store many different images, by either changing the frequency of the laser beam, or changing the angle at which you split the original laser.

The brain's storage systems can be modeled on the hologram. For example, the neurons' different firing rates could represent frequencies, and a different number of connections could represent angles. This type of modeling could be very powerful. It would be a model that could store a lot of information in a very small volume, and could "tag" information using combinations of frequency and angle, as well as retrieving related memories or information because of similarities in frequencies or angles. This model would easily permit storage of an almost infinite amount of information in a small mass.

An elegant, potential retrieval system could be modeled using these different angles and frequencies. It could neatly explain why memories can fade over time (the hologram is smaller) or why a particular memory brings up a whole series of associated memories or ideas (a similar angle or frequency). This model, however, would stand as a mathematical substitute for the real neuronal networking, and would only serve as a metaphor of how vibrations (firing rates) and angles (connections) can create memories of past events. It doesn't even begin to tackle the problem of attention and awareness. It would just explain a mathematically possible method of storing information. Similarly, just because the computer can retrieve information with an instruction, doesn't mean the computer is in any way aware of what the information means.

Memories have a contextual as well as an emotional component. The context and the emotion serve to establish specific handshakes that interconnect all the various elements of an episode. The memory becomes easily accessible in the future under the presence of the same emotion because the specific chemistry generated by the emotion was present during the storage of the memory, and is necessary to recreate the memory. Likewise, when sensory signals detect similarities in context in the environment, handshakes relating to context are activated, and it becomes more probable that the memories relating to that context will be activated. Unconscious memories in the Freudian sense do not exist. Memories are unconscious only in the sense that they are inaccessible for various reasons: wrong chemistry (emotion), not the right context (wrong handshakes), lost handshakes (not a very important memory, displaced by other more significant memories), and even physical trauma (an area of the brain is damaged).

Most likely, different strategies encode an event; subsequently, a different match between the stimulus and the echoes is needed to retrieve the event. When people drink alcohol or smoke marijuana during an encoding phase, they later have difficulty remembering – but if they have similar doses of alcohol or marijuana, they can recall the past event easier. Known as state-dependent retrieval, this process has been observed

across a wide range of drugs, dosages, and experimental materials.[159] Inducing the same intoxicated states helps to more readily match stimulus to echoes revealing an improved match between encoding and retrieving.

When an echo is matched, the stimulus is mirrored to the cortex and a cascade of handshakes is sent out. The cortex uses known sequences to anticipate what comes next and to resolve ambiguity. Individual words often cannot be understood out of context, yet when an ambiguous word is heard in a sentence, the meaning is understood.

The brain ultimately engages in an act of "construction" during the retrieval process. Posterior regions of the cortex (area 37, auditory-visual integration) that are concerned with perceptual analysis hold on to fragments of sensory experience – bits and pieces of sights and sounds. Various other regions of the cortex contain tags that bind sensory fragments to one another and to preexisting knowledge, thereby constituting complex records of past encodings. A memory is triggered when an echo and its tags simultaneously link sensory fragments that were part of an episode. This retrieved memory is a temporary constellation of activity in several distinct regions – the voices, the images, the sensations, and the feelings – a reconstruction with many contributors.

Through PET scans, we have found explicit retrieval of memories activates the hippocampus.[160] We have mentioned the hippocampus plays a role in encoding novel experiences. This suggests that coding of a novel experience and explicit recall have a similar architecture.

Attention initiates recall by sending handshakes with tags to many areas of the cortex. When the handshakes activate the frontal lobes (particularly the right lobe) during explicit retrieval, an increased blood flow reflects the mental effort involved in searching memory. This search for handshakes and tags that could be a close match to the required retrieval quest is slow and methodical. These handshakes activate more potentially related echoes that will in turn be projected to the hippocampus. The hippocampus with its ability to activate many neurons electrically at the same time will send out the appropriate signals to many areas simultaneously, and in this way increase the likelihood that a match will be found and retrieved. This process is known as strategic retrieval.

When the hippocampus and the related medial temporal lobe structures (area 40 and 22) are probing for handshakes and tags that might be related (without the aid of the right frontal lobe), they are searching for associations (similarities in the echoes or tags) between the stimulus and stored memories. This process is called associative retrieval. The associations can be contextual.

Without the aid of the frontal system (area 9 and 10), the medial temporal system must wait for the right stimulus to make contact with the engram (matching stimulus with echo). The medial temporal region (area 40) works cooperatively with regions toward the rear of the brain (area 39) where engrams are stored, including areas in the parietal (somatosensory associative area 7) and occipital cortices (visual area 19 and 18), forming distributed networks that allow us to encode and recall our recent experiences.

Damage to the medial temporal system leads to severe memory loss of recent experiences, whereas frontal system damage typically does not. When the automatic retrieval system is dysfunctional, the signals sent to the strategic system are fruitless; as a

[159] Daniel L. Schacter, *Searching for Memory*.
[160] Ibid.

result it is difficult to remember recent events. However, if the strategic retrieval system is impaired and the automatic retrieval process is intact, it should be possible to remember reasonably well when the right stimulus matches an echo.

Even though specific areas of the cortex learn to represent familiar objects, through associative handshakes, these areas can modify its classifications. New classifications are created to produce better and more often expected patterns that are matched to sensory signals. The feedback and forward handshakes are constantly interacting, changing all the time and are modified thus by experience.

For the rememberer, the engram (the stored fragments of an episode) and the memory (the subjective experience of recollecting the past event) are not the same thing. The stored fragments contribute to the experience of remembering, but they are only a part of it. Another important part is the matching between stimulus and echoes, which is generally referred to as the cue. The match (cue) activates the engram, which produces a new, emergent entity – the recollective experience – that differs from its constituents.

When we encode an experience, connections between active neurons become stronger, and this pattern of brain activity becomes the engram.[161] Later, as we try to remember the experience, a retrieval cue (stimulus matched to an echo) will induce another pattern of activity in the brain. If this pattern is similar enough to a previously encoded pattern, remembering will occur. When we remember, we complete a pattern with the best match available in memory.

Memories are an emergent property of the cue and the engram. The question becomes, how do we convert the fragmentary remains of experience into an autobiographical narrative that endures over time and constitutes the stories of our lives?

The rate of forgetting is relatively rapid at first and then slows down with the passage of time. However, more recent time periods yield more memories and more distant time periods produce fewer memories. As time passes, we encode and store new experiences that start to interfere with our ability to recall previous ones.[162] As more time elapses the engram becomes more "blurry" (some of the handshakes are lost), the range of cues (matching stimulus and echoes) that elicit a specific episode narrows. This means that when we suddenly and unexpectedly remember a forgotten memory, it may be because we have luckily stumbled upon a retrieval cue that matches perfectly with a faded or blurry engram.

Weakening and blurring engrams are an unpleasant reality of memory. It can be frustrating, even disturbing, to realize that past experiences are constantly slipping away from us, some rapidly and others imperceptibly. Forgetting, though often frustrating, is an adaptive feature of our memories. It is like rats chewing away at our papers in our filing cabinets. Luckily, we don't need to remember everything that has ever happened to us; engrams that are never used are probably best forgotten. We are better off forgetting trivial experiences than clogging our brains with each and every ongoing event, just in case we might want to remember one of these incidents some time in the future. We do need to form an accurate picture of the general features of our world, and we are reasonably adept at doing so.

Events are composed of multiple things, like a scene is composed of multiple objects. The memories that compose an event are nested hierarchically, the same as the

[161] Ibid
[162] Ibid.

objects that make up a scene. The memory of your house does not exist in one area of the cortex; it is stored hierarchically reflecting the hierarchical structure of the home. Large-scale relationships are stored at the top of the hierarchy and small-scale relationships are stored towards the bottom. Higher regions keep track of the big picture while lower areas deal with fast-changing, small details.[163]

Long-term memory involves a process known as protein synthesis and appears to be accompanied by the growth of new synapses. On a cellular level the switch from short term to long term might be a switch from a process-based memory to a structure-based memory.[164]

Mounting evidence also points toward a kind of consolidation that operates over time periods of months, years, and even decades. That is, some engrams appear to become more resistant to disruption by brain injury as the years pass. Patients with memory disorders from damage to structures deep within the temporal lobes provide evidence for this kind of consolidation. These amnesic patients have trouble remembering everyday experiences that take place after the onset of the brain damage (anterograde amnesia). Many of them also have problems remembering facts and events from periods prior to the brain damage (retrograde amnesia). In some cases patients have great difficulty remembering experiences from relatively recent time periods and less difficulty, sometimes none at all, remembering experiences from the distant past. People with damage to structures in the inner parts of the temporal lobes, including the hippocampus are better able to remember experiences from the distant past than from the recent past.

Other amnesic problems are associated with other problems. Lengthy alcoholism sometimes results in thiamine deficiencies that wreak havoc with a part of the brain known as the diencephalon, which is closely connected with the medial temporal lobe; these thiamine deficiencies produce retrograde amnesia. If memories consolidate over time, and the medial temporal region plays an important role in the consolidation process, then a medial temporal lesion should have relatively little effect when it is made long after initial learning and a much more drastic effect when it is made soon after learning.[165]

Summarizing, it takes sometime after initial encoding for a memory to become fully established in the brain. At the level of brain systems, the hippocampus and related structures in the medial temporal region probably play a role in memory consolidation, though only for a limited time after the event occurs. Long-term storage of memories appears to occur in cortical networks outside the medial temporal region, with different cortical networks representing different kinds of information. For instance, storage of visual memories depends on networks in the occipital lobes, which are essential for visual processing. Patients with lesions to a structure at the junction of the occipital and temporal lobes, known as the fusiform gyrus, have great difficulty recognizing faces, and may also have problems recognizing other kinds of visual objects.[166]

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[163] Jeff Hawkins, *On Intelligence.*
[164] Daniel L. Schacter, *Searching for Memory*.
[165]Ibid.
[166] Daniel L. Schacter, *Searching for Memory*.

Learning and Filing: The Hippocampus

The hippocampus lies laterally and slightly below the caudate nucleus and the putamen and runs closely parallel to the tail of the caudate nucleus. It maintains rich afferent and efferent connections with the cortex and the thalamus.

The hippocampal formation is a primitive form of allocortex, termed the archicortex, with three principal cell layers: the molecular, the pyramidal (or granule) and polymorphic. (The other type of allocortex is paleocortex, which is primarily olfactory cortex.) The hippocampal formation is divided into the dentate gyrus, hippocampus and subiculum. Each division has three principal layers. The three layers of the hippocampus and subiculum are analogous to those of the dentate gyrus, except that the pyramidal layer of the hippocampus and subiculum replaces the granule layer of the dentate gyrus. The pyramidal neurons are the projection neurons of the hippocampus and subiculum. The granule cells' bodies are in the second layer of the dentate gyrus and project to other neurons of the hippocampal formation. The dendrites of granule cells receive signals from the molecular layer. The polymorphic layer contains interneurons.[167]

Under particular conditions, postsynaptic activity can alter presynaptic impulses. Acetylcholine and glutamate act synergistically via their actions at nicotinic ACh receptors (nAChRs) and NMDA receptors respectively. A pulsed ejection of nicotine onto apical dendrites selectively enhances glutamatergic excitatory postsynaptic potentials (EPSPs) mediated by NMDA receptors. This suggests that nicotine acts at rapidly desensitizing presynaptic *alfa*7nAChRs to increase glutamate release onto postsynaptic NMDA receptors. This finding, however, suggests that the synergistic actions mediated by *alfa7*nAChRs and NMDA receptors may contribute to experience-dependent synaptic plasticity in the sensory cortex only during early postnatal life.[168]

The perforant-path forms a monosynaptic excitatory connection between the cells of layer II of the entorhinal cortex and the pyramidal cells in hippocampal area CA3. The distal location of these synapses suggests that somatically recorded perforant-path excitatory postsynaptic potentials (EPSPs) may be influenced by activation of voltage dependent channels in CA3 cells. The perforant-path EPSPs are reduced by roughly twenty-five percent by blockade of postsynaptic low-voltage-activated calcium and sodium channels. This indicates that in CA3 pyramidal cells both of these channels contribute to the amplification of perforant-path EPSPs. Stimulation of perforant-path synapses results in strong, rapid activation of CA3 pyramidal cells.[169] Here is an example of how the echoes of the entorhinal cortex can be altered postynaptically, and very subtly alter the signaling and functioning mode of the cortex.

The hippocampus and the amygdala form distinct neural circuits with mutual afferent and efferent connections that mediate two major functions, learning/memory and memory/emotions, respectively. They receive major inputs from the limbic association

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[167] John H. Martin, *Neuroanatomy.*

[168] Riekkinen M. & Riekkinen P. Jr., *Nicotine Selectively Enhances NMDA Receptor-Mediated Synaptic Transmission During Postnatal Development in Sensory Neocortex,* The Journal of Neuroscience, Oct 15, 1998, 18(20): 8485-8495.

[169] Nathaniel N. Urban, Darrel A. Henze, and German Barrionuevo, *Department of Neuroscience and Center for the Neural Basis of Cognition, University of Pittsburgh, Amplification of Perforant-Path EPSPs in CA3 Pyramidal Cells by LVA Calcium and Sodium Channels.*

area located primarily in the cingulate girus. The hippocampal circuits receive extensive information from the cortical association sensory areas. This architecture involves the hippocampus as a major processor of emotional context and association to other memories.

To illustrate the complexity of the inter-connections and the activity of just one neurotransmitter, glutamate, in relation to the hippocampus, (and not including the NAMDA receptors) I list the following: AMPA glutamate receptors are found primarily in CA1 of the hippocampus, the molecular layer of the cortex and the lateral septal nucleus. Kainate glutamate receptors are found in CA3 of the hippocampus, in layers V and VI of the cortex, the reticular nucleus of the thalamus and the granule cell layer of the thalamus. Metabotropic (mGluR1) glutamate receptors are found in the hippocampal dentate gyrus granule cells, CA4 cells, CA2-CA3 pyramidal cells, and neurons of the thalamus, lateral septal nucleus and the mitral and tufted cells of the olfactory bulb; mGluR5 receptors are found in the dentate gyrus, the cerebral cortex, CA1-CA4, the subiculum, the lateral septal nucleus, the striatum, the nucleus accumbens and the anterior olfactory nucleus; mGluR2 receptors are found on dentate gyrus, the pyramidal cells of the entorhinal cortex and the mitral cells of the accessory olfactory bulb; mGluR3 receptors are found on the dentate gyrus, the cerebral cortex, the thalamic reticular nucleus, the caudate putamen, the glial cells in the corpus callosum, the anterior commissure and throughout the brain; mGglur4 receptors are found in the thalamus, the lateral septum the pontine nucleus and the entorhinal cortex; mGlur8 receptors are found in the central nervous system-retina, the hippocampus, the hindbrain and the cerebral cortex and the olfactory bulb.[170]

The hippocampus works closely with the adjoining entorhinal cortex, so much so that the two are almost inseparable. These structures receive complex sensory and cognitive information from the limbic association cortex. The entorhinal cortex is prominently involved in processing olfactory signals.[171] It receives pooled information from the visual and auditory systems as well. The glutamate receptors in common with the olfactory bulb seem to suggest an associated evolutionary path between spatial orientation and smell, which makes sense to help find opportunities that emit odors (i.e., food and sex) or avoid threats (i.e., predators that emit odors).

The hippocampus receives inputs from a cascade of polymodal association cortices. The perforant-path projects principally from the entorhinal cortex's layers II (medial) and III (lateral) with minor contributions from layers IV (medial) and V (lateral) to the hippocampal formation. Projections from layers II and IV project to the granule cells of the dentate gyrus (DG) and pyramidal cells of the CA3 region, while those from layer III and V project to the pyramidal cells of the CA1 and the subiculum. The perforant path is divided into medial and lateral pathways, depending on whether the pathway arises in the medial or lateral entorhinal cortex. CA3 neurons receive input from the DG and project to CA1 pyramidal cells via the Schaefer collateral pathway, as well as to CA1 cells contralaterally through the associational commissural pathway. They skip the CA2 region. CA1 cells project to the subiculum, which in turn sends a feedback

[170] LabVelocity, *Excitatory AA (Glutamate)Receptors,* 2001.
[171] John H. Martin, *Neuroanatomy.*

projection (the main hippocampal output) to layer V-VI of the medial and lateral entorhinal cortex.[172]

Pyramidal cells of the hippocampus and subiculum have extrinsic connections, sending their axons to cortical and subcortical targets. The hippocampus and the subiculum have extensive back projections to the entorhinal cortex, which projects widely to other cortical regions. The principal subcortical targets are the mammillary bodies, which receive projections from pyramidal cells of the subiculum and the lateral septal nucleus. The lateral septal nucleus also receives a projection from the hippocampus. These axons run through the fornix. Both sides of the hippocampal formation are interconnected through commissural neurons whose axons course in the ventral portion of the fornix.[173]

The perforant pathway seems to be sending echoes from layers II-III to the hippocampal formation. The subiculum in turn mirrors back extensive signals to layers V-VI of the entorhinal cortex, which project to the cortex, as well as an intralaminar projection back to layers I-III,[174] to reinforce and establish echoes and handshakes to store events and memories, and through their interrelations construct a context, along with the projections from the pyramidal cells of the hippocampus and the subiculum to the cortex. The double signaling strengthens the echoes and handshakes in the cortex and makes memories durable and easier to recall later. Here we see, in detail, how the handshake signals are transmitted from layers V-VI to layers I and III. If the echoes are disrupted for whatever reason, the hippocampus can't mirror signals to the cortical areas through these clusters. As an end result, the handshake signals are disrupted, and recall of memories becomes impossible.

The projections from the subiculum to the mammillary bodies and the lateral septal nucleus send information about the context in relation to the present emotion. These signals help evaluate the positive or negative aspects of the present unfolding events. Because of the various feedback connections, this evaluation depends on previous (experience) stored echoes and handshakes and the associated emotions.

The entorhinal cortex has afferent and efferent connections with the parahippocampal, the perirhinal and the association cortico. Damage to a specific cluster of cortical structures in the medial temporal lobe (the entorhinal, perirhinal, and parahippocampal cortices) that are adjacent to, and a major source of input for, the hippocampus and amygdala produce severe deficits of recognition memory.[175]

The principal afferent connections of the hippocampus are from the parahippocampal gyrus, comprised of the parahippocampal, perirhinal and entorhinal cortices. The parahippocampal gyrus has afferent connections from the temporal association cortex (areas 41, 42 and 22), and afferent and efferent connections with the lateral cortex (superior temporal gyrus (areas 22 and 38), middle (area 21) and inferior temporal gyri (area 20), posterior parietal cortex (area 40) and the insular cortex). The medial prefrontal and orbital gyri have afferent connections to the cingulate gyrus and through the retrosplenial cortex to the parahippocampal gyrus. The parahippocampal gyrus has direct afferent connections to prefrontal and orbitofrontal cortical areas.

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[172] *http:/www.bris.ac.uk/synaptic/images/figures/pathways/hippocampus.gif*
[173] John H. Martin, *Neuroanatomy.*
[174] *http:/www.bris.ac.uk/synaptic/images/figures/pathways/hippocampus.gif*
[175]Daniel L. Schacter, *Searching for Memory.*

Through the divergence of connections emerging from the entorhinal cortex to cortical association areas, the hippocampal formation can influence virtually all association areas of the temporal, parietal and frontal lobes, as well as some higher sensory areas, after as few as three synapses.

There are two ways the hippocampus can alter the signaling of the entire cortex. First, the hippocampus has fused neurons that can act, electrically speaking, as one. These fused neurons are GABAergic and because of their electrically joined gaps will fire together controlling many projection cells simultaneously, in this way affecting many areas of the cortex concurrently. Second, through the extensive connections of the perforant-path between cells of layer II of the entorhinal cortex and the pyramidal cells in hippocampal area CA3, it can postsynaptically change the types of echoes emanating from the cortex and adjust the entire brain.

The hippocampus receives simultaneously many signals from the thalamus and echoes from the cortex. The thalamus, in the absence of a match between incoming signals and echoes, automatically determines this is a new and novel event, and it signals the hippocampus. With this ingenious architecture, the hippocampus, through the sodium and calcium channels, alters the echoes postsynaptically and thus finds looser matches from the echoes of the cortex and uses these to determine how to encode the novel event. The closer (not exact) matches will produce more related echoes that increase the chance of recalling the event in the future. In this way the hippocampus aids in storing and retrieving experiences.

The synchronized firing of the hippocampus establishes handshakes of the event in the cortex related to their echoes. The related echoes thus establish a contextual setting for the event with their related memories. In the future, when an event has sufficient similarities to past contexts, the related memories are quickly activated. Emotions, through signals from the amygdala, also affect the behavior of the hippocampus. When emotions are triggered, their particular brain chemistries single out events and their associated memories are easier to store or recall.

It is known that neurogenesis occurs in the hippocampus.[176] The exact role that this has on forming new memories is not clear yet. It has been suggested that the formation of new neurons is necessary for the plasticity required for learning.

The dentate gyrus in the hippocampus is special because it generates new neurons. In neural network models patterns are stored in a distributed fashion in the synaptic weights, and the traces of old patterns degrade, as new patterns are stored, a phenomenon known as catastrophic interference. The stability-plasticity dilemma arises from the fact that one can either choose a low learning rate to make stored patterns more stable, or a high learning rate to make the network more plastic, and enable it learn new patterns, but not both. New neurons would continuously be used for learning new patterns, as the old ones suffer from catastrophic interference.

It is commonly assumed that the hippocampus helps in resolving the stability-plasticity dilemma for the cortex. Accordingly, the hippocampus stores patterns quickly, and suffers to some extent of catastrophic interference, and then replays the stored patterns to the cortex where they are basically learned. The hippocampus has three stages: the dentate gyrus (DG), CA3 (corno ammonis), and CA1 (plus subiculum). CA3 is

[176] Henriette Van Pragg, Alejandro F. Schinder, Brian R. Christie, Nicolas Toni, Theo D. Palmer & Fred H. Gage, *Functional Neurogenesis in the Adult Hippocampus*, Nature, Feb. 2003.

assumed to be the actual storage while DG performs an encoding (mirroring and setting the echoes) and CA1 a decoding of the patterns (detecting the echoes from the cortex) to permit an efficient storage of patterns in CA3.

According to this model, the signals from the DG to CA3 indicate that learning occurs with neurogenesis.[177]

This model, however, doesn't consider the effect of the signals being relayed from the anterior thalamic nucleus via the cingulate gyrus to the hippocampus.

The hippocampus has connections to the amygdala and the entorhinal cortex. The entorhinal cortex has extensive input from the cingulate gyrus, the temporal lobe, the amygdala, the orbital cortex and the olfactory bulb. The entorhinal cortex has projections to the DG, CA3 and CA1. Information received at the DG is passed on to CA3 and from CA3 it is passed on to CA1. CA1 sends its output to the subiculum and back to the entorhinal cortex.[178]

Damage to the entorhinal cortex disables the entire medial temporal-diencephalic network. There is now considerable evidence that the major pathological signs of Alzheimer's disease are initially concentrated in the entorhinal cortex, as well as the hippocampus.[179]

In contrast, damage to other cortical regions impairs different kinds of knowledge. Patients with parietal damage forget once familiar layouts and have difficulty navigating routes they used to travel with ease. Parietal regions become active when people remember the location of objects. Long-term memory for the sound of a word depends on networks that involve part of the temporal lobes in the left cerebral hemisphere known as Wernicke's area (area 42). Damage to this area often produces inability to understand spoken language and people often speak a bewildering gibberish.[180]

The medial temporal region can be thought of as a critical zone for assembling explicit memories (area 21). Past episodes typically include many different kinds of information: visual, auditory, spatial, verbal and so forth. The medial temporal region sends echoes and tags and handshakes to locations of different kinds of information that are stored in separate cortical regions. The tags are needed to keep track of all the sights, sounds, emotions and thoughts that together comprise an episode, until the engram is established enough to produce its own echoes. The medial temporal region contains instructions that help assemble the puzzle (area 40 and 39); eventually the instructions are shifted to cortical regions that contain all the components of the puzzle.

Later on, we will establish the deep relationship between remembering and attention and the importance of cortical area 40 with its triple efferent and afferent pathways to the thalamus in these processes.

The adjacent amygdala has strong afferent and efferent connections with the hippocampus. The hippocampus's main output signals, aside from the perforant path, are through the fornix to the septal nucleus and the mammillary body. The mammillary body projects to the anterior thalamic nuclei, which relays signals to the cingulate gyrus[181]

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[177] Gerd Kempermann and Laurenz Wiskott, *Adult Neurogenesis in the Hippocampus*.
[178] Henriette Van Pragg, Alejandro F. Schinder, Brian R. Christie, Nicolas Toni, Theo D. Palmer & Fred H. Gage, *Functional Neurogenesis in the Adult Hippocampus*, Nature, Feb. 2003.
[179]Daniel L. Schacter, *The Search for Memory*.
[180]Ibid.
[181] John H. Martin, *Neuroanatomy*

(areas 23, 24, 29 and 32). The amygdala helps regulate the associational aspects of memory and emotions.

The cortex is arranged in a hierarchical manner, with lower areas interpreting smaller and smaller details of the environment. Going up the hierarchy, more and more complex memories are stored. At the top of the hierarchy we find the hippocampus. Yet, the hippocampus has strong connections with the structures deep in the brain. This architecture suggests that the hippocampus acts as a bridge, closing circuits between the newest, evolutionary speaking, and the oldest, between the cortex and the basal ganglia.

When the highest areas of the cortex cannot interpret a stimulus because it has never been stored, the hippocampus is activated to form a new memory. The new memory is not only composed all the sensory signals that together make it, but also by the internal state of the brain. Hence the connections to the basal ganglia and the cortex.

Dreaming: What We felt, Not What We Remember

Most brain neurons are at or near their maximum levels of activity while the subject is awake. However, when the subject is asleep, neurons display a wide range of behaviors. There is REM (rapid eye movement) and non-REM sleep, and the brain behaves differently in these two states.

During non-REM sleep most neurons in the brain stem reduce or stop firing, whereas most neurons in the cerebral cortex and adjacent forebrain regions reduce their activity by only a small amount. In this state, adjacent cortical neurons fire synchronously with a relatively low frequency rhythm. This synchronous electrical activity generates higher-voltage brain waves than waking does, yet consumes less energy when the brain idles this way. In contrast, during the awake state, neurons more or less go on about their individual business.[182] This synchronous activity helps strengthen the echoes and handshakes that were recently established, following the old principle of neurons that fire together, stay together. In this way, memories are made more durable.

During non-REM sleep a very small group of neurons (about 100,000) at the base of the forebrain is maximally active. These cells have been called sleep-on neurons and appear to be responsible for inducing sleep.

Brain activity during REM sleep resembles that of waking. Brain waves remain at low voltage because neurons are behaving individually. And most neurons in the forebrain and brain stem are quite active, signaling other nerve cells at rates as high – or higher than – rates seen in the waking state. The overall consumption of energy is the same as when awake. The greatest neuronal activity accompanies the familiar twitches and eye motion that give REM sleep its name. Cells located in the brain stem, called REM sleep-on cells become especially active during REM sleep, and in fact, appear to be responsible for generating this state.

Most movement during REM sleep is inhibited by two complementary biochemical actions involving neurotransmitters. The brain stops releasing neurotransmitters that would activate motoneurons, and it dispatches other neurotransmitters that actively shut down those motoneurons. The key neurotransmitters affected are serotonin, norepinephrine and histamine, all monoamines. Brain cells that

[182] Jerome M. Siegel, *Why We Sleep*, Scientific American, 2003.

produce these monoamines, continuously active in waking, stop discharging these neurotransmitters completely during REM sleep. The interruption of monoamine release during REM sleep may allow the receptor systems to "rest" and regain full sensitivity.[183]

However, the visual attentional mechanism that controls eye movements is not affected when we are in REM sleep and the eyes move rapidly, especially when we are dreaming. It is possible that the eye saccades are intimately involved in the process of seeing and are an active component of vision that focuses on small details of a bigger picture, aiding the construction of a scene.

REM sleep also affects brain systems that control the body's internal organs. Heart rate and breathing become irregular during REM sleep, just as they are during waking.[184]

It has been established that dreaming is another player in the consolidation of memories, especially during the rapid eye movement (REM) stage when we dream most frequently and intensely.[185] There is some dreaming during non-REM sleep, but the dreams are less vivid. Obviously, when dreaming, the visual system is activated to create all the visuals of the dream experience. Sounds, speech, and other sensations are integrated into the dream to establish different handshakes for the recent memories so that they can be *stored into longer-term memory in relation to emotional context.* Dreams have content of the last few days but the recent emotional context is referenced to our earliest and very most important emotions; dreaming is a cataloging process of recent important experiences (important, meaning producing an emotional response, otherwise they would not be important) indexed with previous similar emotions for quick recall when encountering an emotional competent stimulus. In the future, events that trigger emotions will activate all the relevant memories. In this elegant way, only the relevant (to an emotion) memories are stored and in the future will be activated and brought to bear on particular situations where an emotion was triggered and the context is similar to past experiences. Response will not be hindered or delayed by searching through all memories.

People who are sensory impaired reflect this deficit in their dreams if they have never experienced that sensory modality. People that became blind before 5 years of age do not have a visual component to their dreams as opposed to people that became blind later in life.[186] People's memories will be built around the sensory modalities through which they were initially experienced.

Helen Keller, blind and deaf since she was a baby, related in a letter, "My dreams have strangely changed during the past twelve years. Before and after my teacher [Anne Sullivan] first came to me, they were devoid of sound, of thought or emotion of any kind, except fear, and only came in the form of sensations. I would often dream that I ran into a still, dark room, and that, while I stood there, I felt something fall heavily without any noise, causing the floor to shake up and down violently…I dreamed of a wolf, which seemed to rush towards me and put his cruel teeth deep into my body! I could not speak (the fact was, I could only spell with my fingers), and I tried to scream; but no sound escaped from my lips"

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[183] Ibid.
[184] Jerome M. Siegel, *Why We Sleep*, Scientific American, November 2003.
[185] Gerd Kempermann and Laurentz Wiskott, *Adult Neurogenesis in the Hippocampus*.
[186] Richard Catlett Wilkerson, *Dreams of the Blind*, 1995.

Keller went on to say, "I do not think I have seen or heard more than once in my sleep. Then the sunlight flashed suddenly on my eyes, and I was so dazzled I could not think or distinguish anything. When I looked up some one spelled [with their fingers] hastily to me, 'Why, you are looking back upon your babyhood!'"

In Jastrow's major study of dreams of the blind (Jastrow was blind) in the early part of the twentieth century noticed, "The dreams of seeing and hearing probably reflect far more of the conceptual interpretation and imaginative inference than of true sensation; yet they are in part built up upon a sensory basis."[187]

After experiencing events that produce a strong emotional arousal (like 9/11), people's dreams are more emotionally intense.[188]

Not surprisingly activation patterns during REM sleep using PET scans show notable arousal of the extrastriate visual cortex, as well as a decreases in activation of the primary visual cortex. This seems to reflect the fact that secondary visual areas, without participation of the primary visual areas that process the visual sensory signals, generate the visuals of dreaming. Significantly, activation is also seen in limbic structures, most significantly in the anterior cingulate and the amygdala.[189] In dreaming, these structures are mimicking the chemical state representative of each emotion as needed in relation to the recent events that are being stored in long-term memory. These emotions become a part of the memory, and later the emotion will be enough to activate the memory.

Solms, whose work is at the interface of neurology and psychoanalysis, has presented data indicating that the control mechanism of dreaming is critically mediated by anterior limbic orbitofrontal structures.[190] These same regions are involved in evaluating the significance of emotional stimuli, as well as guiding free association activities. Normal activity in these brain circuits during sleep allows for the processing of information by symbolic representational mechanisms during dreaming, while failures in regulatory functioning caused by stressful[191] events causes a breakdown in dreaming, disturbed sleep, and nightmares.

A prominent feature of REM sleep is the presence of large PGO (pontine-geniculate-occipital spikes which originate in the brainstem pass through the LGN and then to the occipital lobes where they exert powerful cholinergic stimulation.[192] This cortical excitation by the PGO spikes allows the ongoing patterns of activity (memories) to rearrange into forms determined by the emotional and cognitive influences present during the event.

Dreaming transfers the recent (last couple of days) salient events, that is the ones with an emotional content, to long-term memory. In the process older, primarily, childhood memories interact with the recent events, because of their emotional commonality. The results are a rich, dynamic panoply of cognitive and emotional memories influencing the dream content in strange (attractors) ways.

Dreaming is a slow constructive, autobiographical process that stores the important, salient points of our lives to guide our responses; it helps us know who we are,

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[187] Ibid.
[188] Barbara Kantrowitz and Karen Springen, *What Dreams Are Made Of*, Newsweek, Aug. 9, 2004.
[189] Ibid.
[190] Allan Schore, *Affect Regulation and the Repair of the Self.*
[191] Ibid.
[192] Barbara Kantrowitz and Karen Springen, *What Dreams Are Made Of*, Newsweek, Aug. 9, 2004.

how we got here, where we are going and more importantly, how we are going to get there.

Roughly about one quarter of sleep time is devoted to REM sleep. One of the most active areas during REM sleep, not surprisingly, because of the role in emotions, is the limbic system and the anterior cingulate cortex. Mark Solms of the University of Cape Town reports that the parts of the brain that are most active during dreaming control emotion.

MAO inhibitors block REM sleep and selective serotonin reuptake inhibitors, another antidepressant, reduced REM sleep by a third to a half. However, the lack or reduction of REM sleep hasn't produced any detectable effects.[193] Some studies show that when we are deprived of REM sleep, we begin to have more vivid, REM-like dreams during non-REM sleep. When people who are sleep deprived, finally lie down, they experience extra-long REM cycles, which can lead to hypervivid dreams and even nightmares, which typically are more intense psychologically.[194]

The monoamines also play a role in rewiring the neurons in response to new experiences. Turning the monoamines off during REM sleep may be a way of preventing changes in brain connections that might otherwise be inadvertently created as a result of other neurons' intense activity during REM.[195] In this way, while dreaming, the emotional context and connections are strengthened and reinforced without affecting the memories themselves. It is important to note that the REM activity is a process to consolidate memories relative to emotional context, not to consolidate the memory itself. In this way learned results of previous similar emotional situations will activate all relevant thoughts and experiences.

Research in rats suggests that during sleep the hippocampus is "playing back" (making the same or similar connections and relays of) recent experiences to the cortex where it will eventually be stored. It seems likely that as we sleep, our brain is working hard to save the experiences that have most meaning (emotion-content) and that we will carry around for much of our lives. Experiences that receive little attention during waking probably receive fewer or no nocturnal playbacks (dreaming), paving the way for forgetting.[196]

What Do We Remember?

The brain also uses other tactics to store important information. There are three kinds of autobiographical knowledge arranged hierarchically. At the highest level we find lifetime periods: lengthy segments of our lives that are measured in years or decades, say living in Carmel, or when the kids were little. In the middle of the hierarchy we find general events: extended, composite episodes, which are measured in days, weeks or months such as playing soccer in college, vacationing at the Grand Canyon, or the first professional job you had. The bottom of the hierarchy would cover event-specific knowledge: individual episodes that are measured in seconds, minutes or hours, such as

[193] Ibid.
[194] Karen Springen, *Sweet, Elusive Sleep*, Newsweek, Aug. 9, 2004.
[195] Jerome M. Siegel, *Why We Sleep, Scientific American*, November, 2003.
[196]

the guy that knocked your teammate unconscious, the moment you first saw the Grand Canyon, or the day you got to work late.[197]

As the cortical centers mature, words and sentences are used to express increasingly complex ideas. As the frontal cortex expands and interconnects, memory improves. A sense of time slowly emerges with autobiographical memory beginning to connect places, events and the self in time. Events are combined with emotional value and organize the sense of self.[198]

General events appear to be the entry point to find handshakes to activate our autobiographical memories. General events may enjoy this privileged status because they simply have more handshakes that can activate the engram. When you repeatedly do something, like going to a specific class for a whole semester, it is easy to remember the course, but not the specifics of any one single class. The losses at the event-specific level are turned into gains at the general-event level. General events capture a good deal of the distinctive flavor of our pasts. They are readily accessible because they have been strengthened through repetition.

Lifetime periods help us to find general-event knowledge and event-specific knowledge; they provide the skeletal structure of our autobiographical memories. This leads to the prospect that there is no single representation or engram stored in memory that has a one-to-one relationship with the mental experience of recollecting one's past. Instead, such experiences are always constructed by combining bits of information from each of the three levels of autobiographical knowledge. Just as memories for individual events resemble jigsaw puzzles that are assembled from many pieces, so do the stories of our lives.

In 1993 some researchers described a sixty-seven-year-old patient who suffered a stroke in the thalamus. He had great difficulty remembering ongoing events. He was also unable to remember just about everything that had happened to him before the stroke – except for one period of his life. He insisted that he was on leave from the navy during World War II. He firmly believed that he was still in active duty and that it would soon be time for him to return to his ship. He remembered a few other things, but his life was dominated by the delusional conviction that he was living nearly a half century in the past. He could recall a few general events but hardly any event-specific knowledge.[199]

The thalamus is a key switching station that activates systems in the cortex of the brain. In this case, the frontal lobe's assistance in searching (sending handshakes) for a specific memory could not be activated to search for lifetime period knowledge (activating related echoes and tags), and through this to look for a specific event. The neural representation of the lifetime period "when I served in the navy" seems to have become continuously and irreversibly turned on. It was the only memory where echoes and tags were accessible, and as a consequence he is trapped in that time period of the 1940's. The damage to his thalamus prevented any activation of the frontal lobes to search for different tags. The hippocampus was locked into one context. Unable to remember any other lifetime periods, emotionally locked, he could not escape the persistent feeling that he needed to return soon to his ship.

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[197] Daniel L. Schacter, *Searching for Memory*.
[198] Louis Cozolino, *The Neuroscience of Psychotherapy*.
[199] Daniel L. Schacter, *Searching for Memory*.

When different components of autobiographical knowledge are not accessible, it becomes easier to see a great deal of structure and complexity beneath the surface of our normally "seamless" recollections of our pasts. What we experience as an autobiographical memory is constructed from knowledge of lifetime periods, general events, and specific episodes. These in turn are constructed from images, sounds, thoughts and feelings related to the event.[200]

In this way the encoding process can add information to memory that later results in a distorted recollection. For instance, verbally describing a face, a color, or even a taste of wine can impair subsequent recognition when an imprecise verbal description overrides a more nonverbal memory. Knowledge of what we expect to happen could become incorporated into a new memory, even when the expected event did not occur. Our memories can be distorted by the same pre-existing knowledge that usually aids our ability to acquire and retrieve new information.

As an example of memory distortion, pay careful attention to the following words: candy, sour, sugar, bitter, good, taste, tooth, nice, honey, soda, chocolate, heart, cake, eat, and pie. Turn away and write them down.

Now, without looking at the original list, consider if these three words were on your list: taste, point, sweet. Many people who studied this list confidently reported (and insisted they remembered vividly) that sweet was on the list – but it was not.[201] Presentation of so many associations to sweet can produce handshakes that elicit a whole category of sweet things and, later on, a false recognition of sweet might be elicited by the gist or meaning of the word list.

True recognition of the words on the list and false recognition of sweet requires accurate retention of the general meanings of words on the list, which in turn depend on the left hippocampus and other medial temporal lobe structures. PET scans have confirmed this. In contrast, areas in the temporal and parietal lobes that store information about the sound of a word were active when people recognized words on the list – but not when they falsely recognized nonpresented words such as sweet.[202] Because of similar echoes or tags, pre-existing knowledge, which often aids in the construction of elaborative encoding, can sometimes seep into and corrupt new memories. New memories are inevitably influenced by old memories, which make a distortion of past events a common occurrence.

The specific manner in which we encode an event determines what retrieval cues (stimulus matched to echoes and their tags) will later help us remember it. This has been termed the encoding specificity principle. Accurate recollection depends critically on our ability to recall precisely when and where an event occurred, a process referred to as source memory. Source memory is extremely fallible. Failure to remember correct sources of acquired information is responsible for various kinds of errors and distortions in eyewitness recollections and other aspects of everyday memory.

The reconstructive nature of memory for time is underscored by various illusions and distortions. One common distortion is known as a scale effect. Can you recall the time and date of your visit to the museum in 1995? You may remember correctly that you went in the evening, in June or summer, when it was actually in August. If there were a

[200] Ibid.
[201] Ibid.
[202] Ibid.

literal record of time in memory, it would be impossible to misremember the date by several months but still remember the exact time of day. The fact that such scale effects occur implies that people infer and reconstruct time on the basis of other kinds of retrieved information.

In some cases, damage to the hippocampus and other medial temporal lobe areas that are implicated in explicit memory, and also extensive damage to the frontal lobes, produces people that seem entirely normal in most respects – except for a total inability to remember their past experiences explicitly. These people, in some instances, can learn new facts and repeat them, but have no idea of how or where they learned them. This form of memory failure is known as source amnesia.

Patients whose damage is restricted to specific regions in the frontal lobes and who are not globally amnesic have great difficulty remembering source information. They also have problems remembering temporal information, such as which of two events came first. In some cases of frontal lobe damage, failures of source memory are accompanied by extensive and even bizarre confabulations – false recollections of events that did not occur and, in some instances, could not have occurred.

Associative retrieval is an involuntary form of remembering that is triggered automatically by an object or what somebody says. It is an automatic activation of handshakes triggered by matching a stimulus to a related echo. Strategic retrieval is more laborious and voluntary; the kind of retrieval you would undertake to remember what you did last Thursday six weeks ago.[203] When no easy match is found between stimulus and echoes, the signal is relayed to the frontal lobes and attention is focused as handshake signals are sent out searching for relevant information: Thursday, six, weeks, past, what, where. When some matches are found, the memory starts to be constructed.

When there is damage to the right frontal lobe, strategic retrieval is impaired and people tend to be stuck at the general-event level and fail to engage in the effortful search that is necessary to recall an event-specific knowledge.

In experiments with split-brain patients, whose left and right cerebral hemispheres have been surgically disconnected from each other (primarily to alleviate life threatening convulsions), researchers can present information separately to each hemisphere. The left hemisphere falsely recognizes novel words that are similar to the ones it has been shown recently. But the right hemisphere claims to remember only those words that match exactly the ones it was shown. The left hemisphere makes inferences and associations that render it susceptible to memory distortion, whereas the right hemisphere retains a more veridical representation.

There seem to be three different long-term memory systems: episodic memory, which is for recollecting specific incidents from our pasts; semantic memory, part of the vast network of associations and concepts that underlies the general knowledge of the world; and procedural memory, which allows us to learn skills and know how to do things.[204]

Schacter reports that a person sustained significant damage to his left temporal lobe and its connections to other regions of the left cerebral cortex, but his right hemisphere was spared. His verbal memory and his ability to understand language were obliterated. Nonverbal and spatial functions are more dependent on the right hemisphere.

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[203] Ibid.
[204] Ibid.

Memory is similarly lateralized. People with damage to the left hippocampus and medial temporal lobe tend to have difficulties explicitly remembering verbal information but have no problem remembering visual design and spatial locations. People with damage to the right hippocampus and medial temporal lobe tend to show the opposite pattern. Of course damage on both the left and right medial temporal regions results in poor memory for both verbal and nonverbal information.

Lesions to the hippocampus produce marked deficits for the memory of recent experiences, particularly spatial layouts.

When there is specific damage to the front of the temporal left lobe, semantic memory is impaired; people have great difficulty accessing general knowledge about familiar objects, places, or words.

Damage to the amygdala does not produce a serious impairment of recognition memory, but the amygdala does play a major role in memory of emotional experiences.[205] There have been cases of people with damage to the amygdala that believe their parents are impostors because their presence lacks any associative emotion; hence the belief that they must be impostors.[206]

Echoes become established to represent past experiences, and an integral part of the echo is the associated emotion (we will come back to this point in the chapters dealing with emotions). Memories with an associative emotion become a representation of past reality. An idea or an imagined event, even though rooted in past experience, lacks this emotional association. This lack of emotional association will be rightly perceived by the brain as separate from reality, and will be interpreted simply as an idea or imagined event. When the thalamus matches echoes associated with an emotion, it triggers the associated emotion by sending signals to the amygdala. The amygdala serves as a memory of emotions and as such triggers the associated emotion of the particular echo. However, when a concept becomes bonded to an emotional state, it becomes a belief. In this way, beliefs are also represented by echoes, which are processed by the brain as true past experience, precisely, because they have an associated emotion. Most beliefs are established early in life and serve as shortcuts to produce particular behaviors by triggering particular emotions. The beliefs serve to take the place of experience; they are quick and dirty shortcuts to trigger an emotion and guide responses.

The nucleus accumbens is 95% composed of medium spiny GABAergic (inhibitory) projection neurons, which are part of the main output of this nucleus. Most of the rest of the interneurons are cholinergic (excitatory). The output neurons of the nucleus accumbens send axon projections to the ventral pallidum (VP), which are GABAergic. Two serial GABAergic projections become excitatory. The VP, in turn, projects to the mediodorsal (MD) nucleus of the thalamus, which projects to the prefrontal cortex (glutamata and aspartate-- excitatory).[207] Major inputs to the nucleus accumbens include the prefrontal cortex, amygdala, hippocampus, and dopaminergic neurons located in the ventral tegmental area (VTA) in the midbrain, which connect via the mesolimbic pathway. Thus the nucleus accumbens is often described as one part of a cortico-striato-thalamo-cortical loop.

[205] Antonio Damasio, *The Feeling of What Happens*
[206] V.S. Ramachandran, *Phantoms of the Brain.*
[207] John H. Martin, *Neuroanatomy.*

The nucleus accumbens is regarded as the limbic-motor interface, in view of its limbic afferent and somatomotor and autonomic efferent connections. Within the accumbens, there appear to be specific areas in which limbic afferent fibres, derived from the hippocampus and the basolateral amygdala, overlap. These afferent inputs have been suggested to converge monosynaptically on cells within the accumbens and are hypothesized to play a role in paradigms such as conditioned place preference (in rats).[208]

Cocaine and alcohol change the accumbens' activity as dopamine release is increased and serotonin is inhibited. Serotonin has to with satiety. The action of dopamine in this circuit reinforces behaviors or desires by sending dopaminic projections to the prefrontal cortex (via de MD). When urges or desires are satisfied, more dopamine is released, producing a positive emotional feeling. This why it is called, by many, the reward circuit. The hippocampus' projections to the nucleus accumbens have to do with creating needs or desires (in rats, preferring certain places), whereas the amygdala's projections (because of their emotional component) create or reinforce beliefs that guide responses.

This is a good example of how different components of a memory—its context or its associated emotion—modify the interpretation of the memory, and as a consequence produce a different behavioral response based on a need or on a belief. Signals from the hippocampus produce a need (or aversion, depending on whether the context is positive or negative), and the signals from the amygdala produce a belief. The two combined become an unbearable urge to act. However, it is possible that the brain, under certain conditions, can construct a belief contrary to a need or vice-versa, i.e., the urge to have sex with the belief that sex is wrong.

In the early 70's exploration of the cellular basis of memory lead to the discovery that electrical stimulation produces a long-lasting increase in the activity of synapses within the hippocampus. Called long-term potentiation, or LTP, this persisting effect of stimulation showed that hippocampal synapses could be altered by experience – a necessary property of any memory system in the brain. The hippocampus seems to have some role in explicit memory (searching for a matching echo to a stimulus), but not all aspects of explicit recall and recognition.[209] It can put a stimulus into context, using tags and mirroring signals to the relevant cortical areas, which will send out handshakes, as well as serve as a map of the environment, which is crucial to remembering the spatial locations of objects and events.

Amnesic syndromes can result from damage either to the medial temporal lobe or to the diencephalon. Two prominent components of the diencephalon are the thalamus and the mammillary bodies (a nucleus of cells located just below the thalamus). The diencephalon and the medial temporal lobe are connected by a structure known as the fornix, which is a major pathway of the hippocampus. The interconnectedness of the two areas suggests that these regions play a key role in explicit memory, and that any damage to these can produce memory problems.[210] These areas funnel inputs from earlier processing stations all over the brain that deal with different aspects of experiences – the sights, sounds, smells, and emotions that make up everyday episodes. The signals with

[208] French, SJ, Totterdell, S, *Individual nucleus accumbens-projection neurons receive both basolateral amygdala and ventral subicular afferents in rats.* Neuroscience. 2003;119(1):19-13.
[209] Daniel L. Schacter, *Searching for Memory.*
[210] Ibid.

emotional content go to the amygdala, signals that put the stimulus in a context go to the hippocampus, and the signals with the modification or confirmation of an initiated action, if it is necessary go to the striatum. Through handshake signals to other areas of the cortex, attention is brought to bear, and the clear sensation of thinking or remembering is felt. This is how all the different inputs are linked together to form an engram that underlies the explicit memories for day-to-day episodes. The sensory incoming signals, in a forward network of handshakes represent the events in the world and with their emotional component and context are stored in memory. The recollections of the events are a feedback network of handshakes that reconstruct the past. However, the present is constructed from feedback loops of existing memories, the present is not independent of the past.

What we see and what we hear, what we think and what we feel are linked together to form new explicit memories by this medial temporal-diencephalic neural system. Thus they are also essential for episodic memory as well as contributing to the formation of new semantic memories. This system is highly selective of novel events.

Semantic memory can be partially preserved even when episodic memory is entirely dysfunctional. It has been generally assumed that semantic memory can be defined as a network of associations and concepts that make up our knowledge of the world – word meanings, categories, facts and so on. But semantic memory might also form the basis of a good deal of autobiographical knowledge.

The opposite is also true: patients with semantic dementias show us that semantic memory can be seriously impaired even when episodic memory functions reasonably well.[211]

When people have been shown pictures of animals, brain scans show areas with heightened activity in the lower parts of the temporal lobes that participate in the perception of complex objects. When they were shown pictures of tools, the same area showed heightened activity plus there was also an increase in blood flow in the left premotor cortex – an area that becomes extremely active when people simply imagine moving their hands to grasp an object. Identifying tools was also associated with heightened activity in a part of the left hemisphere (the middle temporal gyrus, area 21) that is involved in producing action words (such as writing). These results suggest that knowledge of tools, but not animals, depends on brain regions that represent movements and actions: things people do with tools. It also suggests that part of cognition involves knowledge of different properties of objects, like what you can do with them.

The brain systems that support episodic and semantic memories allow us to recognize objects in the world, to travel in time, and to construct our life stories in a seemingly effortless manner.

Implicit memory has been defined as when people are influenced by a past experience without any awareness that they are remembering. An interesting study with amnesic patients who cannot recall any words from a list shows that when given a cue (the first three letters of the word), they did not appear to be aware of recalling words, but they performed extremely well, and acted as if they were in a guessing game. They showed memory for the words, but they were not remembering in the ordinary sense.

Implicit memory is produced by echoes that trigger subtle emotional responses that change the internal state. These somatic changes serve to evaluate how “good” or

[211] Ibid.

"bad" the stimulus is. We then "know by a gut feeling." Implicit memories have to be transferred to the left hemisphere to be known explicitly. In other words, the emotional content (nonverbal), the emotional knowledge, has to be translated into words (verbal) to become known.

When amnesic patients are given word beginnings or other cues, and are instructed to think back to the list to try to remember target words, they perform quite poorly. But when given the same cues with instructions to guess or to provide the first word that comes to mind, they perform as well as people with no memory problems. Likewise, depth of encoding influences later retention when normal volunteers try to remember the target words yet has little effect when they respond with the first word that pops to mind.

Also, amnesic patients can learn perceptual skills without remembering when and where they learned them. Such skill learning depends on a procedural memory system that is spared in amnesia. This system is selectively involved in knowing how to do things: ride a bicycle, type words, or piece together a jigsaw puzzle. It seems that priming and procedural memory are part of implicit memory in contrast to explicit memory. It has also been shown that amnesic patients have implicit memory for emotional experiences that they could not remember explicitly.

Implicit memory, by definition, does not involve source information. Merely seeing a familiar word activates a specific part of the occipital lobe, the region that is essential for visual perception; the automatic matching of the signal to an echo activates a handshake. This visual memory is involved in visual encoding of words and has nothing to do with other memory systems.[212] This area (37) is an auditory-visual association area.[213]

In another case, a patient with damage to the occipital lobes who had lost much of his vision, had a light flashed in the part of his affected visual space, and he claimed to see nothing. But when asked to guess the location of the flash, he performed extremely accurately! There is a form of unconscious perception. This ability has been called blindsight. (See chapter Five.)

Schacter reports that when people are shown a list of words like assassin, octopus, avocado, mystery, sheriff, and climate, and later tested to fill in the missing parts of a word, for example: ch----nk, o-t—us, -og-y---, -l-m-te, they have a hard time coming up with a correct answer for two of the word fragments (chipmunk and bogeyman). But octopus and climate jump out at them because they had been studied. This kind of memory is called priming. People were tested one hour or one week after. Conscious memory was, of course, much less accurate after a week than an hour, but there was just as much priming on the word fragment-completion test after a week as there was after an hour. The results suggest that priming occurs independently of conscious memory. Amnesic patients have little or no episodic memory, but often show normal priming.

Subjects were shown line drawings of possible and impossible objects (like drawings of M.C. Escher) briefly on a computer screen and then asked whether the object was possible or impossible. Decision about possible objects was primed by exposure to the object several minutes earlier. Surprisingly, there were no priming effects for impossible objects. Amnesic patients confirmed this priming pattern. When people make

[212] Ibid.
[213] Jean Tailarach, Pierre Tornoux, Co-Planar Stereotaxic Atlas of the Human Brain.

decisions about briefly flashed possible objects, there is extensive activity in two adjacent regions at the interface of the temporal and occipital lobes known as inferior temporal gyrus and the fusiform gyrus. But there is little or no activity in these areas when people made decisions about impossible objects. Cells in the inferior temporal lobe respond selectively to the general shape of an object, as opposed to its size or isolated parts. Other studies have shown that the fusiform gyrus is involved in perceiving and recognizing faces, which we see as unified wholes. These two areas are involved in the encoding of the overall shape of an object.

This shows that a perceptual system plays a role in priming. This system has been called the perceptual representation system and allows us to identify objects and to recognize words on a printed page. The perceptual representation system specializes in dealing with the form and structure of words and objects, but it does not know anything about what words mean or what objects are used for. Meaningful concepts and associations are handled by semantic memory.[214] Different echoes and different handshakes are produced by the various sensory and memory systems. This redundancy in the brain allows various memories to operate in a seamless cooperative mode that allows recognizing words (spoken or written), and immediately becoming aware of their meaning, and when we see objects we easily recall how to use them.

The auditory priming effect, like the visual priming effect, is nearly identical after deep and shallow encoding, even though explicit memory for spoken words was much higher after deep encoding than shallow encoding.[215] In priming and implicit memory, the thalamus finds a match between stimulus and an echo from the appropriate cortex area; in explicit memory the thalamus sends a signal to the frontal lobes and activates a search mediated by handshakes to other cortical areas in search of a potential or close match. The result is also different; in one case we don't know how we remember, in the other we explicitly know we remember.[216]

The hippocampus is not active in priming, because it is left out of the sensory (visual or auditory) information extraction. The hippocampus is active when people consciously recollect words recently studied. The hippocampus with its specialized GABAergic (inhibitory) neurons, which are electrically coupled by gap junctions, can activate many interconnected cells at once. In this way signals can be sent simultaneously to many different regions to find a match (or a close match) and activate parts of a memory. This in turn will send out handshakes to other associated memories and in this way start the reconstruction process of an episode. Quickly the when, the how, with whom, at what time, in what period of my life and so on, are remembered, not necessarily with complete accuracy. It is a reconstruction process that can be affected by newer experiences as well as by similar memories.

The perceptual representation system plays a role in our ability to recognize words and objects. Priming reflects the fact that this system changes with encounters with words and objects. Reading words, hearing voices, or seeing objects that populate the world sometimes produce subtle alterations in our brains, alterations that later influence the way we respond to the environment or that make it more likely for a particular idea or image to spring to mind, seemingly out of nowhere. We are entirely unaware that any of

[214] Daniel L. Schacter, Searching For Memory.
[215] Ibid.
[216] Ibid.

these changes is taking place. Priming and other kinds of implicit memory operate invisibly. They are silent parts of our mental lives, but important sources of memory's fragile power.[217]

Implicit memory might play a role in the perplexing experience of déjà vu. The influence of a fragment of an experience is activated by the present situation, but cannot be recollected explicitly, thus creating the feeling that this has already happened before.

Implicit influences on our judgments and behaviors might be especially pernicious because they operate outside awareness. We maintain stereotypes about groups of people that may be automatically and unconsciously activated when we interact with, or are asked about, members of the group. The implicit memories we are considering arise as a natural consequence of everyday activities like perceiving, understanding and acting. The systems that perform these functions often change, perhaps imperceptibly, as they go about their business. Our brains are constantly changing and adapting to the world, and when these changes persist, they can affect our thoughts, judgments and behaviors in surprising ways.

Recent work on procedural learning has shown that in addition to the basal ganglia, the cerebellum, long known to be involved in motor performance, is crucial for motor skill learning. The cerebellum plays a key role in carrying out the timing of operations that allow us to arrange motor movements in their proper sequence. The basal ganglia in turn are responsible for refining the sequence and storing it as an organized motor program. The basal ganglia and the motor cortex play an important role in this kind of procedural memory. When people practice a sequence of finger movements (like playing the piano), and they learn the sequence better, there is a gradual expansion of activity in the motor cortex. A motion routine is established by handshakes with areas that are necessary for a smooth execution of specific movements.

Procedural memory is also involved in the development of habits – those well practiced and mostly unconscious behavioral routines we all carry out in everyday life. Human amnesic patients with damage to the medial temporal lobes, who show poor memory for recent experiences, show forms of habit learning. Conversely damage to the basal ganglia disrupts habit learning as well as motor skill learning.

Yet because priming generally reflects small changes in the perceptual representation system or semantic memory, and acquiring skills and habits involves slow procedural learning that builds up over time, additional systems are required that allow rapid association and recall of sights, sounds, places, and thoughts that come together in a single episode.[218] The structures in the medial temporal lobes are closely associated with linking together, through echoes and handshakes, all the parts necessary to reconstruct past episodes.

A novel and shocking event might activate a special brain mechanism. The event is so important that the memory might be stored as if a picture has been taken. This "freezes" whatever happened at the moment we learnt of the shocking event. It is as if we took a picture and a flashbulb went off. Appropriately, this phenomenon is known as flashbulb memory. Although flashbulb memories are not one hundred per cent accurate, a high level of confidence in a memory is a hallmark of flashbulb memory.

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[217] Ibid.
[218] Ibid.

Memories of episodes that are highly emotional are different from ordinary memories. It might be that traumatic emotional memories are unusually accurate and depend on special brain mechanisms. Stress hormones act on the brain and create a state of heightened alertness and reinforce the circuitry involved in memory formation.[219]

When the brain detects a threat, a number of structures go on alert, including the amygdala, the hypothalamus and the pituitary gland. They exchange information with each other, then release signaling hormones and nerve impulses to the rest of the body and brain to prepare for fight or flight. The adrenal glands release epinephrine (adrenaline), which makes the heart pump faster, and the lungs work harder to flood the body with oxygen. They also release extra cortisol and glucocorticoids that help the body convert sugar into energy. Nerve cells release norepinephrine, which serves to tense the muscles, and sharpen the senses to prepare for action. Digestion and other unnecessary body functions shut down. When the threat passes epinephrine and norepinephrine levels drop, but if danger comes too often, the increased epinephrine and norepinephrine levels can damage the arteries. Low-level stress keeps the glucocorticoids in circulation, leading to a weakened immune system, loss of bone mass, suppression of the reproductive system and memory problems.[220] These memory problems can be acutely important in cases of depression.

Individuals with poor emotional attachment histories display empathy disorders because of a limited capacity to perceive the emotional state of others. Part of the problem is the inability to read subtle facial expressions, which lead to a misrepresentation of emotional states and thus the intention of others. Such individuals also exhibit a poor ability to appraise internal cues of their bodily states. This also leads to a diminished adaptive capacity to evaluate external-social and internal-physiological signals of safety and danger[221]

The lack of emotional involvement with others during childhood leads to a diminished set of echoes for social interaction, and later in life will be manifested as an inability to activate certain memories and their accompanying emotions when presented with emotional expressions of others.

In the great majority of cases of individuals who have experienced extreme or unusual traumas, the most commonly observed symptom is a repetitive, intrusive recollection of the event. The memories keep intruding, bringing feelings of sadness, anxiety, depression and even detachment. It is very similar to grieving. Nearly one in three people report experiencing “memory difficulties” after the traumatic event, probably because they were so upset and distracted that they did not pay attention to ongoing events normally.[222]

In extreme cases it is known as Post Traumatic Stress. This is manifested by the unbidden recollection of the trauma in the context of emotional disturbances and spotty memory problems. The frequency of the intrusive memories tends to diminish with time.[223]

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[219] Ibid.
[220] Robert M. Zapolsky, *Why Zebras Don’t Get Ulcers*.
[221] Allan Schore, *Affect regulation and the Repair of the Self.*
[222] Daniel L. Schacter, *Searching for Memory.*
[223] *Diagnostic and Statistical Manual of the Mental Disorders,* DSM-IV-TR.

Grieving is a process to recalibrate the threshold at which each emotion will be triggered in the future. This makes sense from an evolutionary sense, in that the close loss of a spouse, a child or a sibling implies the cause of the loss might still be a real threat to our kin or us. After we have recalibrated our emotions, when presented with a similar pattern or similar threat, we will react more quickly or at a lower threshold to a similar threat than before the loss. All emotions, one by one, have to be dealt with to restore a homeostatic balance. The added fear of another loss will also help accelerate a response to similar threats. The feelings, while grieving, will be more intense the closer the loss sustained.

Traumatic memories are generally more accurate than other memories, but sometimes are subject to distortion. These distortions are attributable to perceptual errors that occur at the time of the event, caused by the stress of the shocking episode. A related kind of emotional filtering seems to occur with combat "flashbacks" of war veterans, which are often so intense that the veterans report they feel as though they are reliving an actual experience. Flashbacks sometimes contain elements of real, imagined, and/or feared events.

The accuracy of the memory is often directly related to the emotional arousal elicited by an experience, independent of whether it is positive or negative. Arousal may also influence what is remembered from an emotional experience by focusing attention on specific aspects of the experience.

Witnesses to a crime that involves a weapon, such as a robbery at gunpoint, typically retain accurate memories of the gun. But they often have poor memories of other aspects of the event, including the criminal's face. The weapon is the "important" threat. The weapon-focusing effect is more pronounced in people reporting feeling anxiety at the sight of the weapon.

Traumatized war veterans may be chronically vigilant and hyperaroused, and thus prone to treating harmless signals in the environment as serious threats.

Suicidal, depressed patients remember the general emotional gist of past experiences, but do not recollect as many specific details as nondepressed people do. Patients' depressed moods focus attention on the general negative themes in everyday incidents that fit their previous negative experiences. At the same time they tend not to elaboratively encode the distinctive particulars of individual experiences. PET scanning studies have shown a reduced activity in the left frontal lobe. On the other hand, patients with strokes that have damaged the left frontal lobe and the left thalamus quickly become depressed.[224] Patients that are suffering from depression acquire new information more readily when it is negative than when it is positive.[225]

High levels of stress or trauma sometimes sever the handshakes (links) among memory systems. This is known as dissociation. Dissociation does not erase a person's memories; it is a process where some of the handshakes used to activate the memory have been dislocated. Large sectors of the past or periods of ongoing experience become detached from a patient's awareness. Some types of handshakes might survive high levels of stress. Evidence of implicit memory of forgotten events normally accessed by explicit recall could indicate "leakage" of information using different types of handshakes. The

[224] Paul Beger, *Gene Linked to Stress, Severe Depression,* Associated Press.
[225]Daniel L. Schacter, *Searching for Memory.*

idea that memory is composed of many parallel, interacting systems provides fertile ground for the operational theory of dissociative processes.

Attention is important to the process of encoding memories. However, when attention is divided on two tasks, later recall leads to knowing instead of remembering. There is no emotional attachment to such a memory, it is something that is known, but not remembered, because it was not important enough to relate to an emotion.

Low levels of stress strengthen the handshakes of memories, particularly in relation to emotions. A slight increase of levels of glucocorticoids and cortisol during stressful events leads to a higher degree of memory accuracy. Yet, high levels of stress, especially if sustained for prolonged periods, disrupt the normal lines of communication among parallel process. Stress hormones disrupt the handshake signals between certain related memories, but not all.

When either a physical or a psychological stressor affects us, such as a brain injury or an emotional trauma, our brains initiate a cascade of events that culminate with the release of glucocorticoids. They are an essential part of the body's response to stress: they help us mobilize energy where needed, increase cardiovascular activity, and dampen down processes that need to be inhibited during a crisis. Yet as necessary as they are for us to respond effectively to stress, excessive exposure to glucocorticoids can seriously damage neurons. The region of the brain most susceptible to damage is the hippocampus. The hippocampus contains an unusually high concentration of glucocorticoid receptors. Excess exposure produces a permanent loss of glucocorticoid receptors as well as significant damage to hippocampal neurons.[226]

Schacter reports that a study showed that the volume of the left hippocampus in sexually and physically abused women when they were young is significantly reduced compared to a control group. Abused women with large reductions in hippocampal volume tended to have more severe psychiatric problems than abused women with lesser reductions in hippocampal volume. None of these abused women had any memory problems on a standard test of explicit memory, and all of them had remembered their abuse. However, these women showed some problems remembering autobiographical episodes from childhood and adolescence in response to cue words.[227]

There is mounting evidence that inhibitory mechanisms play a role in memory. Neurons communicate by sending excitatory signals that increase each other's activity. They also send signals that cause other neurons to decrease or "turn off" their activity. Without such inhibitory processes, our mental lives would be unbearably chaotic: we would be overwhelmed by a dizzying array of objects and thoughts, sensations and feelings. Our brains must constantly inhibit a good deal of neural activity in order for us to function properly. The process of focusing attention on one subject and ignoring another involves inhibition of the brain's response to the object we ignore.

People, who have been blind since birth, employ the visual system's cortical areas as an added use for their tactile sensations, i.e., identifying objects by touch activates the occipital regions normally used for vision. In experiments involving the rotation of objects, blind people perform similarly to sighted people, except their responses are slower and with a few more errors. It has been determined that blind people use a body-centered or movement-based coding system and ignore the external reference framework

[226] Robert M. Zapolsky, *Why Zebras Don't Get Ulcers*.
[227] Daniel L. Schacter, *Searching for Memory*.

provided by the stimulus and the surrounding objects, which is normally used by seeing people.[228] In other words, the visual-spatial, extrapersonal information is not being integrated to the intrapersonal space. Blind people who are performing complicated tasks, such as reading Braille, use the visual cortex to process these signals.[229] So in a real sense, they are "seeing" with their fingers. Thinking and communicating can also be done by body language, gestures and motion, as in dancing or ice-skating or pantomime.

What can be more real than our memories? Ultimately, we are only what we can remember of our lives. We feel happy when we have many happy memories. If, on the contrary, we have many sad memories, we will feel that our lives have been gloomy. Yet, what we remember is often a reconstruction of past episodes using combinations of memories, not necessarily an exact recall in every detail. Access to the rich, varied, happy and gloomy memories, puts us in touch with that rich internal space we identify with our sense of self. We do, in general, retain the gist of what our lives have been about. We do maintain a general notion of where we came from, who we are, but in a real sense these memories are a great illusion created in our brains to help us survive and project into the future. The brain is betting that what is coming is similar to what has happened. Yet, life can be full of surprises!

7
The Attentional Systems: Are You There?

Arousal is a minimum state of activity of the brain that permits the use of the senses for gathering information from the environment to aid in orienting the organism in space. The reticular formation comprises the central core of the brain stem. It is a complex network of around 100 nuclei that run from the top of the brain stem to the bottom of the myencephalon. These nuclei are distributed throughout the medulla, pons and the midbrain. The reticular formation has numerous downward projections and upward projections. The major inputs originate from the spinal cord (body state information), the solitary complex (gastrointestinal information), vestibular information (balance and motion), the trigeminal nuclei (information from the head and neck), and projections from the tectum, providing visual, auditory and tactile pattern information.[230]

An image or representation of external space is created by the continuous sensory impulses. Likewise, a representation of internal space, or the body is continuously updated by the nervous system. Arousal is a continuous activity that integrates the external space with the internal space to allow for navigation of the body through the environment. The basal ganglia achieve this seamless integration with interactions between the skeletomotor loop and the oculomotor loop; internal body information integrated with external, mostly visual information.

Neurons in the reticular formation region regulate arousal by influencing the excitability of neurons throughout the nervous system. The neurons can affect excitability directly through diffuse projections rostrally and caudally, or indirectly by contacting

[228] Ibid.
[229] *Braille Reading Strategies May Enhance Stimulation of the Brain Responsible for Vision,* Journal of Neurophysiology, Jan 2002.
[230] David Olmsted, *A Brief History of the Reticular Formation.*

other neurons with diffuse projections. Coordinating with the basal ganglia, other nuclei of the reticular formation are involved in basic functions such as movement, muscle tone, cardiac reflexes, circulation, awareness and attention. Another important path by which the reticular formation affects the excitability of cortical neurons is through connections with thalamic nuclei that have diffuse cortical connections.[231] The thalamus regulates the flow of sensory information, and this gate is controlled by neuromodulators from the brainstem reticular formation that are released during arousal. Cells in the brainstem laterodorsal tegmentum increase their firing rates releasing acetylcholine in the thalamus, which depolarizes thalamocortical neurons increasing their spontaneous firing rates in the tonic firing mode and enhancing the transmission of low frequency sensory inputs through the thalamus. The postsynaptic depolarization of thalamocortical neurons during arousal also strongly facilitates the transmission of high frequency sensory inputs through the thalamus.[232] This produces two effects: 1) this ascending system makes the thalamus more sensitive to sensory input and 2) the arousal state activates the cortex to send a stream of echoes to the thalamus to begin directing the flow of sensory signals. This calibration process pinpoints the locations in the cortex for the appropriate mirroring (relaying) of signals.

The acetylcholine neurons of the reticular formation project to both the ventral posterior nucleus and the reticular nucleus. The reticular nucleus of the thalamus has a general inhibitory effect on the other thalamic nuclei. Though both, the ventral posterior and reticular nuclei receive acetylcholine, the reticular nucleus is inhibitory; to this must be added the additional signaling from the echoes of the cortex, whereas the acetylcholine to the sensory nuclei are excitatory. The combination of these two actions is the difference between aroused and asleep, as all sensory information is mirrored to the cortex. However, during REM sleep, the acetylcholine system is activated, but the body remains motionless due to a system of descending inhibition. This inhibition is controlled by a group of cells that descend down the spinal cord and inhibit motor activity.

Sensory evoked responses are suppressed in the cortex during arousal. This sensory suppression results from the activity-dependent depression of the thalamocortical connection caused by increased tonic firing of thalamocortical cells during arousal. Thalamocortical suppression during arousal is associated with a strong reduction in the spread of sensory inputs through the cortex, thus reducing the size of sensory representations. This serves to focus sensory inputs to their appropriate representations in the cortex, which may be computationally helpful for the spatial processing of information.[233] Thus, the calibrated echoes serve to concentrate the sensory inputs and initiate the processing of the sensory signals disregarding many secondary input signals.

Awareness is the minimal processing state of sensory impulses. It involves a preliminary detection of the environment and is mostly concerned with spatial orientation. It is primarily involved with where objects are in relation to the body. In the case of vision, awareness involves what is called the short-range system, and is concerned with movement as well as separating objects from the environment.

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[231] John H. Martin, *Neuroanatomy.*
[232] Castro-Alamancos, Manuel A., *Role of Thalamocortical Sensory Suppression During Arousal: Focusing Sensory Inputs in Neocortex*, J Neurosci. 2002 22: 9651-9655
[233] Ibid.

Awareness is not involved in trying to determine what an object is,[234] but mostly in determining where objects are in relation to the organism.

There are at least three awareness systems: a somatosensory awareness that maps the relative positions of all parts of the body with respect to one another (proprioception), as well as processing information from the tactile signals sent by all receptors in the skin (pain, pressure, vibration and temperature); a hearing awareness; and a visual awareness. These three systems working in unison allow a seemingly effortless body orientation through space. Gustatory and olfactory awareness systems may also be involved.

An automatic mechanism, awareness carefully centers the senses on relevant stimuli by controlling eye, neck and head movements. The superior colliculus receives inputs from the eye, ear and body. These inputs are roughly mapped. The basal ganglia, through the reticular formation, the midbrain and the cerebellum, coordinate body movements automatically to help direct the senses. The colliculus is a three-layered structure. The neurons in the upper level are very selective for movement, small stimuli in the field of vision and momentary changes of light. All of these factors command attention.[235] Genetically pre-wired, the awareness systems are carefully coordinated by the superior colliculus at the top of the mid brain through the thalamic nuclei. Any salient changes in the environment or the body automatically redirects, or focuses the senses on these stimuli; this is the basic function of attention. Attention is the mechanism used by the brain to monitor changes in the external and/or internal space. This allows the organism to orient itself with respect to the environment in a continuous fashion.

Each area of the cortex attempts to interpret the signals reaching it as part of known sequences of patterns, or memories. If they can, they pass on a stable pattern, the name of the sequence, to the next higher area. If an unexpected pattern arrives, then this is what is passed up to the next higher area. The higher area might be able to interpret the pattern as part of it's own sequence. If so, it will feed back to the lower area and produce a stable output. Simultaneously, it will also send a stable pattern up the next higher area. The higher an unfamiliar pattern needs to go to be interpreted, the more areas of the cortex get involved in resolving the unexpected input. Finally when a region thinks it can understand the unexpected event, it generates a new prediction. This prediction propagates down the hierarchy as far as it can go. If the new prediction is incorrect, an error will be detected.[236] Two things happen at this moment: a) an echo is sent to the thalamus, and b) the unknown stimulus will be sent up the hierarchy until some region can interpret it as part of a known sequence or memory. The echo that was sent to the thalamus automatically triggers the attentional systems. This would be a bottom-up initiative. The attentional systems focus the senses on the unknown and thus activate a whole new set of forward handshakes.

In a world that is known and predictable, most of the up-and-down flow of patterns happens rapidly and occurs in the lower areas of the cortex and everything is quickly resolved. Confusion occurs when the cortex can't find any memory that matches the stimulus. Thus the stimulus races all the way up the hierarchy. Until finally, a high level prediction is made. If it is correct, the prediction travels down the hierarchy all the

[234] Francis Crick, *The Astonishing Hypothesis*.
[235] Ibid.
[236] Jeff Hawkins, *On Intelligence.*

way to the bottom. In less than a second all areas are given a sequence that fits the stimulus.[237]

When the highest areas in the cortex can't understand the stimulus, it interprets it as novel, a never encountered stimulus, and as a result it is passed on to the highest area of the brain, the hippocampus. The hippocampus then initiates the construction of the new memory.

There is evidence that the attentional mechanism could "light up" or activate some areas of the cortex; such an increase in excitability level of those areas might facilitate their lengthening the duration of their nerve cell responses to achieve the time-on (about 500 msec) for awareness.[238] In other words, the echoes and handshakes need to be active for about half a second so the sensory or internal brain activity can enter awareness. When subjects received short stimuli to the sensory thalamus (between 15-150 msec) and asked to guess when it was applied, even though not aware of the stimuli, could guess correctly better than a 50-50 if no stimuli had been applied. When the duration of the stimuli was increased (150-260 msec), the subjects could guess up to 75 percent correct. To go from one condition (correct, but no awareness) to another condition (correct, with minimal awareness) required an additional stimulus duration of almost 400 msec.[239]

The thalamus refers in a sequential order the stimuli it receives temporally.[240] A sequence of echoes makes incoming signals be mirrored to various hierarchical areas of the cortex. The expectation, or the memory of what might happen, dictates this temporal order. The thalamus is responsible for closely coordinating attention with these three awareness systems. Under normal conditions the brain processes a multitude of signals in an automatic mode; when this occurs we say that the organism is aware. By processing the sensory signals, the organism orients itself in space and time and navigates through the world to find food and avoid danger. The thalamus activates the attentional systems to focus on particular stimuli. There are two ways to activate attention: One mechanism bottom-up, based on a new and novel stimulus. Another is a top-down mechanism after deciding what is important and consequently focuses the attentional systems on a particular stimulus.

The attentional systems evolved into projections to the cortex from several nuclei of the thalamus that originally interacted automatically with the basal ganglia to produce genetically wired responses. Some researchers have gone so far as to mention up to 25 such automatic responses, such as sleeping, eating, drinking, fleeing, hunting, defecating, grooming, mating and so on.[241]

There are three different thalamo-cortical projections to area 40 in the temporal and parietal lobes. These come from the lateral posterior nucleus, the lateral dorsal nucleus and the pulvinar nucleus.[242] The basal ganglia, through the aid of this system, integrate seamlessly the external spatial map with the body map.

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[237] Ibid.
[238] Benjamin Libet, *Mind Time.*
[239] Ibid.
[240] William H. Calvin, *The Cerebral Symphony.*
[241] David D. Olmsted, *A Brief History of the Reticular Formation.*
[242] Jean Talairach and Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

Attention evolved through natural selection to center the senses on changes in the environment and body for successful locomotion and focus on important stimuli to increase opportunities and decrease threats. When an appropriate stimulus, determined by the thalamus by matching incoming sensory signals with echoes, is detected, or when a certain threshold of change is perceived, the thalamus automatically activates the attentional systems. Sequences of stimuli activate handshakes of expected future sequences, activating memories of what is about to happen. These expected memories generate their own echoes. When the thalamus detects a mismatch between expected events and incoming signals, the attentional systems are activated to focus the senses on the unexpected stimulus. In this way, the unexpected, activates a new sequence.

Jeff Hawkins asked himself what happens if a new object, one he'd never seen before, appeared in the room – say, a blue cup. The answer seemed simple. He would notice the new object as not belonging. To notice that something is different, some neurons that weren't active before would have to become active. Then, how would these neurons know that the blue cup was new and the other objects in the room were not? The brain uses memories to constantly make predictions about everything we see, feel, and hear.[243] The brain uses memories to form predictions by activating handshakes that are associated with what it expects. Conversely, when there is a mismatch (between expected echoes and sensory signals), the cortex detects the unexpected. The unexpected stimuli generate a related echo, and when it is detected by the thalamus, it reinforces the activation of the attentional systems. There is an inbuilt redundancy.

Attention focuses the senses on the stimulus and activates all relevant memories to the stimulus, including all the cortical areas used by the senses that might have encoded events with shared characteristics in order to better examine, interpret and understand the stimulus ant its context. Attention ignores most stimuli to deal more effectively with one object or situation. Attention deals with things serially, first with one object, then another. This natural process helps focus on ever-changing internal or external stimuli concerned mostly with appetites, emotions, thoughts (internal) and the changing environment (external).

Attention is controlled by the thalamus, but integration of external and internal space is achieved by interaction of several neurological loops. Following these loops and the neurotransmitters they use we encounter:

The skeletomotor loop: projecting from the motor areas (primary, premotor and supplementary, areas 4 and 6, GABA) and somatic sensory cortex (glutamate) there are projections to the putamen on to the globus pallidus internal (GABA, substance P and enkephalin) and the substantia nigra pars reticulata (GABA, substance P and enkephalin), which in turn project to the thalamic ventral anterior and ventral lateral nuclei (glutamate and aspartate) and feedback to the motor cortex (glutamate). This loop is primarily concerned with mapping the body and the relation between its parts.

The skeletomotor loop connects with the oculomotor loop, primarily with afferent and efferents between motor areas 4 and 6 with area 8.

The oculomotor loop: efferents from the frontal eye field and supplementary eye field (area 8, GABA, with extensive connections to visual areas 17, 18 and 19) and the posterior parietal (areas 7 and 40, glutamate) and prefrontal to the caudate body and, similarly, to the globus pallidus internal and the substantia nigra pars reticulata, which

[243] Jeff Hawkins, *On Intelligence.*

project to thalamic ventral anterior and medial dorsal (glutamate and aspartate) and feedback to the cortex. This loop is primarily concerned with mapping the exterior space in relation to the body.

The prefrontal cortex loop: efferents from the premotor cortex (GABA and enkephalin), the middle and inferior lobe (areas 20 and 21) and the posterior parietal (areas 7 and 40) to the caudate head (GABA and enkephalin), projecting to the substantia nigra pars reticulata and the globus pallidus internal, which project to the thalamic ventral anterior and medial dorsal nuclei and back to the cortex where the signals originated.

Moreover, there are extensive connections between these two loops, primarily areas 9 and 10 connecting with area 8.

The limbic loop: afferents from the medial and lateral temporal lobes (area 20, glutamate), the hippocampal formation and the anterior cingulate gyrus (areas 24 and 32, GABA and enkephalins) to the ventral striatum (GABA, substance P and enkephalins), projecting to the ventral pallidum and the globus pallidus internal and the substantia nigra pars reticulata (all GABA, substance P and enkephalins), which project to the thalamic medial dorsal and ventral anterior nuclei and back to the cortex.[244]

The output of everyone of these loops provides information for the various thalamic nuclei to coordinate their signaling to the cortex after integrating the visual and body signals into a single map, as well as incorporating what is or isn't important evaluated by the prefrontal loop and integrated with an emotional evaluation through the limbic loop.

The striatum, comprised of the putamen, the caudate and the nucleus accumbens receives signals from the cortex (glutamate and aspartate) and from the substantia nigra par compacta and the ventral tegmental area (dopamine). The striatum's main output is to the globus pallidus internal and external (GABA, substance P and enkephalins). Neurons in the striatum that contain GABA and substance P give rise to the direct path projecting to the globus pallidus internal. Neurons that contain GABA and enkephalin give rise to the indirect path and project to the globus pallidus external. The direct path promotes movement and the indirect path inhibits movement.

The globus pallidus internal projects mainly to the thalamic ventral anterior and ventral lateral nuclei. Whereas the globus pallidus external projects mainly to the subthalamic nucleus, which feeds back to the globus pallidus internal, thus regulating and fine-tuning the output to the thalamus.[245]

Attention is a constructive process in the sense that it interprets all the signals from our senses using our stored memories and experiences, and creates the present. Attention is a process that can focus externally or internally and can be of two kinds; one automatic, bottom-upwards, as small changes in the sensory signals focus the senses on the changes; another top-downwards, focuses the senses on specific stimuli to interpret better or in greater detail, to extract more meaning from the sensory signals. When monitoring the external environment, attention creates the illusion of the ever-present.

Many short-lasting cerebral activities take place without entering awareness: thoughts, imaginations, potential actions, ideas, possible problem-solving. Only when attention is focused, can many of these activities reach a level of awareness. Most brain activities occur without any awareness. It is probable that the matching of echoes to

[244] John Martin, *Neuroanatomy.*
[245] Ibid.

stimuli at the thalamus initiates many brain activities by triggering subtle emotional responses, similarly to making very small body movement adjustments to accommodate the external changing landscape. Quick behavioral, motor responses to sensory signals can be made within 100-200 msec after the signal, well before awareness of the signal can be expected. Few of the thousands of sensory inputs delivered per second to the brain achieve (conscious) awareness, though they (may) lead (unconsciously) to meaningful and psychological responses.[246]

Attention can be voluntarily directed, involving the prefrontal loop. PET scans show such voluntary direction involves the frontal lobes (areas 9 and 10) and a restricted area in the left inferior prefrontal cortex (area 47). These areas are also implicated in executive functions and planning. People with damage to these areas fail to organize and categorize new information as it comes into memory. They have difficulty accessing semantic memory and in that respect interpreting quickly and correctly what they see or hear in the present. Thus it becomes much more difficult for them to encode the experience for later recall.[247] The more attention is engaged in constructing this present, the better this event will be encoded for later recall as a past event. When attention monitors the internal signals of the brain cortex, it searches for stored memories of events, in what is known as explicit recall.

The limbic association cortex (areas 11, 47 and 38) involving the limbic loop and the prefrontal association area (areas 46, 9 and 10) are active when deciding to assess motivational and emotional factors. The posterior parietal cortex (the somatosensory and visual attentional system, area 40 and 7) coordinates the visual information with the premotor areas, important in planning movement. From the premotor areas (area 6) the sequence of movements is directed to the primary motor area (area 4).[248]

Visual attention involves the long-range system, which is primarily concerned with what is moving out there.[249] Attention is necessary for encoding a stimulus for later recall. The handshake (associative) signals that are used to help interpret what the object is, in what context, where in space and time, will be used to represent the event, and later be available for recall. The handshakes include referred (tags) information to help keep events in order.

When attention is focused on extrapersonal space, it constructs the present. Attention remembers the now. Our previous experiences, our memories -- the knowledge that we have stored of objects, people, faces, movements, actions and so on -- will determine how we construct this present, and this construction takes place outside awareness.

There is some evidence that the right hemisphere is more involved than the left hemisphere in visual and hearing attention.[250] The somatosensory attention system is also more strongly represented on the right side, as strokes on this side only, and not the left side, produce body neglect of the left half of the body.[251] The right hemisphere is also

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[246] Benjamin Libet, *Mind Time.*
[247] Daniel L. Schacter, *Serching for Memory.*
[248] John H. Martin, *Neuroanatomy.*
[249] Francis Crick, *The Astonishing Hypothesis.*
[250] Chris McManus, *Right Hand Left Hand.*
[251] Andrea Peru, Giampetro Pinna, *Right Personal Neglect Following a Left Hemisphere Stroke. A Case Report.*

involved in shifting attention to where someone is looking to follow the gaze of another.[252]

Semantic memory is continuously integrated with the incoming signals of our senses to interpret them according to experience. Attention filters out unattended events or objects, and, conversely, an attended event is reacted to more rapidly, at a lower threshold and more accurately. Attention helps encode the present; remembering retrieves the past. The present has the added quality of being accompanied by sensory information that is perceived in almost real time. The past lacks this quality, and attention feels the difference; when the brain interprets this difference, it feels like remembering.

The thalamus automatically and continuously shifts attention by genetically encoded routines, primarily, to changes in the environment that are being registered by the basal ganglia circuits. The thalamus achieves this in three ways:

a) The visual and hearing attentional systems through projections from three different nuclei (lateral dorsal, lateral posterior and medial) to the associative area (40). Area 40 has intracerebral connections to area 39 (another associative area), areas 18 and 19 (secondary visual) and area 22 (auditory association). Areas 40 and 39 have association bundles to the temporal pole and the frontal lobe, and commissural homotopic (same area contralaterally) connections.

b) The somatosensory attentional system through projections from three nuclei (lateral dorsal, lateral posterior and pulvinar) to area 7 (associative somatosensory), which has rich connections contralaterally to areas 1, 2 and 5 and subcortical projections to the lenticular nucleus and the tegmentum.

c) Voluntary and automatic control of the senses through projections from the dorso medial nucleus to the frontal lobes (areas 9 and 10) which in turn have rich connections to many areas (the three other lobes and the hypothalamus), and the areas that control eye movement and speech, and to the tegmentum, which coordinates neck movements to orient the senses.[253] The eyes shift ever so often, generally attracted towards moving objects; the hearing shifts from one sound to another, and then back, mostly checking if the sound is still the same. No change means nothing new.

From the assumption that logic is based on syntactic language-based proofs, or on constructing and manipulating spatially organized mental models, or on imagery based on visual mental abilities, another study, in the absence of any correlated visual input, showed that reasoning activated an occipitoparietal-frontal network, including parts of the prefrontal cortex (areas 6 and 9) and the cingulate gyrus (area 32), the superior and inferior parietal cortex (areas 7 and 40), the precuneus (area 7), and the visual association cortex (area 19).[254] This study shows attention systems activating during reasoning (visual attention/area 40, and somatosensory attention/area 7) along with visual (area 19) and motor (supplementary motor cortex, area 6) regions as well as involving the prefrontal area 9 involved in thought, cognition and movement planning. Moreover, the anterior cingulate gyrus (area 32) involved in emotions is also activated. This implies that reasoning has an emotional component.

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[252] Kingstone, A, Friesen, C.K. and Gazzaniga, M.S., *Reflective joint attention depends on lateral and cortical connections*, Psychological Science, 11, 159-166.
[253] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.
[254] Knauff M., Mulack T., Kassubeck J., Salih H.R., Greenlee M.W., *Spatial imagery in deductive reasoning: a functional MRI study*, Brain Res Cogn Res. 2002 Apr;13(2);203-12.

An emotionally competent stimulus can override the attentional systems and direct the thalamus to focus attention on the new stimulus.

Also, after a certain time interval, and there is evidence that this might be genetically set, when nothing is new, attention shifts to something else, bottom-up. Attention shifts probably entail a three-step process: disengage, move, engage. Attention focuses the senses on the new stimulus; otherwise, attention, when not activated by the thalamus, will be downgraded to awareness. The reticular formation, continuously monitoring the spatial and temporal aspects of our environment, produces awareness. The thalamus is continuously matching expected echoes to expected stimuli. When a mismatch is detected, attention is activated to assist in dealing with the unforeseen. Under certain conditions attention can appear to be absent, but sometimes it simply has shifted inwards: attention is focusing on internal handshakes from the entire cortex. Attention can focus on thinking or on the body or it can be in "remembering" mode.

There have been reports[255] of neglect in both extrapersonal and personal space. People with extrapersonal neglect fail to detect half of the visual and auditory stimuli in the contralesional side of space. Patients with personal neglect are unable to orient towards the contralesional hemisoma, and in some cases lose the perception of the contralesional half of the body (hemisomatoagnosia). In other words, the person doesn't feel one half (the left half) of his or her bodies.

In general, extrapersonal and personal neglect occur together; however, they do happen independently of each other. Personal neglect is much less frequent than extrapersonal neglect. When they do happen together, it always involves lesions to the right parietal area. Extrapersonal neglect has been reported on both sides, but curiously there is no evidence of right personal neglect with lesion to the left side. Theoretically, there could be a left-handed person that might have this situation reversed. Personal neglect might involve not feeling some parts of one half of the body, not necessarily the whole half, depending on the extent of the injury.

Personal neglect is associated with a lesion of the right infero-posterior parietal region, or damage to subcortical structures, like the thalamus and the basal ganglia, the internal capsule and the parietal subcortical white matter. Such lesion or damage affects the upper limb more than the lower, the elbow more than the shoulder and the hand more than the elbow. When it occurs in the absence of extrapersonal neglect, it is not very severe. Although it is usually associated with marked impairment of motor and somatosensory functions and with visual field defect (VFD), its presence is surely compatible with a normal visual field. In spite of their frequent co-occurrence, anosognosia for hemiplegia, somatoparaphrenia, and hemisomatoagnosia are dissociable phenomena rather than different aspects of a unitary syndrome. A full awareness of motor impairment is compatible with the inability to orient toward the paretic limb.[256]

A patient with a right hemisphere stroke (left side paralyzed) sending a command to move his left arm receives visual feedback informing that it is not moving, so there is a discrepancy. His right hemisphere is damaged (highly sensitive to discrepancies), but his intact left hemisphere goes about its job (when confronted with a discrepancy, it tends to smooth it over, pretend it doesn't exist and forge ahead) of denial and confabulation,

[255] Andrea Peru, Giampetro Pinna, *Right Personal Neglect Following a Left Hemisphere Stroke. A Case Report.*
[256] Ibid.

smoothing over the discrepancy and concluding that all is fine. On the other hand, if the left hemisphere is damaged and the right side is paralyzed, the right hemisphere is functioning properly, so notices the discrepancy between the motor command and the visual feedback.

For a person to deny that he or she is paralyzed is quite bizarre, but even more amazing is when some patients also deny that another patients is paralyzed. According to experiments done by Giaccomo Rizzollati on monkeys there are neurons in the frontal lobes that fire when a monkey performs certain specific movements. One cell will fire when the monkey reaches out and grabs a peanut; another cell will fire when the monkey pushes something, yet another cell will fire when the monkey pulls something. These are motor command neurons. Rizzollati found that some of these neurons would also fire when the monkey watches another monkey performing the same action. The same thing happens in humans. The visual image of someone performing a movement is completely different from the image of you performing the movement. The brain must produce an internal mental transformation. Only then can a neuron fire both in response to your own and to another person's movement. Rizzollati calls these mirror neurons. It is possible that these neurons were damaged in the case of the patient in the paragraph before. This system of neurons might not be working properly in patients that suffer anosognosia.[257]

Neglect dyslexia presents itself in two forms: reading only the right-hand half of words, i.e., women as men, train as rain, date as ate, etc.; alternatively, the word read is of the correct length, but the left half of the word being guessed at, i.e., sawmill as windmill, cake as make, or together as whether.[258]

Neglect generally involves the left half, whether it is the food on the left half of a plate or applying makeup to only the right half of the face. Essentially, attention is not being paid to the left side.

Vision, hearing, thinking and feeling are linked together by a medial temporal-diencephalic neural system and this system is essential for episodic memories and the formation of new semantic memories.[259]

The architecture of the interconnections between the different attentional areas strongly suggests that these systems are working together. Area 40 in the parietal region (infero-posterior parietal) is strongly linked with associative functions.[260] I will call this area the visual and hearing attentional area. It is strongly connected to the adjacent area 39 (slightly posterior to area 40), which also has associative functions. This particular area (39) neighbors the auditory-visual integration area (area 37) and somatosensory associative area (area 7) in the right side, which was mentioned in personal neglect previously. The somatosensory associative area (7) has connections to the lenticular nucleus and the tegmentum, which are related to controlling neck and head movements to center the senses on new stimuli.

There are three different pathways from the thalamus (pulvinar, lateral dorsal and the medial nucleus) to the visual and hearing attentional area. This area (40) in turn has intracerebral connections to visual integration area (18), another visual area (19) that is connected to adjacent areas and is connected contralaterally (to the other hemisphere) via

[257] V.S. Ramachandran, *A Brief Tour of Human Consciousness.*
[258] Chris McManus, *Right Hand Left Hand.*
[259] Daniel L. Schacter, *Searching for Memory.*
[260] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

callosal radiations. This visual area (19) is connected to the primary visual area (area 17) through the visual associative area (18). These two visual areas (18 and 19) are connected to the frontal oculomotor center (area 8), to the sensorimotor cortex and to the auditory cortex by long association bundles.[261] This architecture shows a strong integration of visual and hearing attention with somatosensory attention, particularly to control movements of the head, neck and eyes. Saccades, the rapid eye small movements which focus on different details of an object are probably controlled through this circuit.

When the visual and hearing attention area (40) is activated by the thalamus, it immediately sends handshakes to the visual associative area and in turn starts the visual attentional system by moving the eyes to the focus of attention. This area 40 also has projections to the auditory integration area (area 22 in the mid portion of the superior temporal convolution). If the brain is seen from below, a portion of area 22 lies exactly in the middle of the brain, behind the brain stem, connecting the two hemispheres. This auditory integration area (22) in turn is connected to an auditory associative area (42) and to the associative somatosensory area (5).

The visual and auditory attentional systems are biased to the right hemisphere, especially when dealing with prosody and facial expressions, as these specializations are lateralized to the right.

This auditory integration area (22) also has efferent connections to the neighboring temporal area (area 21). This last area (21) receives projection fibers from the inferior temporal lobe (area 20) and has some efferent fibers to the parietal and occipital cortex.

The auditory associative area (42) is in turn closely connected to the area in control of speech (areas 44 and 45, which, not surprisingly, happen to lie between the supplementary motor area and the frontal lobes) and the area in control of voluntary eye movement (area 8), also adjacent to the supplementary motor area. Through the handshakes and signals sent to the auditory integration area (area 22), thought and hearing are focused on the stimulus.

In a quick and direct manner, the thalamus produces a tremendous flurry of activity as attention is brought to bear on a stimulus. With the appropriate relay of impulses, the thalamus quickly activates visual attention (area 40 projects to visual areas 18 and 19), auditory attention (area 40 projects to area 22 and is relayed to area 42), and simultaneously brings on line the somatosensory attention of the body (area 7 with connections to area 5). Each of these attentional systems sends out its own sets of handshakes to each other to reinforce the activity initiated by the thalamus as it coordinates and integrates all the attentional systems.

Elegantly enough, the somatosensory attention system (somatosensory associative, area 7) is the only other area in the cortex that also has three different pathways to and from the thalamus (lateral dorsal, lateral posterior and the pulvinar nucleus).[262] This area happens to be neighboring with the main associative area (area 39) and the visual and hearing attentional area (area 40) just mentioned above. Area 7 connects contralaterally to the somatosensory region (areas 1 and 2) and the somatosensory associative area (5).[263] In this way coordination between the two halves of

[261] Ibid.
[262] Ibid.
[263] Ibid.

the body becomes possible. Area 7 also connects to the visual, auditory and tactile integration area (31) to the neighboring somatosensory associative area (5) and through this to the auditory associative area (22). Area 7 on the right side is involved with body awareness, and on the left side is involved with the manipulation of objects and the execution of symbolic body language. The thalamus, by signaling to area 7, activates the other attentional systems with the proper set of handshakes: the visual with direct connections to area 40, and indirectly from here, and by projections from the other associative somatosensory area (5) to the auditory attention system (area 22) and on to the auditory integration area (42).

The activation of these three attentional systems can be achieved by the efferents from the lateral dorsal or the lateral posterior nuclei. If the signal is relayed by the medial nucleus, only the visual and hearing attentional systems will be engaged and the somatosensory attentional system will be activated indirectly. Alternately, if the signal is relayed by the pulvinar nucleus, only the somatosensory attentional system will be engaged, and the visual and hearing attentional systems will be activated indirectly.

The thalamus relays signals from our senses or bodies through these different pathways to these two areas (7 and 40): the somatosensory associative area (7) on the right, the manipulation of objects on the left (7), and the main visual and hearing attentional area (40) on both sides,[264] but with a slight dominance from the right side.

The visual and hearing attentional systems, even though they are bilateral, present asymmetries, depending on the type of stimulus or in the type of memory used to encode or retrieve information. Explicit retrieval or episodic nonverbal retrieval activates the right frontal lobe more, whereas episodic verbal retrieval activates the left inferior prefrontal area.[265]

In an interesting series of experiments people were shown two shapes: a kiki and a booba. A booba is sort of an amoebic shape, or and abstract caricature of a cloud. Whereas a kiki looks like a piece of shattered glass with jagged edges. Ninety-eight percent of people identify the jagged shape as a kiki and the bulbous amoeboid shape as a booba. The shape kiki and the sound kiki share one property. The kiki visual shape has a sharp inflexion, and the sound "kiki" represented in the auditory cortex, also has a sharp sudden inflexion. Tamillians, who don't speak or write English, produce the same results. Other shapes can also be paired with sounds in this manner: for example, if you show a blurred or smudged line and a sawtooth and ask people which is "rrrrrr" and which is "shhhhh" they spontaneously pair the former with "shhhhh" and the latter with "rrrrr."[266]

Attentional area 40 is the crossroads between the visual and auditory attentional systems. Hearing is in the temporal lobe and vision is in the occipital lobe. This area is also commonly called an associative area. It should not be surprising that here is where the common denominator of different sense modalities can be extracted. Patients with left angular gyrus lesions tested abysmally at interpreting proverbs and metaphors and also failed the booba/kiki test. Ramachandran conjectures that visual-auditory metaphors are processed on the left side (the TPO junction—e.g., "loud shirt," "sharp cheese") and

[264] Ibid.
[265] A.D. Wagner, R.A. Poldrack, L.L. Eldrige, J.E. Desmond, G.H. Glover, & J.D.E. Gabrieli, *Material-Specific Lateralization of Prefrontal Activation During Episodic Encoding and Retrieval.*
[266] V.S. Ramachandran, *A Brief Tour of Human Consciousness.*

spatial metaphors ("tested abysmally," he "stepped down" from his post) are processed on the right side.[267]

In the 1980's Jeffrey Holtzman of Cornell University Medical College, studying the attentional systems of split brain patients, found that each hemisphere is able to direct spatial attention not only to its own sensory sphere but also to certain points in the sensory sphere of the opposite, disconnected hemisphere. This suggests that the [visual] attentional system is common to both hemispheres, and is operating via some interhemispheric connections[268] (the anterior and posterior commissures, the corpus callosum having been severed during split-brain operations).

Holtzman's work shows that the attentional resources are finite: the harder the task, the more of these resources are needed – and the more one half of the brain must call on the subcortex or the other hemisphere for help. In 1982, Holtzman discovered that the harder one half of the split brain worked, the harder it was for the other half to carry out another task simultaneously.

More recent investigations show that another aspect of [visual] attention is also preserved in the split brain. When a person searches a visual field for a pattern or an object, the researchers found that split-brain patients perform better than normal people do in some of these visual-searching tasks. The intact brain appears to inhibit the search mechanisms that each hemisphere naturally possesses.

Alan Kingstone of the University of Alabama, studying split-brain patients, found that the left hemisphere is "smart" about its search strategies, whereas the right is not. In tests where a person can deduce how to search efficiently an array of similar items for an odd exception, the left does better than the right. Thus, it seems that the more competent left hemisphere (in this case) can hijack the attentional system.[269]

When these areas, the somatosensory associative (7) and, through area 40, the visual associative (18 and 19), and the auditory integration (22) become activated we feel that we are paying attention. Through these two subsystems and their interconnections we are simultaneously activating the three attentional systems: auditory, visual and somatosensory attention. In this way, attention to where our body (intrapersonal space) is in relation to the extrapersonal space (visual and auditory attention focused on the environment) is achieved seamlessly.

Any one of these attentional systems could be activated alone for specific tasks, for example, listening to music or watching a tennis match. When one of these systems is not functioning properly, we might not be aware of this, as we can't pay attention to it.

Depending on the nature of the stimulus as well as the sensory type of input, the thalamus will use a different pathway to relay the stimulus to each of these areas. The thalamus, with the help of the striatum, can help speed up a response time when needed by getting ready to relay the proper action signals to the body.

The caudate nucleus has many clumps of axon terminals that receive signals. They are called striosomes when they receive information from the amygdala. Striosomes also receive information from the orbital frontal cortex and the anterior cingulate girus. All these areas are related to emotions. There are other clumps of axon terminals that receive signals from the thalamus, the lateral prefrontal cortex and the orbital frontal

[267] Ibid.
[268] Michael S. Gazzaniga, *The Split Brain Revisited,* 1998.
[269] Ibid.

cortex (areas related to control and elaboration of higher mental functions). These latter clumps are known as matrisomes. Between them lie tonically active neurons (TANs). The output of the TANs is sent to the basal ganglia; the outputs of the medial globus pallidus, the lateral globus pallidus, and the subthalamic nucleus are sent back to the thalamus and relayed to the premotor and motor cortex to automatically execute responses if necessary.[270] The caudate nucleus, because of its architecture, when it detects a strong emotion, will signal the thalamus and override the thalamus's control of attention. In this way, attention is shifted to whatever caused the emotion: the ECS. This also has the advantage that if motor responses are needed in a flight-fight response or in a mating encounter, they are activated automatically without further processing.

In the world we live, we need to deal with objects moving at various speeds, generally somewhere between zero and 200 miles per hour (terminal velocity through air is about two hundred miles per hour). The slower an object is moving, the quicker we can shift attention from one object to another. We need to respond, sometimes in twenty milliseconds, to various stimuli, for example, a big cat swinging a paw at us at 100 miles per hour, (20 milliseconds correspond to about a movement of 2.5 feet). It has been proven that it takes somewhere between 300 and 500 milliseconds for an event to reach consciousness,[271] much too slow to consciously respond to an attack by a lion at close quarters. Yet, we are capable of deftly moving a few inches out of the way, and then quickly picking up a thick stick and proceed to fend off the next swing, and in quick succession, counterattacking with a blow to the head with the stick. All this elapses in about half a second. Focusing simultaneously on the personal and extrapersonal space, attention coordinates all necessary movements of our body in response to the moving threat in the environment.

Actual awareness of a signal must be clearly distinguished from the detection of the signal. Human and nonhuman beings can discriminate between two different frequencies of tactile vibration, even though the intervals between the two pulses in each vibration frequency are only a few milliseconds in length. Becoming aware of the two frequencies requires a relatively long time.[272] However, if a response is needed, the response will be initiated by the matching of echoes to the stimulus long before the stimulus reaches awareness; before an individual can report deciding to produce a response. The echoes serve as a neurological shortcut to initiate action as soon as possible.

Attention also refers events sequentially in time in such a way that the episode, when it becomes part of our immediate past memory, will be perceived as being in concurrence with all our past experiences. Echoes from the cortex help the thalamus index the episode so it will be remembered in the right sequence. Even though most everything happened outside consciousness, we still feel that we were not only witnesses to the event but were active participants and decision makers during the event. We might even remember the event in slow motion, as the adrenalin rushing through our system temporarily sped up everything, including all our cognitive and perceptive functions as well as our motor responses.

[270] Jeffrey M. Schwartz, *The Mind and the Brain*.
[271] Nick Herbert, *Elemental Mind*.
[272] Benjamin Libet, *Mind Time*.

The attentional systems have at their disposal all the memory systems (visual, hearing and somatosensory) that aid the brain to interpret the signals relayed by the thalamus sent by the senses and body. Each attentional system will impart their input sensory signals (visual, auditory, tactile, proprioceptive) with a particular quality or feeling in spite of the fact that the neurons in each cortical area must be doing exactly the same.

The attentional systems can be directed inwards to search for past memories as in explicit recall. As we have seen, this involves a systematic search and effort. This use of the attentional systems in what we call remembering is also a constructive process. The past is reconstructed from fragments of memories of the event. The reconstruction of a past episode will not only depend on how the different parts of the episode -- the where, with whom, when, the how, and so on were encoded -- but also on the specific cue that was used to elicit the memory. The difference between remembering and the present is a distinct feeling that the memory is a past part of our lives -- we know we are not actually seeing or hearing or feeling the past event, even though we can clearly re-enact what made up the past event.

There are strong connections between areas 21 and 20 in the temporal lobe with the visual and auditory integration area (37) and the auditory integration area (22). This architecture suggests that this area could be a strong candidate for thinking, but we must keep in mind that thinking will not be restricted to this area alone. There are too many other memory systems needed in the process of thinking to actually limit this activity to one area. The handshakes are established throughout wide areas of the cortex.

The brain uses speech to communicate what it is thinking to other brains. When it is not communicating with others, the brain uses an internal speech to think, except that the mouth, tongue and vocal chords are not being activated. It is a process similar to imagining moving a finger, but not really moving it. The brain imagines speaking, but doesn't speak. The brain uses auditory areas to think, creating, in effect, an internal "voice". When the brain focuses internally on these areas, attention is paid to what it is "saying," that is, thinking.

In the same way that the brain uses the memory systems of our hearing sense to interpret speech, to speak and to think (verbally), the brain uses the memories of the visual system to imagine or visualize, and to manipulate and turn objects in our "mind's eye". The brain can think visually, even though it can only communicate this form of visual thinking by translating it to speech, which can produce distortions of the original thought.

The brain also communicates feelings by using gestures and body language, which are easily understood. Some of these gestures are universal among cultures and even across species.

When we focus attention on the memory subsystems of cognition and perception, we feel we are thinking or remembering or imagining. Memories stream by in odd combinations of associations and cues -- lifetime or episodic memories of events, real and imagined. Memories can be primed by new sensory information; objects or body movements might activate semantic and procedural memories. This type of brain activity feels similar to thinking, but our attention can distinguish between memories (remembering) and thought.

When attention is focused internally, using all of these three attentional systems, we access the rich internal space that we call ourselves -- our memories, our thoughts, our visions, our aspirations, and our feelings. Thinking happens in the brain, independent of the body, and that is why it feels like it is separate from the body, even though the brain is an integral part of the body. The brain creates a model of the body, but not of itself.

The brain is continuously processing a multiplicity of flows of signals in parallel. In order to deal with them effectively, the brain has a tendency to automatize as many as possible in order to free attention to deal with threats or novel situations. Attention focuses on new opportunities and sudden dangers. If this were not so, we would be using our scarce attentional resources to coordinate our body movements to walk and to calculate the spatial relationship of objects relayed by our eyes. The automatic routines set up by the brain continuously and effortlessly coordinate our visual and motor systems, among many other functions.

Early processing of signals from the senses is done in parallel; many of these activities proceed simultaneously. At some point these signals reach a higher level and are interpreted as a particular object. When attention focuses on an object, it can only deal with one (or a few at most) at a time. This is done by temporarily filtering out information coming from unattended objects. The attentional system then moves fairly rapidly to the next object. Attention, like remembering, is a serial process that activates relevant areas one at a time, then shifts to another stimulus or memory, respectively. The thalamus matches an echo from the memory system to a stimulus. It activates these memories by mirroring the stimulus. These areas then send out handshakes to other relevant areas. As the signals move upwards in a hierarchical manner, handshakes are also sent back downwards, modulating the upward signaling. In a quickly cascading manner pertinent experience and knowledge are activated.

Two distinct processes can shift attention. One is emotional; it switches the focus of attention to the emotional competent stimulus (ECS) if it is considered more important. The other is a voluntary control, which also plays a role in deciding if the emotional competent stimulus is or is not more important. The prefrontal lobes (areas 9 and 10) have rich connections to the thalamus[273] and can signal it to shift attention. These areas have also been associated with executive functions, and are involved in weighing alternative possible courses of action as well as implementing them. This is where decision making takes place, allowing you to choose from different courses of action according to what is happening in the present -- what you remember and know about the situation and what can possibly happen with different actions, according to past experience. The orbital frontal cortex (area 11) is involved in evaluating the ECS. For this purpose, afferent and efferent projections to the caudate determine the nature of the emotion in relation to the stimulus and reinforce or defuse the caudate's signaling. Similarly, the thalamus will reinforce the activation of the emotion or allow it to decay. In this manner, the whole operation of the brain is quickly changed.

In complex tasks involving multiple kinds of mental activities, executive functions plan the sequence of mental steps and schedule the various activities, switching attention as needed. Voluntary control, like attention, can only do one thing at a time. It can initiate a multiplicity of movements or a sequence of activities, but these, once

[273] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.

initiated, become automatic. The executive system can be overloaded if it has to work on unrelated goals at the same time, especially if the goals conflict with one another.

There are rich connections from the frontal lobes (areas 9 and 10) to the area that controls the motor functions of speech (44 and 45), as well as to the frontal oculomotor field for voluntary conjugate movement of the eyes (area 8) as well as connections to the hypothalamus and brain stem.[274] These anatomical connections imply that voluntary control of the eyes and speech, as well as the initiation of other voluntary movements is coordinated from these areas (9 and 10). We can think of these areas as the seat of free will only in the sense that voluntary actions are initiated here. For this purpose, these two areas have rich connections to the other three lobes[275] and have access to all memory systems to enable them to activate useful information in the context of deciding a future course of action from several alternatives. Motivational and emotional processes are in place to help direct the organism to more favorable outcomes, and strongly influence free will. So the will is free, but it is not as free as it seems.

The hippocampus has strong projections to and from the prefrontal area. It has been strongly implicated in forming memories about relations between stimuli, regardless of the kinds of relations. The relations can be among different memories or memories about spatial arrangements. The hippocampus, with signals from the prefrontal areas, helps activate these related, stored memories. The hippocampus with its strong connections to the amygdala (basal nucleus) will provide information about emotional context.

Aside from thalamic projections, the amygdala's output is fine tuned by other afferent projections from several areas: the medial prefrontal cortex (which includes the anterior cingulate and orbital area) as well as the infralimbic and prelimbic cortex which interact with the amygdala [central nucleus], and the brainstem outputs to the central nucleus. These afferent projections allow cognitive functions organized in the prefrontal regions to regulate the amygdala and its emotional reactions.[276]

The so-called where and what visual pathways are also connected to the prefrontal area. The where pathway involves impulses from the primary visual cortex to the temporal cortex, and the what pathway goes from the primary visual cortex to the parietal lobe.[277] This allows the "what" and "where" to be brought to bear in the decision process. The shifting of attention by the thalamus is involved in directing the "what" pathway and in this manner selects what the "what" is at a given moment.

In a careful orchestration of signals, the prefrontal cortex sends handshakes to all memory systems, which echo signals to the thalamus to be prepared for action (by sending signals to the motor areas to start the general movement to approach or flee) and/or shift attention, and signals the hippocampus to activate related memories needed for the task at hand. Once all the activities necessary for a decision have been implemented, the prefrontal cortex initiates action by controlling speech and eye movement and sending signals to the brain stem to be prepared for signals from the motor cortex.

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[274] Ibid.
[275] Ibid.
[276] Joseph LeDoux, *The Emotional Brain.*
[277] Francis Crick, *The Astonishing Hypothesis.*

It has also been determined that the prefrontal area can activate cells in the where pathway.[278]

The activation of all the subsystems mentioned is called by some, working memory: a memory that holds for short periods of time the relevant stimuli and memories to achieve some end. The classical brain area implicated in coordinating all this is the lateral prefrontal cortex (area 46 adjacent to areas 9 and 10). Depending on the task at hand (interpreting a stimulus, response selection, conflict resolution or decision making), the working memory circuit engages different areas of the prefrontal cortex to different degrees.[279]

By focusing attention, the proper mental resources are allocated to the task at hand. The executive function keeps lower levels engaged in activities that support the task. However, if the lower level subsystems detect some event that is unrelated to the current task but is more important than the current task (generally determined by the activation of an emotion), resources are allocated to processing the new event. Attention shifts and new memories related to this emotion are activated.

Even though the result of executive functions (monitoring, resource allocation, task management, conflict resolution, memory retrieval and so on) enters working memory, it is important to recognize that these executive processes function outside awareness.

8
Were You At Our Tennis Match this Morning?

Consider the simple case of a tennis doubles match. Your opponent serves to you at a modest one hundred miles per hour. While the ball is approaching, you have to decide to go cross-court, down the line, or lob. You also need to decide if you will do this with a forehand or a backhand shot; and once you decide that you are going cross court with a backhand, you also need to determine if it will be an under spin or top spin shot.

Then, from the corner of your eye, you detect a slight motion, perhaps just a hint of the net man leaning towards the center of the court indicating his intention to poach. In that split second, you change your mind, and change your body motion, primarily the orientation of your shoulders so you can execute a shot down the line to take advantage of your opponent's movement.

Experiments on the subjective evaluation of the interval of time that represents the present indicate that this "present" is about three seconds long: all else is mere reminiscence or anticipation.

How finely can we divide this little three-second present? The shortest perceivable time division – called the fusion threshold – is between two and thirty milliseconds, depending on the sensory modality. Two sounds seem to fuse into one if they are separated by less than two to five milliseconds. Two successive touches merge if they occur within ten to twenty milliseconds of one another, while flashes of light blur together if they are separated by less than twenty to thirty milliseconds. Humans consider

[278] Ibid.
[279] Daniel L. Schacter, *Searching For Memory*.

two events as presently perceived if their temporal separation is between three milliseconds and three seconds.

Consciousness has many definitions. The philosopher John Searle defined it as, "Consciousness consists of those states of sentience, or feeling, or awareness, which begin in the morning when we awake from a dreamless sleep and continue throughout the day until we fall into a coma or die or fall asleep again or otherwise become unconscious.[280] I try to avoid the use of the word unconscious because of the multiple interpretations the words has. In the context of the model presented here, consciousness is the capacity of the brain to experience perception and cognition explicitly through the attentional systems, what is called perceptual consciousness (as opposed to reflective consciousness) by others.[281]

Antonio Damasio of the University of Iowa differentiates core and extended consciousness. Core consciousness is all about the here and now through sensory awareness. Extended consciousness requires a sense of self, a self-referential aspect that includes the past and the anticipate future. As we have seen, this difference resides in how the attentional systems are focused: whether they are focusing externally or internally, respectively.

Benjamin Libet has done extensive experiments demonstrating that a stimulus must last about 500 milliseconds before producing a conscious sensation. He has also demonstrated that this is also true independent of the abnormal route of activation following stimulation directly at the sensory cortex. Even when electrode contacts were located in the medial lemniscus leading into the thalamus (for therapeutic purposes), the time requirements to produce a conscious sensation were the same. Logically, the longer the path a signal travels, the longer for a response in the cortex, the event-related potentials (ERPs). With a stimulus to the hand the ERP begins after a delay of 14-20 msec, where a signal from the foot may take 40-50 msec.

A striking feature of the ERP is that it is neither necessary nor sufficient for eliciting a conscious sensation. A conscious sensation can be elicited with a weak stimulus applied to the surface of the sensory cortex without eliciting an ERP. A single stimulus on any part of the specific sensory pathway *that is located in the brain* does elicit an ERP response of the sensory cortex, but doesn't elicit any subjective sensation at all.[282] The ERP is the nervous pulse that activates the handshake signals, and when an electrical stimulus is applied directly on the sensory cortex it takes the place of the handshake signals.

However, if a sensation on the skin lasts less than 500 milliseconds, an enormously long time compared to the 10-20 milliseconds of transit time required for the nerve signal to travel to the cortex, the stimulation is not consciously perceived. This does not mean that a skin shock has to be at least half a second long in order to be felt, but only that the handshake signals produced by skin shock at the cortex must last at least a half second before the skin shock can become part of the conscious experience. If we had to wait half a second before experiencing what we touched, our tactile sense would be useless for all but the slowest of physical activities. Typical tactile reaction times are on the order of 100 milliseconds – the time it takes to perceive a touch and push a button.

[280] Christof Koch, *The Quest for Consciousness.*
[281] Donald R. Griffin, *Animal Minds.*
[282] Benjamin Libet, *Mind Time.*

How can we reconcile the observation that 0.5 second of neural activity is needed to build up a conscious touch sensation with the fact that we can feel a touch and take action five times faster than the time these perceptions are required to become conscious?[283]

Axonal spikes travel down a neuron at speeds of 1.5 to 90 millimeters per millisecond, depending on the type of neuron and whether the axon is myelinated or not. In 20 milliseconds this is equivalent to the spike moving between three and 180 centimeters (roughly one inch and six feet respectively). Messages between different areas of the cortex travel at speeds of 1.5 to 5 millimeters per millisecond. Messages traveling down the spine move at speeds between 20 and 90 millimeters per millisecond. A neural message takes about the same time to go from one half of the brain to the other as it does to travel all the way down to the leg.

What seems to be going on is this: the tactile signal reaches the cortex in about 10-20 milliseconds and is not consciously perceived. But this arrival time is unconsciously noted[284] by the thalamus with a tag. If the cortical activity due to the tactile stimulus is not disrupted and is allowed to proceed for the minimum time adequate to produce a conscious sensation (about 0.5 seconds), the touch is registered as part of the ongoing flow of awareness (becomes part of conscious experience). However, the touch is not experienced 0.5 seconds later: it is instead "referred" to the previous time indexed by the initial pulse arrival at the thalamus. It is as if the initial tactile pulse sets a "marker" in time, and this "marker" is redeemed if future cortical events produce enough sustained neural activity to promote the touch signal into awareness (consciousness).[285]

Subjective referrals of the spatial and temporal features of a sensory event have the effect of subjectively correcting the neuronal distortions of the sensory event. The distortions are imposed by the way in which the neurons represent the event, both in space and in time. So in our conscious experience of a sensory event, the event seems to occur when it actually happened, instead of 0.5 sec. later (when we, in fact, became aware of the event).[286]

This parallels Kornhuber's arguments made in 1965, that there is brain activity almost one second before the subject makes a decision to move. One second is a long time on the neural scale, certainly much longer than the time from the neural impulse to traverse from the motor cortex to the muscles. In his words, "The readiness potential far antedates the subject's decision to make a movement."[287]

Awareness is a constructive process that requires neural activity lasting half a second, but is a continuous on-going process. It is different to measure a small tactile stimulus and the brain's response to it than to measure the brain's activity as a response to the on-going stimuli received by all sensory pathways. The real world is not made of isolated impulses lasting less than 20-30 milliseconds. Just like movies have 30 frames per second, it doesn't mean we see a jerky motion with 30 jerks per second. We see a continuous movement. The brain fills in the gaps and spaces. Of course evidence of subjective awareness is an introspective report of awareness by the individual who has the experience of it. Some short-term memory formation must occur for the subject to

[283] Nick Herbert, *Elemental Mind.*
[284] Ibid.
[285] Ibid.
[286] Benjamin Libet, *Mind Time.*
[287] Nick Herbert, *Elemental Mind..*

recall that awareness and report it. Some have argued that the 0.5 –sec duration of activities for awareness is simply a reflection of the time it takes to produce a short-term memory trace of the event (see Dennett discussion on Libet, 1993).[288]

There exist certain types of amnesia (I experienced this on one occasion after getting hit in the head) where new memories can't be formed, yet the immediate past (about 30 seconds or less) is recallable. The individual in this condition is clearly aware, even of his memory shortcomings and his incapacity to form new memories. It is this very short-term or working memory that is involved in awareness.

An alternative way of looking at this is that an echo (the memory of the sensation) was matched to the incoming sensory signal; the signal was mirrored to the area where the echo originated, and the appropriate handshakes were sent out to activate the related circuits, and only after all this is accomplished will the brain perceive the stimulus. It is not that the stimulus wasn't received in the cortex, but that it is only later perceived.

Small lesions to the brain stem or the intralaminar nuclei of the thalamus produce a coma.[289] It could be argued that the echoes and signals cease to be matched and loss of consciousness is the result. This does not mean that the intralaminar nucleus is the seat of consciousness, but just a necessary component.

In classical conditioning, a conditioning stimulus (CS) is presented just before and during the unconditional stimulus (US). The CS can be a tone that does not produce a response initially; the US can be an air of puff to the eye that elicits an eye-blink response. After some trials of this combination, the subject responds with an eye blink to the tone alone. That of course requires a memory process for the CS-US relationships. This simple delay conditioning is intact even in animals with bilateral hippocampal lesions. An echo to blink when a puff of air hits the eye is long established, another echo to blink is established when it is continuously matched to a CS (a tone). There is no memory involved per say, just a matching of sensory incoming signals with echoes that trigger responses automatically. In trace conditioning the CS is arranged to end about 500 to 1000 milliseconds before the onset of the US. Animals with bilateral hippocampal lesion fail to acquire trace conditioning. Amnesic patients with damage to hippocampal lesions fail to acquire trace conditioning but are able to learn standard delay conditioning.[290] In trace conditioning a memory relationship has to be established, which is impossible with hippocampal damage.

A case for free will (at least for moving our bodies under certain conditions) can be made analyzing a tennis match. First, consider that every decision by each player to make a particular shot is made independently, completely unbeknownst to his partner and two opponents. They in turn only have fractions of a second to choose what to do in response to a returning shot. After executing their choice of shot, you now have a fraction of a second to decide your response, but ultimately you do choose from several choices, perhaps constrained by your abilities. Every split second, before answering each shot, every player makes a free will choice as to what he will do. There is nothing preordained in how each point will develop.

Back to our tennis game. My opponent serves at 100 miles per hour, which is the equivalent of 146.5 feet per second. The court is 72 feet long, so, roughly, I have about

[288] Benjamin Libet, *Mind Time*.
[289] Penfield W. *The Excitable Cortex in Conscious Man.* Liverpool: Liverpool University Press. 1958.
[290] Benjamin Libet, *Mind Time.*

0.5 seconds to respond between the time he hits his serve and the time the ball reaches me. My vision could potentially process about 16 “snapshots” (of 30 milliseconds each) to calculate where the ball is going to be when the time comes for me to hit it (one snapshot about every 4 feet). I don’t see a strobe light effect of a ball every four feet; instead, my brain fills in the details and I see the ball in a perfectly continuous trajectory. In that half second I have to decide everything mentioned earlier.

If I change my mind at the last split second and decide to go down the line as my opponent tries to poach, this decision has to be made about 100 milliseconds (as the ball hits the court and bounces towards me) before I make contact with the ball. Both my opponent and I wait until the last possible moment, he to move and me to change my shot. Part or all of this decision process was done outside awareness, “referred” back to the sequential times when the sensations arrived in the cortex.

I, however, vividly feel that I consciously experienced all this; that I saw my opponent move about 100 milliseconds before I hit the ball, and that I was a direct participant in this last split-second decision and shifted from a cross-court to a down-the-line shot. I am aware that I changed my mind (and my motions) as a consequence of the movement I detected about 100-200 milliseconds (three or four visual snapshots of 20-30 milliseconds each) before hitting the ball.

Consider also that when my opponent serves to me, the sound of the ball as it is hit by his racquet (traveling at the speed of sound of roughly 800 feet per second) takes roughly 90 milliseconds to reach my ear. I, however, experience the sound as being in synchronization with what I am seeing and not as the sound happening when the ball is almost one quarter of the way towards me. I experience the sound simultaneously with the visual image of the racquet touching the ball, even though this is physically impossible. And also, the sound of the ball hitting the ground is not experienced when the ball reaches me, but when the ball hit the ground. Again, I am “referring” in time the information relayed by my senses so that I experience reality as it really is, as my experience dictates, not as the information reaches my senses. Also, this reality is experienced as being “out there,” not inside my head.

After my opponent serves, the sight of the ball automatically triggers a memory of the expected trajectory, there is no time to perform a calculation. This memory recalls a sequence of muscle commands that have been well rehearsed. This sequence is stored in memory and can be adjusted within certain limits. If the serve is outside these limits, we cannot answer the serve.

A good experiment would be to film tennis players and determine how late can they change their mind about a particular shot, and still execute it without error. While I wait for my opponent to serve, I try to relax. This puts my brain in an optimum state to not favor some echoes over others, to not obstruct all the echoes stored in memory. While my opponent’s body goes into motion as he starts to serve, I can begin to “read” his intentions. Then as the ball begins a trajectory towards me, using all possible clues, such as speed, spin and so on, my brain determines with certain degree of accuracy where the ball will be when it reaches me. All these visual signals will be matched to stored echoes, which will activate (through handshakes to the various motor areas) the possible motions that my body will make to place my body in the best possible position to hit the ball. The more experienced a player, the more echoes stored, and the more exact the response will be. If the trajectory falls into a well established (and practiced) zone, the response will be

very smooth. Many athletes report that if they try to "think" about what they are doing they perform less well than when letting their bodies do "it."

Watching professional tennis players receive serve, it is easy to observe that they begin the motion to return serve, sometimes even before the server hits the ball, because they can "read" the serve by the server's body motion. Occasionally, when there is a "let" serve (the ball touches the net but falls into the service area) the receiver has enough time to change their movements from returning the serve to catching or stopping the ball. This seems to indicate that between the time the ball touches the net and reaches the receiver (about 250 milliseconds or less) there is enough time to change your mind and initiate a new action, seemingly before it can be consciously reported.

Typically a tennis player gets ready to answer an opponent's shot, especially when it is within reach. Similarly, if the return shot is on a trajectory that will take the ball out of bounds and is within reach, there is a brief time period (again, about 250 milliseconds or less, depending on how hard it was hit) to determine that this is so, and refrain from hitting the ball or calling, "out," to your partner so he won't hit the ball. When the ball is approaching too fast, within reach, and the time period is less than 100 milliseconds, it becomes impossible to refrain from trying to answer the shot.

Immediately after hitting a winning shot, sometimes within one or two steps (about 100-200 msec.), body language -- positive emotional expressions, such as fist pumping or jumping high -- is initiated, which proves that this knowledge was processed. Likewise, when a bad shot is hit, negative emotional expressions are manifested, like slumping or dropping the tennis racquet. This shows that the brain can process this information in less than 100 msec, and can trigger the appropriate emotional response within 100-200 msec.

According to the arguments presented, neurologically speaking, between 100-250 milliseconds can be the latest that one can change his or her mind. If I change my mind later than that, the result will be a strange movement, that is partially the original intent, mixed with the new intended movement, resulting in a completely botched shot

In experiments with subjects presented with pictures associated to "good things" and "bad things," it has been determined it takes about 120 milliseconds to activate the regions in the ventromedial prefrontal region that react to unpleasant or pleasant stimuli.[291] Can it be that to feel consciousness requires about the same time or more to be activated? However, there are numerous movements and reactions that need to be coordinated in 10-20 millisecond time responses.

Retroactive or backward masking between two peripheral sensory stimuli has long been known. When a visual stimulus consisting of a small weak spot of light, a stronger larger flash that surrounds the first one can block the subject's awareness of the first one. The second flash has this effect even if it is delayed by up to 100 milliseconds after the initial weak flash.[292]

Retroactive masking has also been reported for electrical stimulation of the skin.[293] With a test stimulus at threshold strength on one forearm, a suprathreshold

[291] Daniel Schacter, *Searching For memory.*
[292] B. H. Crawford. *Visual adaptation in relation to brief conditioning stimuli.* Proceedings of the Royal Society Series B (London) 134;283-202.
[293] A.M Halliday and R. Mingay. *Retroactive raising of sensory threshold by contralateral stimulus.* Quarterly Journal of Experimental Psychology 13:1-11. 1961.

conditioning stimulus on the other forearm raised the threshold for the test stimulus. The conditioning stimulus was effective even when it followed the test stimulus by 100 milliseconds, but not when it followed by 500 milliseconds. This establishes that the masking takes place at the level of the brain rather than in a peripheral sensory structure, but must occur close to the 100 millisecond interval. A delayed cortical stimulus can mask or block awareness of a skin pulse when it is applied between 200-500 milliseconds later. However, cortical trains lasting less than 100 milliseconds, or single pulses, were not effective for this retroactive inhibition.

The dynamics of calcium in thick dendrites and cell bodies spans the right time scale (on the order of hundreds of milliseconds) for perception. Indeed, it has been established experimentally in the cricket, that the concentration of free, intracellular calcium in the omega interneuron correlates well with the degree of auditory masking, a time-dependent modulation of auditory sensitivity in these animals (Sobel and Tank, 1994.)[294]

Measurements of reaction times to respond by pressing a button as quickly as possible after the appearance of an agreed signal were between 200-300 milliseconds.[295] With training, I believe this reaction time can be reduced. Reaction times are examples of free will (to choose to press a button). It is necessary to take into account the neuronal activity preceding the measurement of reaction times because it is during this period that the echoes to anticipate pressing a button are activated. The free will is independent of the awareness to do so, or the awareness of pressing the button. The decision to press a button with the appearance of the agreed signal, antedates the neuronal process of reacting to the signal, pressing the button and becoming aware of doing so.

Returning to tennis players: the motion to produce a topspin forehand can be a memorized (practiced) motion, and the cross-court or down-the-line shot might be a small variation (changing your feet and shoulders) of this movement, and these movements might be outside consciousness, but we know what the correct motion feels like, and we know that we voluntarily changed our shot at the last split second. We couldn't have been conscious (thinking) in the real sequential times (or at all) of all events (the sounds and images matched to the echoes) that our senses relayed to us. If our movements weren't well practiced (memorized), we would not have had time to coordinate all the signals our brain relayed to our muscles to achieve the cross-court shot, much less, when at the last split second we changed our minds and went down the line. We can only produce shots that we have stored in memory either through practicing, or less frequently, through watching others. Novice players continuously attempt to execute motions that work when the ball is in certain zones, even when the ball is out of those zones, and they consequently miss the shot.

Because of the phenomena called "referred in sequential time," everything was presented to our consciousness in the correct temporal sequences, and sights and sounds were synchronized to match our experience. We couldn't have been conscious in real

[294] Christof Koch, *The Quest for Consciousness.*
[295] Benjamin Libet, *Mind Time.*

time; however it feels like we were there, and didn't miss a thing! The brain is a great illusionist. Subjective time need not be identical to neuronal time.[296]

There is the free will to decide to make a number of particular shots, but only within narrow constraints. The process leading to producing a voluntary shot is initiated by the brain before any awareness of the movement. We can only produce shots according to the echoes stored, matched, and activated by our opponent's movements and the trajectory of the ball. Any decision to do anything else will produce a "bad" shot. Additionally, if we have never seen a particular trajectory, or our opponent makes movements we have never observed, no echoes will match the incoming signals and the cascade of neural activity that will produce the right movements is not initiated, or at best, executed incorrectly. In other words, we simply won't be able to return the ball.

Professional tennis players (that can hit balls above 100 miles per hour), have about one second between shots (0.5 sec for the shot to travel to the opponent's base line and 0.5 sec for it to return). This means that from the moment they hit the ball, they have to finish the motions they used to return the ball, stop, set themselves and get ready to respond with a second shot. Careful observation shows that they do all this, even when they "know" that the opponent won't be able to return the shot. This reinforces the observation that to change the course of their actions requires 400-500 msec of neural processing. Interestingly, when a player hits what they consider a winning shot (it takes 500 msec for the ball to travel to the opponent's base line) but the opponent makes an extra effort and manages to somehow return the shot, the player misses the next shot, even when it is a relatively easy shot. Once the player felt (decided) their shot was a winner, he or her initiated the process of "stopping play." Once this decision is carried out, yet, unbelievably to the player and most spectators, the ball is returned, it requires (400-500 msec) to "resuming play." This explains neatly why the player in this mental state executes a missed return. It also explains why all coaches insist on training to never assume a point is over and continue play even when the ball is "out" (the umpire might call it incorrectly). With such training, echoes are set in memory, which will guide the continued play even though it might seem to be over.

The will to win can be instilled by proper training: the echoes set in memory to never give up and to not stop play. This is the belief that a player needs in order to win. The interaction of the sensorimotor system (moving the body, having the correct grip on the racquet, making the racquet an extension of the body, executing the correct motions when making contact with the ball, and so on) with the other sensory modalities (mostly vision and sound to track the ball, the opponent, and "know" where the boundaries of the court are) and with the will (free will) to win and the appropriate training (setting the echoes in memory to guide action) all come together and when perceived by the brain are felt as consciousness. Consciousness is what it feels to be here, to perceive ourselves through our memories and feelings, what it feels like to perceive the world.

The conscious will (W) does appear 150 msec before the motor act, even though it follows the onset of the cerebral action (RP) by at least 400 msec. That allows it, potentially, to affect or control the final outcome of the volitional process. (Actually only 100 msec is available for such effort. The final 50 msec before a muscle is activated is the

[296] B. Libet, W. Wright, Jr. B. Feinstein and D. K. Pearl. *Subjective referral of the timing for a conscious sensory experience: a functional role for the somatosensory specific projection system in man.* Brain 102:193-224. 1979.

time for the primary motor cortex to activate the spinal motor nerve cells, and through them, the muscles. During this final 50 msec, the act goes to completion with no possibility of its being stopped by the rest of the cortex.)

The conscious will could decide to allow the volitional process to go to completion, resulting in the movement itself. Or, the conscious will could "veto" the process, so that no motor act occurs. The conscious decision to veto could still be made without direct specification for that decision by the preceding unconscious processes[297] (the echoes going from the cortex to the thalamus). So at minimum, we are free to do or not to do. Many acts like driving a car become automatic and can be performed in a seemingly effortless fashion. As these acts are going on, no awareness or volitional control of them is necessary.

The voluntary appropriate motion begins with a series of echoes matching the visual sensory stimuli received at the thalamus. These echoes are used to calculate the projection and speed of the trajectory and determine where body and ball can meet. Thus many echoes, simultaneously, begin to select which movements are possible (according to the visual signals) and initiate action. The feeling of consciousness arises when the brain perceives thoughts as the cause of the action, or as it remembers the recent experience.

What about a voluntary decision to act (like writing this book)? Write, leads to sitting down, to thinking about the subject. It does not originate with a sensory signal (like a tennis ball approaching), but originates with the act of focusing attention on an idea. This begins a cascade of brain processes, which through handshakes activates many memory systems. Attention allows the brain to capture, here and there, briefly, an emerging idea. Speaking or writing it down requires an extra effort; an effort that can improve the results through repetition and practice; similar to how an athlete improves his performance with practice.

In certain situations we can act with free will and control of whether to act. A simple example of this was employed in an experimental study (Libet et al, 1993, 1994)—the conscious will to flex the wrist in a freely capricious manner. This provides a kind of prima facie evidence that mental processes can actually control some brain processes. Of course, the nature of this experience must be qualified. His experimental findings showed that conscious free will does not initiate the final "act now" process; the initiation occurs unconsciously. But conscious will certainly has the potentiality to control the progress and outcome of the volitional process. Thus, the experience of independent choice and of control (of whether and when to act) does have a potentially solid validity as not being an illusion.

Fast responses to sensory signals are developed unconsciously (below awareness). These are evident is almost all sports activities, but also in everyday responses to danger signals. There is experimental evidence that responses in test to reaction times are made unconsciously. The origin of words being spoken as well as the playing of musical instruments, especially for fast runs of notes must be unconscious in nature.

Perceptions that never reach awareness have an impact on later neural processes. In patients recovering from general anesthesia (Bennet et al, 1985; Bonke et al., 1986), vocal expressions in the operating room that were not consciously heard and could not be recalled later still had an impact on the patients' responses after recovery.

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[297] Benjamin Libet. *Time Mind.*

A curious twist to the idea of free will is presented in what is called alien hand syndrome. Alien hand syndrome is a loosely defined cluster of symptoms characterized by involuntary movement of an upper limb in conjunction with the experience of estrangement from or personification of the movements of the limb itself. Alien hand syndrome was initially used to describe cases involving a disconnection of the hemispheres via corpus callosal lesion. The term alien hand syndrome requires only the "feeling that one limb is foreign or "has a will of its own," together with observable involuntary motor activity. The term has been defined as involuntary movement occurring in the context of feelings of estrangement from or personification of the affected limb or its movements.[298]

Patients suffering alien hand syndrome may find that the hand and arm on the affected side perform curious purposeful actions, such as undoing a buttoned shirt when the subject is trying to button it up. All this occurs without, or even against, the subject's intention and will.[299] A well-known (popular) case is that of Peter Seller's character in the movie *Fail Safe*, directed by Stanley Kubric. In the movie, the president's (of the U.S.A. is Peter Sellers) right hand involuntarily and unpredictably rises and does a "Heil Hitler" salute.

At present, there seem to be three broad clusters of behavioral and subjective symptoms subsumed under the diagnosis "alien hand syndrome." The patient in this study and other examples suggest that posterior alien hand syndrome may not be as closely associated with focal, critical lesion sites as its callosal and callosal-frontal counterparts (callosal and callosal plus medial frontal lesions). Rather, it seems to be a disorder of involuntary movement in the context of alterations in body schema sufficient to cause feelings of estrangement from those movements. These symptoms may arise independently from one another and may arise from either single or multiple lesions.[300]

Another curious example of free will is people with Tourette's syndrome. They uncontrollably exhibit urges to produce vocal outburst, often with obscene language and other abnormal behavior. Brain imaging studies (Wolf et al, 1996) have found that the caudate nucleus is involved in this malady. The caudate appear to be involved in organizing intentional movement. In persons with Tourette's syndrome, the caudate exhibits a heightened sensitivity to dopamine.[301]

These cases show that each hemisphere has their own set of echoes and these in turn can generate actions without volition or even against one's own will. The echoes are stored at a level below awareness.

When the brain detects an emotion (a particular body state), it is experienced as a feeling. Similarly, the feeling of thinking or paying attention is what the brain interprets as consciousness. There is a difference between a programmed, deterministic mechanical response and the mental process we call consciousness. Consciousness is more than perceiving and knowing; it is knowing that you know. *The brain feels conscious when it*

[298] T. Bundik Jr., M. Spinella, *Subjective experience, involuntary movement, and posterior alien hand syndrome.* J Neurol Neurosurg Psychiatry 2000;68:83-85 (January).
[299] Benjamin Libet. *Time Mind.*
[300] T. Bundik Jr., M. Spinella, *Subjective experience, involuntary movement, and posterior alien hand syndrome.* J Neurol Neurosurg Psychiatry 2000;68:83-85 (January).
[301] Benjamin Libet, *Mind Time.*

feels, when it is thinking, and when it knows, when it remembers, and when it exercises volitional action.

In these last two chapters I have been trying to argue that human consciousness (of the reflective kind) is a lot less than what we like to think, and that animal consciousness (at least of the perceptual kind) is a lot more than we tend to give them credit for.

It is impossible to deny that most animals (vertebrates, at least, but perhaps other genus as well) have a perception of the environment and their bodies. After all they do move, and they navigate through the world. How finely can they determine what is out there, or exactly what their bodies are doing while they are moving is an open discussion. I would venture to say that when an animal moves, and when we consciously decide to move, our nervous systems are performing very similar actions. We are not necessarily conscious of the exact sequence in which our muscles moved, nor even of the small changes of the ground under our feet, or even of the seeming movement of the world as we move through it, but we definitely must have some awareness (perceptual consciousness) in the form of a neural representation of our bodies and the space around us.

As I have argued in previous chapters, memory systems increase (evolutionarily) to deal with ever finer and more complex interpretations of our sensory signals. Ultimately, these expanded memory systems are co-opted for other uses. The hearing memories to produce speech and "spoken" thoughts, the visual memories to produce "visual imagery" and to "turn objects in our minds eye," both of which are variations or modes of thinking. As we move up the evolutionary ladder, as animals develop more complex memory systems, at which point is reflective consciousness enacted, is anybody's guess. Exactly how animals think might be very hard to determine. How do bats perceive the world through echolocation? Do dogs see the past while they are sniffing the environment? Do they know how long ago someone walked by? Do they race tracking a smell to ultimately join the past to the present as they rush to meet the subject that left the trace? The relation between perceptual consciousness and reflective consciousness is probably just one of degrees. Consciousness is simply an expansion of cognition and the memory systems that evolved to aid the senses.

9
Right, Left

There are asymmetries in the brain, not only slight differences in the anatomy of each hemisphere, but also in functions. There is some variability of the sulci and gyri in the two hemispheres. Whereas we are bilaterally symmetric, at least on the outside, this symmetry is not perfect; the left hand is not exactly the mirror image of the right hand. And we definitely are not symmetrical in the disposition of our internal organs, the heart on the left side being a good example.

In general, the left hemisphere controls the right side, and the right hemisphere the left side. The right hemisphere controls the hand and fingers of the left; the left hemisphere controls the right. Both hemispheres, however, dictate the movement of the

upper arms. Moreover, there are myriad functions the brain performs that do not involve bilateral pairs, i.e., a left and a right eye, or foot, or ear, etc.

The brain evolved greater efficiency and speed when performing tasks that do not require bilateral pairs (i.e., language, reading, mathematics, recognizing objects, etc.) by concentrating the task to adjacent neurons in one hemisphere, and foregoing the time consuming (10-20 milliseconds) contralateral communication. Having adjacent neurons form clusters that specialize in particular functions is more efficient than splitting the task into two areas, one on the left and one on the right. However, many functions located on one side are complemented by other functions performed on the opposite side.

The anatomical allocation of certain major functions to particular areas of the cortex is approximate and varies from individual to individual. In other species, the lateralization of functions is much less; so some of the brain studies of other animals cannot be used to infer the same functions in Homo sapiens.

One of the many known asymmetries is that we find the region involved in sensory-motor integration on the right side, while the supplementary motor cortex on the left side controls both sides of the body to a much greater extent than the right supplementary area.

During explicit retrieval, an increased blood flow, particularly in the right frontal lobe, reflects the effort involved in searching memory. The right frontal lobe sends handshakes with tags to many areas of the cortex. This search for related handshakes to the required retrieval quest is slow and methodical. These handshakes will activate more potentially related echoes that will in turn be projected to the hippocampus. The hippocampus with its ability to activate many neurons simultaneously will increase the likelihood that a match will be found and retrieved.

PET scans have confirmed that the left hippocampus and other medial temporal lobe structures are involved in accurate retention of the general meanings of words on a list.[302] This probably has to do with the fact that language and speech are generally a left hemisphere specialization, primarily in Broca's area, including semantic, phonological and syntactic processing.

Based on lesion data, prosodic processes have been related to right hemisphere function. However, linguistic pitch discriminations, as applied to lexical discrimination by native speakers of tone languages, activate the left inferior frontal lobe.[303]

Affective aspects of language, such as intonation (or prosody) are represented in the right hemisphere, and rather strikingly, the neural organization of the affective elements mirrors the organization of the logical content of language in the left hemisphere. Damage to the right temporal area corresponding to Wernicke's area in the left temporal region leads to disturbances in comprehending the emotional quality of language, such as appreciating whether a person's tone of voice convey sadness or happiness.[304]

The right hemisphere excels at visual motor tasks. Using fMRI to compare prefrontal activation elicited by verbal and nonverbal material during encoding and during retrieval showed greater left inferior prefrontal activation for verbal encoding and

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[302] Daniel Schacter, *Searching for Memory.*
[303] Ralph-Axel Muller, Natalia Kleinhans and Eric Courchesne, *Broca's Area and the Discrimination of Frequency Transistions: A Functional MRI Study.*
[304] Eric Kandel, James Schwartz, Thomas Jessell, *Principles of Neural Science.*

retrieval, whereas nonverbal encoding and retrieval resulted in greater right inferior prefrontal activation.[305]

Most people's right hemisphere cannot handle even the most rudimentary language. Nevertheless, in at least one case of split-brain surgery, one patient developed the capacity to speak from the right hemisphere – thirteen years after the surgery. This patient can now speak about information presented exclusively to the left or to the right hemisphere.

When presented with new information, people usually remember much of what they experience. When questioned, they also usually claim to remember things that were not truly part of the experience. If split-brain patients are similarly tested, the left hemisphere generates many false reports, whereas the right hemisphere does not; it provides a much truer account.

Interesting findings in other split-brain patients, suggest that the left hemisphere seeks the meaning of events. It constantly looks for order and reason, even when there is none, which leads it to continually make mistakes. The left hemisphere excels at developing schemata and has the ability to determine the source of a memory, based on the context or the surrounding events. The left hemisphere actively places its experiences in a larger context, whereas the right simply attends to the perceptual aspects of the stimulus. It has been demonstrated that the left prefrontal regions of normal subjects are activated when they recall false memories.

A region in both the right and left hemispheres is active when a false memory is recalled; yet, only the right is active during a true memory. False memories are constructed in the left hemisphere, reflecting an error in the reconstruction of past experience.

The left hemisphere seeks explanations for why events occur. The right hemisphere does not try to interpret an experience and find deeper meaning. It continues to live in the present. It appears that the inventive and interpreting left hemisphere experiences events very differently from that of the truthful, literal right brain.[306] However, the richness of the experience is the sum of both, even though the left brain's experience might seem to surpass that of the right.

The principles underlying hemispheric specialization are still poorly understood. Using functional magnetic resonance (fMRI) during tasks such as letter and visuospatial decisions with identical word stimuli, researchers determined the following: first, hemispheric specialization depended on the nature of the task rather than on the nature of the stimulus; second, analysis of front candidate regions for cognitive control showed increased coupling between the left anterior cingulate cortex and left inferior frontal gyrus during letter decisions, whereas right anterior cingulate cortex showed enhanced coupling with right parietal areas during visuospatial decisions. Cognitive control is localized to the same hemisphere as task execution.[307]

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[305] A.D. Wagner, R.A. Poldrack, L.L. Eldrige, J.E. Desmond, G.H. Glover, & J.D.E. Gabrieli, *Material-Specific Lateralization of Prefronta Activation During Episodic Encoding and Retrieval.*

[306] Michael S. Gazzaniga, *The Split Brain Revisited.*

[307] Stephan K.E., Marshall J.C., Friston K.J., Rowe J.B., Ritzl A., Zilles K., Fink G.R., *Lateralized cognitive processes and lateralized task control in the human brain.*, Science. 2003 Jul 18;301(5631):384-6.

Apraxia (difficulty producing skilled, complicated movements) is caused by damage to the left frontal lobe, but problems generally occur with both the right and the left hand. The left hemisphere processes instructions for carrying out complex movements with both hands.[308] Regions in the left lateral surface are involved in speech, writing, understanding language, figure drawing and reading.[309] Since speech and writing also involve fast, intricate, carefully coordinated movements, this might indicate a relationship, evolutionarily, between movement and language, between communication with gestures and hand movements and speech. The left side medial surface is involved in organizing reading as well as movement in relation to language.[310] Different cultures use hand gesticulation in various forms, which seems to indicate that this is a learned behavior, much like speech. The differences in hand gesticulation can be as notorious as the differences in spoken language, such that careful observation of hand and body movement (without hearing the spoken language) might be enough to determine the culture of the individual in question.

In almost five per cent of right-handed people language is located on the right side. Handedness and language dominance are undoubtedly associated, right-handers being more likely than left-handers to have language in the left hemisphere. Almost twenty-five per cent of left-handers have language on the right side. Left-handers are about four or five times more likely than right-handers to have language located in the right hemisphere.

We tend to talk about handedness (left or right), but it might be better to talk of sidedness. If sidedness were decided randomly, then the chance of finding each function on one side or the other would be equal. In humans, we are mostly right-handed, but the one-in-ten left-hander doesn't necessarily have everything else reversed in his or her brain. It is more efficient to master certain tasks with one hand, especially if the task only requires one hand, like writing or hammering. This, of course, doesn't mean that the non-dominant hand cannot learn to do complex activities.

Observations of gorillas and felines show that individuals have a consistent preference for using the left or the right hand or paw, respectively. However, half are right-handed and half left-handed. About half of chimpanzees in the wild prefer their right hand and half their left. When given more exacting tasks, the tendency to use their right hand increases to about sixty per cent, particularly in bimanual tasks where one hand supports and the other acts upon the object. In the case of mice, right-handedness dominates, but slightly less than in chimpanzees (about fifty-five per cent). Only humans show a very distinct predominance of right-handedness (ninety percent).

A study of some chimpanzees fishing for termites revealed that some chimpanzees fish with either hand. Others, however, are more specialized, always fishing with the same hand, and they do far better, collecting thirty-six percent more termites, independent of which hand was preferred. Handedness gives an advantage.

Many aspects of behavior occur preferentially on one side, not only with the hands, but also the arms, legs, eyes, ears and feet. Some behaviors seem to relate to handedness, but many don't.

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[308] Chris McManus, *Right Hand Left Hand.*
[309] Jean Tailarach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[310] Ibid.

Footedness is related to handedness, right-handers mostly being right footers, and left-handers are mostly left footed. However, there are almost twice as many left footers than left-handers. Ear dominance, preferring to hold the phone to one ear, is about sixty per cent on the right and forty on the left, with right-handers tending to prefer the right ear, and left-handers the left ear.

Checking which eye is used when looking through a camera or a microscope can assess eyedness. Again, most right-handers prefer the right eye; left-handers, the left; but there are many who are cross-lateral.

There are other lateralities, i.e., hand clasping and arm folding, with either the right or the left on top; more people chew on the right side than the left.

One in five people can wiggle their ears; and of those that can wiggle just one ear, twice as many can move the left ear as the right ear.

Ninety per cent of fetuses suck their right thumbs. Fetuses of ten weeks gestation do not suck their thumbs, but eighty-five percent move their right arm more than the left. This can't be taken as an indication that the brain is already asymmetric at such an early stage, because this early in development the neurons in the brain have not become connected to the spinal cord. Such early behavioral asymmetries seem to arise in the spinal cord.

Elegant studies have shown that preference comes before skill. This indicates that the skill is acquired after giving one side preference over the other.

In studies with rats, which were given high doses of amphetamines that induce highly repetitive sequences of actions, such as paw washing, some of the rats kept turning in circles until the drug wore off. It was observed that some rats consistently turned clockwise whereas other consistently turned counter-clockwise. A detailed pharmacological analysis revealed that the amphetamine was affecting the concentration of dopamine, and that normal rats do not have the exact same amount of dopamine on the left and the right sides of the brain stem. The amphetamine was amplifying this small normal difference.

Left brain damage, depending on the size of the area injured, can affect speech, writing, reading and/or spelling. An intriguing condition that has been reported is alexia without agraphia, where patients can write perfectly but can't read what they wrote. The overall picture, however, isn't as simple. The production of language isn't entirely a left hemisphere task. If it were, patients with right hemisphere damage only should have normal language skills. Certainly they can talk with a wide vocabulary and good grammar, but their speech is not normal; it lacks the musical quality of speech, prosody, whereby the tone goes up and down, and the words accelerate and slow down, or get louder or softer, providing emotion and emphasis. Speech without prosody is like a computer-synthesized voice. Metaphor, humor and sarcasm also are generated from the right side. What we call language depends on both the right and left hemisphere working together, each making its own contributions.

However, language skills, like reading, writing, speech and spelling, which normally appear on the same side, don't always necessarily do so. Some of these abilities can be on one side and others on the other.[311]

During speaking as opposed to singing, relative increases in activity have been observed in the left hemisphere, in classical perisylvian language areas (area 44)

[311] Chris McManus, *Right Hand Left Hand.*

including areas 42 and 22, the attentional hearing system (area 40), the frontal operculum (part of area 44 and 45), as well as the somatosensory cortex (parts of areas 3, 2 and 1) and the putamen. Relative increases during singing were observed in the right hemisphere: these were maximal in the right anterior superior temporal gyrus (parts of area 38 and 22) and contiguous portions of the insula, the right anterior middle temporal gyrus (part of area 22), the right superior temporal sulci (area 38 and 22), the right medial (area 32) and dorsolateral prefrontal cortices (part of areas 46 and 45), the mesial temporal cortices and the cerebellum, the somatosensory cortex (parts of areas 3, 2 and 1) and the nucleus accumbens. The production of words while singing is associated with right hemisphere areas that are not mirror-image homologues of the speech areas of the left hemisphere.[312]

The right hemisphere is also important for music, specifically recognizing and remembering melodies, and singing. Rhythm and pitch, on the other hand, are a left hemisphere specialty. This goes to show, again, that rich, complex activities require the integration of both sides. Musical hallucinations and musicogenic epilepsy – convulsions produced by particular pieces of music – have been reported after right hemisphere damage.

The right lateral surface specializes in visual perception and integration. It is involved in the recognition of space and perception of body images and gestures. Not surprisingly, the ability to orient the position of the head in space is controlled from the right.[313]

The two hemispheres complement each other; they do not work alone. The left hemisphere handles logic and the right hemisphere knows facts about the world. The two working together produce a powerful combination. If one or the other has to work on its own, the results can be absurd and strange.

Apart from personal neglect and neglect dyslexia, which neglect the left half of the body or the left half of words, there are other forms of neglect of the left half space. For example, eating only the food on the right half of the plate, reading only the right half of a page, remembering only the buildings on the right hand, washing or applying make up on only the right half of the face, and so on. Some patients with neglect only draw the right half of objects. Patients with right-hemisphere damage ignore the left half, but normal individuals give it attention and over-exaggerate it. This also explains why people are more likely to bump into objects on their right side.

Damage on the right side of the brain can also result in other unusual syndromes. In a condition known as misoplegia, patients suffering paralysis show a virulent hatred to the affected limb. In extreme cases, patients may violently hit the affected limb or shout abuse at it. In extreme cases, a patient might not even recognize the paralyzed limb as his or her own and think that it actually belongs to someone else.

There are some motor activities that are lateralized. Swallowing is one of them. Dysphagia (difficulty swallowing) occurs in over one-third of patients with strokes in one half of the brain. About half the general population control swallowing with the right hemisphere; the rest, the left.

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[312] Jeffries K.J., Fritz J.B., Braun A.R., *Words in melody: an H(2)150 PET study of brain activation during singing and speaking.*, Neuroreport, 2003 Apr 15;14(5):749-54.
[313] Jean Talairach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

The left hemisphere is more accurate at naming and identifying smells. Damage to the right hemisphere can lead to a curious condition known as "gourmand syndrome" in which there is a sudden onset of an obsessional interest in fine foods.

Some aspects of sex are lateralized. In experiments showing sexually explicitly films, sexual arousal activated two areas in the right hemisphere associated with motivation, and one area in the left hemisphere involved in involuntary responses. Again, sex, like other activities, depends on the two halves working together.[314]

Similarly, some emotional reactions are lateralized. A study in England showed that blood flow was greater in the right thalamus, the pallidum and putamen in subjects with Chronic Fatigue Syndrome or Depression compared to healthy controls.[315]

People in the first year after a stroke on the left side are twice as likely to develop depression as are others. Research suggests that strokes in the left frontal lobe are particularly likely to disregulate emotion.

Brain activity asymmetries have been observed with specific emotions. Anger shows greater changes toward left frontal activation than fear, and conversely, fear shows greater right frontal activation. However, both fear and anger present right parietal activation (area 40),[316] indicating that the visual and auditory attentional systems have been activated.

Damage to the left temporal lobe and its connections to other regions of the left cerebral cortex obliterate verbal memory and the ability to understand language.

Nonverbal and spatial functions are more dependent on the right hemisphere. Memory is similarly lateralized. People with damage to the left hippocampus and medial temporal lobe tend to have difficulties explicitly remembering verbal information but have no problem remembering visual design and spatial locations. People with damage to the right hippocampus and medial temporal lobe tend to show the opposite pattern.

A specific damage to the front of the temporal left lobe impairs semantic memory; only with great difficulty can general knowledge about familiar objects, places, or words be accessed.[317]

In another study, one woman had transient acute depression when high frequency stimulation was delivered to the left [but not the right] central substantia nigra.[318]

In the case of a three-and-a-half year-old girl whose left hemisphere had suffered severe developmental abnormalities that produced chronic seizures, it was decided to perform a left hemispherectomy (but leaving the brain's deep structures -- the brainstem, thalamus and basal ganglia -- intact). The brain of a child is incredibly resilient and plastic, such, that after removing the entire left hemisphere (where all the brain's language centers reside), the girl still learned to talk, read and write. This plasticity apparently remains until age two. If the brain suffers damage before this age, it usually reorganizes itself to reassign the lost functions to another area. Similarly, if the right

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[314] Chris McManus, *Right Hand Left Hand.*

[315] Klaus P. Ebmeier, Br. J Psychiatry 2000;176:550-556

[316] Jack Wacker, Marcus Heldman, and Gerhard Stemmler, *Separating Emotion and Motivational Direction in Fear and Anger: Effects on Frontal Asymetry*.

[317] Antonio Damasio, *The Feeling of What Happens.*

[318] Boulos-Paul Bejjani, Philippe Damier, Isabelle Arnulf, Lionel Thivard, Anne-Marie Bonnet, Didier Dormont, Philippe Cornu, Bernard Pidoux, Yves Samson, and Yves Agid, *Transient Acute Depression Induced by High-Frequency Deep-Brain Stimulation*, Centre d'Investigation Clinique, Federation de Neurologie and INSERM Unite 289.

hemisphere is removed, the left hemisphere will take on the removed tasks. It is reported that the worst a child suffers from losing half his or her brain, is some impairment of the peripheral vision and fine motor skills on one side of the body.

A great example of brain plasticity is offered by Paul Bach y Rita, professor of biomedical engineering at the University of Wisconsin. He has developed a method for displaying visual patterns on the human tongue. The subject wears a small camera on his forehead and a chip on his tongue. In this way, visual images are translated pixel for pixel into points of pressure on the tongue. A visual scene is turned into a pattern of hundreds of tiny pressure points. The brain quickly learns to interpret the changing patterns correctly. Wearing this device, blind people are learning to "see" via sensations on the tongue.[319]

After therapy following Dr. Jeffrey Schwartz's methods, using PET scans on OCD patients during a ten-week study period, scans after treatment showed significantly diminished metabolic activity in both the right and left caudate, with the right-side decrease particularly striking. There was also a significant decrease in the abnormally high and pathological correlations among activities in the caudate, the orbital frontal cortex, and the thalamus in the right hemisphere.[320]

Considering the neuroanatomical sex differences observed in structures that connect the two hemispheres, particularly in the size of the anterior commissure and the massa intermedia (when present), which are, respectively, 12 % and 53% larger in women than in men, even when the brains of males were larger, this may, in part, underlie functional sex differences in cognitive function and cerebral lateralization.[321] This can explain neatly (in general) why men are more single-goal oriented and women can multitask better.

10
Thinking and Intelligence

Defining thought or intelligence is difficult at least. If we define thinking as a brain process that produces the appropriate response given a specific stimulus, natural selection has certainly made sure that all life would have to be considered as thinking, even though not necessarily sentient. If intelligence is defined as the brain's ability to process memories and experiences in novel ways to produce a greater and better range of responses, then homo Sapiens would be at the top of the list, but we couldn't very well say that we are thinking, as novel responses don't necessarily produce the appropriate or best responses at all times. If intelligence is defined as being able to produce the appropriate response in a never-before-encountered experience, then intelligence is just a degree of more or less thinking. Then intelligence has to be defined as a thought process that involves emotions minimally, that is to say intelligence is a process where emotions are not the most important guiding force; reason and logic are. Asking the question differently, in light of what we have presented before, is intelligence a more potent way of arriving at a response than emotions and memories? Or is intelligence just a process

[319] Jeff Hawkins, *On Intelligence.*
[320] Jeffrey M. Schwartz, *The Mind and the Brain.*
[321] Allen LS, Gorki RA, *Sexual dimorphism in the anterior commissure and massa intermedia of the human brain,* J Comp Neurol. 1991 Oct 1;312(1):97-104.

that leads to understanding? And lastly, is communication a part of thinking and intelligence?

Another definition of intelligence is the ability to make predictions about the future. This in turn is tied into understanding, which is an internal metric of how the brain remembers things and uses its memories to make predictions. Intelligence is not just a matter of behaving intelligently. Behavior can be a manifestation of intelligence, but isn't the primary ingredient of being intelligent. You can be intelligent doing nothing, just thinking and understanding. To understand what intelligence is, what creativity is, we must understand how the brain makes predictions.[322]

Can you think more than a lizard?

Lizards can do almost anything we do; and some things better than most of us. Lizards can locate food; they can run and seek cover when something bigger approaches; they try to stay out of trouble; they mate without hanging around bars and getting intoxicated. When lizards are first born, without much help from their parents they prosper and grow. Humans as newborns certainly can't do so. And as adults they continuously get into all sorts of problems.

Rodolfo Llinas, at the New York University School of Medicine, wrote, "The capacity to predict the outcome of future events – critical to successful movement – is, most likely, the ultimate and most common of all global brain functions."

Predictions are not always exact. Rather the brain works with probabilistic predictions concerning what is about to happen.[323] More likely, the handshakes that are generated when and echo matches a stimulus activate associative memories, which include memories of what is expected to happen next. Thus the cortex through past experience (stored associated memories) anticipates the future.

But do lizards really think? When they act, do they consider among a series of options and then choose the best one? Probably not. Most lizards' responses, possibly, are genetically wired; their thalami trigger emotions (instinctive behavior) automatically when certain stimuli are detected without further processing of the signals, because a match is made between incoming stimulus and stored echoes. The emotion only allows for a limited range of responses (memories) to be activated. Their brains might not even be wired to perceive the emotion. Yet, the emotion will guide their behavior. In this sense, we certainly feel more and think more than lizards, but is this always a better strategy?

Memories are stored in the cortex, or can be pre-wired genetically. These memories are echoes of ECS, and because of this quality, when a similar stimulus is encountered, an emotional reaction is triggered. Intuition, common sense or instinct is guided by the same mechanisms. A stimulus is matched to an echo representing an emotionally competent stimulus, and a subtle emotional response is automatically triggered. In general, learning and experience will promote behaviors that produce a positive emotion, or avoidance behavior when it causes a negative emotion. A big

[322] Jeff Hawkins, *On Intelligence.*
[323] Ibid.

moving object will cause a lizard to seek a hiding spot, irrelevant of whether it is a friendly (or not) object – fear will trigger a run-under-that-thing-over-there reaction.

Thinking in different modalities basically is an exadaptation of our auditory, visual and somatosensory systems. The memory systems that are used by these three sensory systems have been greatly expanded (compared to reptiles, birds and most other mammals) and are also interconnected through semantic memory and our attentional systems. The cortex is basically a memory storage system.

Hearing memories used by the brain to interpret information from our ears integrated to specialized motor memories control speech and allow our brains to communicate with other brains. Language and speaking are two sides of the same coin and co-evolve. Hearing memories allows us to make sense of speech sounds and build sounds into words; in turn, this gives words a syntactical and grammatical meaning, allowing us eventually to "think" (using this speech ability) in terms of a "voice in our head." I actually experience several "voices" going on continuously "inside" my head. Thinking, in terms of voices in our head, is an expanded use of our sense of hearing.

Some forms of social language probably evolved from grooming and hand-gestures as well as from unconscious reflexes and learned reactions in response to social situations and constraints, which in turn can facilitate interpersonal relationships.

In terms of circuits, thinking is mostly done by afferent and efferent connections between the cortex, hippocampus and thalamus.

Gestures universally, across cultures, accompany speech. Indeed, even individuals who are blind from birth and have never seen others gesture purposefully move their hands as they talk. Whenever there is talk, there is gesture. Gestures can beat the tempo of speech, point out referents of speech, or exploit imagery to elaborate the contents of speech. Gestures participate in communication, yet they are not part of a codified system. As such they are free to take on forms that speech cannot assume and are consequently free to reveal meanings that speech cannot accommodate.

Gesture and speech never convey exactly the same information. However, gestures convey meaning that is integrated with speech and are semantically and pragmatically co-expressive with speech. Typically, gesture precedes the word with which it is co-expressive, and the time lag between the onset of the gesture and the onset of the word is quite systematic – the gap between word and gesture is larger for unfamiliar words than for familiar words. The systematicity of the relation suggests that gesture and speech are part of a single production process.

There is evidence that gestures are learned shortly before words, but become integrated with speech quite early in development. At that point gesture and speech become unified into a single system characterized by both semantic and temporal coherence.

Languages differ in various parts of the world and as might be expected, gestures vary according to language. Italians are big gesturers and attend to gestures more than English speakers. Gestures, in general reflect special features of each language. For example, to describe someone swinging on a rope from one building to another, in English, the term "swing" describes an arch trajectory, and the hand gesture used would move in such a way. Whereas, in Japanese there is no corresponding verb, and consequently, Japanese speakers use verbs such as "iku" (go) or "tobu" (fly) that do not encode the arch, and they use straight gestures.

Predominantly, in the spatial and visual domain, gestures are particularly well suited to represent visual concepts, like movement and shapes. Thus having the ability to express a concept in gestures does not guarantee that the speaker can express the concept in speech. However, having the ability to express a concept in speech almost always does mean that the speaker is able to express the concept in gesture.[324]

In the Penfield motor map in the cortex, the hand and mouth area are right next to each other. Also, think of the shape the lips or mouth take when speaking a word. "Big, large, enormous, gigantic," are all words that open the lips wide, whereas the words, "little, small, diminutive, tiny weeny," purse the lips mimicking the visual appearance of the meaning of the word. Mirror neurons (in the prefrontal cortex) might be responsible for aiding to mimic a complex three-way congruence between the phoneme sound, the appearance of lips and tongue and their felt position that is required for lip-reading and learning to speak in childhood.

It is very common for people who are doing complex manual tasks, such as cutting with a pair of scissors or playing music on an instrument, and having the jaw clench and unclench, or the lips pulling or pursing into various shapes as the finger move to produce the music, mimicking the manual movements.

Sounds can also have a visual representation as in the case of the visual amoebic symbol "booba" and the jagged visual "kiki."

Here are three mechanisms that could culminate in the emergence of a primitive language: a hand to mouth mapping; second, mouth in Broca's area to visual appearance in the fusiform gyrus and sound contours in the auditory cortex; and third, auditory to visual, the booba/kiki effect.[325]

To this add an emotional component of communication through facial expressions, gestures and body postures as well as grunts, shouts or crying. Gestures, body postures and facial expressions, as a means of communicating emotions, and hand signals and gesticulations as a sign language to communicate intentions, probably antedate, evolutionarily speaking, spoken language. Greater numbers of neurons in the cortex allow for more specialization areas; specialization leads to lateralization. The evolution of spoken language is not only the history of developing motor commands to emit meaningful sounds, but also the story of the evolution of the cortex with specialized areas to interpret those sounds. Spoken language and thinking (in terms of voices) evolved from emotional expressions and sign language. This involves the evolution of emotional and motor systems. In turn, this implies there is a motor and emotional basis for thinking, if not in language terms, at least in terms of actions and responses. Emotions, after all, are automatically triggered in response to particular stimuli to generate genetically wired and learned reactions. Emotional responses could be considered a form of logic, i.e., when this happens, react this way.

Understanding speech and speaking go hand in hand, or should I say, go hand in mouth? It is no accident that the areas of motor speech control (left side frontal lobe area 44) are adjacent to the supplementary motor cortex (area 6, limb and eye movement planning). On the right side, area 44 has specialized in orienting the head in space. And, as mentioned, the hand area and the mouth area are side by side. Thinking and ideas, in

[324] Susan Goldin-Meadow, *Hearing Gesture.*
[325] V.S. Ramachandran, *A Brief Tour of Human Consciousness.*

the form of silent speaking, is a feedback cascade of handshakes emanating from the higher auditory regions down towards the lower auditory areas.

The efferent connections from area 24 (coordinating emotions, learning and memory) in the anterior cingulate gyrus to areas 6 (communicating through gestures and planning movements), 8 (control of voluntary eye movements as another means of communication), 9 and 10 (prefrontal association cortex having to do with thought, cognition and planning) as well as the subcortical targets of this area to the striatum, hypothalamus and tegmental area become more understandable. Thinking in terms of voices inside our brains uses an incredibly complicated network of sound memories to construct or interpret words, movement memories to generate sounds, emotional reactions to guide meaning and prosody, and thus create a grammar and syntax. We are all aware of the voices we hear and the conversations we carry on as we think. Evolutionarily speaking, prosody -- the musical quality of speech, whereby the tone goes up and down, the words accelerate and slow down, or get louder or softer, providing emotion and emphasis -- might be proof of the emotional component of speech. Prosody is controlled from the right hemisphere. Speech without prosody is like a computer-synthesized voice. Metaphor, humor and sarcasm also are generated from the right side and also have an emotional component.

This emotional type of guidance of our thoughts and behaviors often departs from social communication. This level of thought is reflexive and might mirror a parallel evolution to social communication allowing for survival-enhancing deception.

Like over-learned motor skills, these two origins of thought, motor and hearing, allow us to integrate intentions and feelings with behaviors.

Vision is intimately related to movement. The basal ganglia (the putamen and globus pallidus, the substantia nigra and the subthalamic nucleus) and the thalamus, integrate the external space with the internal body map using the visual signals and the somatosensory body signals, so that the premotor and motor cortex can ultimately sequence and control necessary movements. This integration of both spaces into one map permits the effortless motion of the organism through the environment. The same visual memories that help us construct a map of extrapersonal space and interpret what is in our visual field allow us to “see” in our “mind’s eye” and to imagine as well as to manipulate objects in “space” and “turn” them in our “heads”. Thinking, with visual imagery, is an expanded use of our vision memories. Logic and deduction evolved as more powerful accessories in thinking using the same architecture and the areas of the incredibly rich memory sequences used to control movement.

The left lateralization of speech, logic and deduction probably led to the left supplementary motor cortex controlling both sides of the body to a much greater extent than the right supplementary area. Correspondingly, the right lateralization of visual-motor, spatial and non-verbal tasks is probably a consequence of this as well.

Automatic responses or behavior come first – evolutionarily speaking, then intelligence. Most of what organisms sense depends on what they do and how they move through the environment. It follows that prediction and behavior are closely related. Mammals evolved a large cortex because of a survival advantage, and such an advantage must be rooted in behaviors. But in the beginning, the cortex served to make more efficient use of existing behaviors, not to create entirely new behaviors.

What is the difference between a human brain and a lizard's? A lot and a little. A little, because to a rough approximation, everything in the lizard's brain exists in a human brain. A lot, because a human brain has a large cortex. This is a huge difference. And what makes humans smarter than other mammals is the increased cortex.

Lizards have sophisticated senses and sophisticated but rigid behaviors. Through natural selection, feeding sensory signals to an added memory system, not only helped interpret better what the signal is, but the animal could also remember past experiences. When the animal encountered a same or similar situation, the memory would be recalled, leading to a prediction of what would happen next. Thus intelligence and understanding started as a memory system that fed predictions into the sensory system.

The cortex evolved in two directions. First it got larger and more complex types of memories could be stored; it was able to remember more things and make predictions bases on more complex relationships. Second it started interacting with the motor system of the old brain. To predict what you will hear, see, and feel next, it needed to know what actions were being taken. With humans the cortex has taken over most motor behavior. Instead of just making predictions based on the behavior of the old brain, the human cortex directs behavior to satisfy its predictions.[326]

In order for the brain to make predictions, the cortex stores echoes as sequences of patterns. When the echoes match the incoming stimulus they activate associated memories, which include expectations. The memories must be stored in a compact manner, what Jeff Hawkins calls an invariant form. This way, memories are applied to new situations that are similar but not identical to past experience.

Some autistic children have what is known as the savant syndrome. Even though they are retarded in many respects, they have one preserved island of extraordinary talent. A seven-year-old child, Nadia had exceptional artistic skills. She was quite retarded mentally, could barely talk yet she could produce the most amazing drawings of animals. She drew a dynamic horse that could easily compare with one of Leonardo da Vinci's pencil sketches of a cantering horse.[327] Perhaps many of the "normal" echoes that should be present are impaired or nonexistent because of autism. The continuous stream of specialized echoes that are dominant would shape the emotional, volitional and potential responses. In the absence of all these "normal" echoes, her brain would spontaneously allocate all her attentional resources to these echoes. In Nadia's case, since everything else is damaged in her brain, she allocates all her attention to the right parietal (damage to the right parietal causes loss of artistic sense). So Nadia has a hyperfunctioning [relatively speaking] art module in her brain.[328] The lack of interference from many other (normally) competing areas produces a greater than normal ability which could be seen as a specialized form of intelligence.

Returning to the idea of intelligence being related to predictions, predictions are not limited to low-level sensory information like seeing or hearing. The human brain is more intelligent than that of other animals because it can make predictions about more abstract kinds of patterns and longer temporal sequences. Intelligence can be measured by the capacity to predict patterns in the world, including language, mathematics, physical properties of objects, and social situations. Your brain receives patterns from the

[326]Jeff Hawkins, *On Intelligence.*
[327]V.S. Ramachandran, *A Brief Tour of Human Consciousness.*
[328] Ibid.

outside world, stores them as memories, and makes predictions by combining what it has encountered before with what is happening now.[329] However, as we have seen, memories have a strong emotional and contextual component. So it follows that predictions will have an emotional and contextual component. Consequently, intelligence cannot be completely unemotional because of the link between emotions and memories.

Logical or deductive reasoning is more than sentential or spatial. In a study by Goel and associates, measurements of regional cerebral blood flow while subjects performed deductive reasoning tasks determined that the areas of activation when performing logic or deductive reasoning were confined to the left hemisphere. They included the left inferior frontal gyrus (areas 45 and 47), a portion of the left middle frontal gyrus (area 46), the left middle temporal gyrus (areas 21 and 22), a region of the left lateral inferior temporal gyrus and superior temporal gyrus (areas 22, 37), and a portion of the left cingulate gyrus (areas 32 and 24). There was no significant right-hemisphere or parietal activation.[330]

Areas 22 (auditory association) and 45 (Area of Broca, motor speech) are related to spoken language; area 37 is a visual auditory association region; area 21 is the origin of the bundle of Turk, which also receives projection fibers from areas 20 and 22.[331] Areas 20 and 21 are involved in form vision, and surround Heschl's gyri and superior temporal lobe (areas 41 and 42, primary and secondary hearing areas respectively). Area 24 is related to emotions, learning and memory; area 32, to emotions. Both are part of the limbic association cortex.[332] Area 24, in addition to important thalamic connections, has important projections to areas 6, 8, 9, 10, and 29, and other efferents, principally from areas 11 and 12.[333]

In another study comparing deductive and inductive reasoning, Goel and associates report that the deduction condition resulted in activation of the left frontal gyrus (areas 45 and 47). The induction condition resulted in activation of a large area comprised of the left medial gyrus, the left cingulate gyrus, and the left superior frontal gyrus (areas 8, 9, 24 and 32). Induction was distinguished from deduction by the involvement of the medial aspect of the left superior frontal gyrus (areas 8 and 9).[334]

To back these findings, another study, using fMRI while subjects engaged in inductive and deductive reasoning tasks, established the following: there was greater involvement of left frontal gyrus (area 44) in deduction, while left dorsolateral (areas 8 and 9) prefrontal gyrus showed greater activity during induction. Both inductive and deductive reasoning were characterized by activation of left lateral prefrontal (parts of areas 46 and 45) and bilateral dorsal frontal (parts of areas 8 and 9), parietal (attentional systems, areas 40 and 7) and occipital (visual areas 18 and 19) cortices.[335]

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[329] Jeff Hawkins, *On Intelligence.*
[330] Goel V., Gold B., Kapur S., Houle S., *Neuroanatomical correlates of human reasoning,* J Cogn Neurosci. 1998 May;10(3):293-302.
[331] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[332] John H. Martin, *Neuroanatomy.*
[333] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[334] Goel V., Gold B., Kapur S., Houle S., *The seats of reason? An imaging study of deductive and inductive reasoning.,* Neuroreport 1997 Mar 24;8(5):1305-10.
[335] Goel V., Dolan R.J., *Differential involvement of left prefrontal cortex in inductive and deductive reasoning.,* Cognition. 2004 Oct;93(3):B109-21

This architecture suggests that not only do logic and deduction involve use of the memory systems of speech (45 and 22) and vision (18 and19) and integration systems (areas 21 and 37), but also use of areas that integrate cognition, planning behavior, thought and some aspects of eye movement (areas 45, 46, 47, 11 and 12) with added inputs from emotions (areas 24 and 32) as well as use of movement routines (movement planning areas 11 and 12 and the supplementary motor cortex, area 6). Sequencing capabilities for deducting and reasoning are borrowed from motor areas that are especially good at memorizing sequences. Evolutionarily, it seems an economic and efficient way to utilize the increased cortical areas involved with memories of movement sequences and planning motion, for logic and deductive processes. Not by accident is the supplementary motor cortex (area 6) adjacent laterally to area 8 (control of saccadic eye movements) and area 9 (involved in planning movements, cognition and thinking) and adjacent medially to area 8 and area 32 in the cingulate gyrus (emotions).

In contrast to left-hemisphere, formal, logical thinking, right cortical image thinking is adaptive when information is incomplete, contradictory, complex or ambiguous.[336] This is achieved by using the viscero-sensory signals generated emotionally, and evaluating how "good" or "bad" the feeling is. A course of action is determined by "gut feelings" as opposed to a deductive reasoning. In the real world, more often than not, when action is required in the face of uncertainty, when logic, deduction and reasoning have failed, an emotional response is automatically triggered. The ECS echoes that best match the present stimuli guide behavior; responses are generated by thinking emotionally. Many conclusions, achieved in a logical systematic way lack this emotional component, they don't "feel" right, and therefore are never acted upon, in spite of the fact that they might be the right response. As cold and calculating that thinking and intelligence might seem, they have an emotional component. The best results are when the illusion of what "feels" good matches the best "logical" answer; when both hemispheres are acting in concert.

The Cerebellum: How much do we think with the back of our heads?

The cerebellum receives information from virtually all other components of the limb and extraocular motor systems, from the spinal cord and brain stem, and from most sensory systems. By receiving information from the motor pathways, the cerebellum is poised to compare information about the intention of an upcoming movement with what actually occurs from the information received from the sensory systems. It has been shown that the cerebellum may compute control signals to correct for differences between intent and action. The cerebellum, in turn, provides the major input to the brain stem and cortical pathways for limb, trunk and eye movement control.

The cerebellum, reflecting this past evolutionary pathway involving the sensory memories with the emotional response mechanisms, also receives input from areas of the brain that do not play a role in movement control, such as the parietal association cortex (the visual, hearing and somatosensory attentional system, areas 40 and 7) and the limbic association cortex,[337] which help regulate emotions.

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[336] Allan Schore, *Affect Regulation.*
[337] John H. Martin, *Neuroanatomy.*

The multiple roles played by the cerebellum offer a good example of both neural conservation and adaptation. The cerebellum is a very old part of the brain that expanded during the evolution of the cerebral cortex. The vermis, involved with balance, is the oldest part.[338] The newer portions – the cerebellar lobes – evolved along with the cortex, and are involved in neural networks of language, memory and reasoning.[339] The cerebellum's ability to process vast amounts of information has been co-opted to assist increasingly in higher cortical processes.

Oddly, if one is born without a cerebellum or it is damaged, one can lead a pretty normal life.[340]

Just as balance and movement require constant monitoring and the inhibition of unnecessary and distracting movements, so, in parallel ways, do memory, attention [concentration] and language. The same timing and coordination necessary for movements are necessary for sequential processing in language and thought in logic and deductive reasoning.[341] For the process of thinking, the brain has co-opted the cerebellum to help perform the tasks at which it excels: monitoring and sequencing.

The extensive connections to the limbic association cortex reflect the emotional and motivational factors involved in the decision to move. Moreover, emotions affect memories and modes of thinking by changing the chemical milieu of the brain. Emotions, naturally, also alter the functioning of the cerebellum, especially in regard to higher functions like reasoning, logic and thinking.

The cerebellum is divided into the vermis, located along the midline, and two hemispheres. The cerebellum has three functional divisions, named for their major sources of information:

The spinocerebellum, which receives highly organized somatic sensory inputs from the spinal cord and a few other structures: it comprises the vermis, the adjoining intermediate hemisphere, of both the posterior and anterior lobes, and the fastigial and interposed nuclei. It controls movements.

The cerebrocerebellum, which receives input from the cortex: this consists of the lateral hemisphere, in both the anterior and posterior lobes, and the dentate nucleus. It participates in the planning of movement.

The vestibulocerebellum, which receives input from the vestibular labyrinth, and helps in maintaining balance and controlling head and eye movements.

Each functional division is anatomically similar, except each division differs from the others with respect to the specific input sources and the specific structures to which it projects.

The organization into layers and interconnections of the cerebellum rivals that of the cerebral cortex in complexity. The cerebellum is made of an outer cortex containing neuronal cell bodies overlying a region that contains predominantly myelinated axons. The cerebellar cortex has an extraordinary number of neurons and a rich array of neuron types. Two prominent neurons are the projection neurons of the cerebellum, the Purkinje cells, and a class of cerebellar interneurons (the majority in the cerebellum), granule cells.

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[338] Louis Cozzolino, *The Neuroscience of Psychotherapy.*
[339] Jeremy D. Schanahmann, *The Cerebellum and Cognition.*
[340] Jeff Hawkins, *On Intelligence.*
[341] Louis Cozzolino, *The Neuroscience of Psychotherapy.*

The cerebellar cortex consists of three cell layers. From the external surface inward these are: the molecular layer, the Purkinje layer, and the granular layer, which is adjacent to the white matter. The cerebellar cortex contains five types of neurons: (1) Purkinje cells, found in the Purkinje layer, with arborizations into the molecular layer and axons projecting into the white matter; (2) granule cells, in the granular layer; (3) basket cells, in the molecular level with their axons to the Purkinje layer; (4) stellate cells in the molecular layer; and (5) Golgi cells, with arborizations in the granular layer and axons projecting to the molecular layer and to a lesser degree the Purkinje layer.

There are two major excitatory inputs to the cerebellum, climbing and mossy fibers. The climbing fibers synapse to the Purkinje cells; the mossy fibers synapse to granule cells, which give rise to the parallel fibers, which in turn synapse to Purkinje cells. The Purkinje cells are the output neurons of the cerebellum.

There are three types of inhibitory interneurons: Golgi, basket and stellate cells. The Purkinje cells are inhibited by stellate and basket cells. The basket cell synapse is located on the Purkinje cell body and is one of the strongest inhibitory connections in the nervous system. The Golgi interneurons inhibit the granule cells. The Purkinje neuron's output is inhibitory in nature and projects to deep nuclei and vestibular nuclei. The granule cells are excitatory and project to all the rest: Purkinje, stellate, basket and Golgi neurons.[342]

It appears that the control and regulation activities of the cerebellum are inhibitory in nature, preventing any activity until it is needed, thus orchestrating the proper sequences. Thinking, like speech requires a grammar and syntax. Timothy Justus, studying patients with damage to the cerebellum concluded that they understood the same amount of words, but they did differ to a marginally significant extent in the production of required articles; were less affected by the manipulation of subject-verb agreement to a marginally significant extent and were significantly less able to discriminate grammatical and ungrammatical sentences.[343]

The brain to achieve other, seemingly more difficult tasks, like thinking, will indirectly usurp the cerebellum's intimate role in movement control. In the next section we will discuss in more detail how some cortical areas involved in movement are activated during higher thinking functions.

Reasoning, Logic and Thinking

Another study of spatial imagery in deductive reasoning (Knauff, et al) shows attentional systems activating during reasoning (visual attention, area 40, and somatosensory attention, area 7) along with visual (area 19) and motor (supplementary motor cortex, area 6) regions as well as involving the prefrontal, area 9, involved in thought, cognition and movement planning. Moreover, the anterior cingulate gyrus (area 32) involved in emotions is also activated.[344] Reasoning has an emotional component. We will return to this later.

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[342] John H. Martin, *Neuroanatomy.*

[343] Timothy Justus, *The Cerebellum and English Grammatical Morphology: Evidence from Production, Comprehension, and Grammaticality Judgements*, Journal Of Cognitive Neuroscience, 2004:16:1115-1130.

[344] Knauff M., Mulack T., Kassubeck J., Salih H.R., Greenlee M.W., *Spatial imagery in deductive reasoning: a functional MRI study.* Brain Res Cogn Res. 2002 Apr;13(2);203-12.

Knauff's study, because it involves spatial imagery, and probably because of how it was set up, activated the attentional systems, whereas the previously mentioned studies by Goel and associates do not show increased activity in the parietal lobes.

In yet another study (Parson's, et al), probabilistic reasoning was mostly associated with left hemispheric areas in inferior frontal (area 11), posterior cingulate (area 30), parahippocampal, medial temporal (area 21), and superior and medial prefrontal (areas 8 and 6).[345] Here, as well, some motor areas are being activated (areas 8 and 6) and the emotion-related area (30).

McGuire, et al investigated the neural correlates of stimulus-independent thoughts were using PET scans and measurements of regional cerebral blood flow. Subjects rated how frequently stimulus-independent thoughts occurred while they were concurrently performing different sets of cognitive tasks. The main positive correlations between stimulus-independent thoughts and blood flow were in the medial prefrontal (areas 9 and 10) region. An association between medial prefrontal activity and stimulus-independent thoughts is consistent with data linking the region to self-initiated thought and its activation during tasks that entail thinking, which is decoupled from stimuli in the immediate environment.[346]

Subjects were imaged using fMRI while alternately (1) attempting to suppress a particular thought, (2) attempting to suppress all thoughts, or (3) thinking freely about any thought. Suppression of a particular thought, when compared to thinking freely, showed greater activation of the anterior cingulate (areas 24 and 32). When comparing attempting to suppress all thoughts with thinking freely, a more distributed network of brain regions, including the anterior cingulate and the insula (area 43), was activated.[347] Area 24 is related to emotion, learning and memory; area 32 is related to emotions; the insula is related to the secondary somatosensory area and the gustatory area.

Thought initiation is regulated in the medial prefrontal region (areas 9 and 10) adjacent to areas involved in thought suppression (areas 24 and 32). The effort to attempt suppression of thoughts involves activating some emotions. The suppression is achieved by activating emotions, which in turn activate other thoughts. There are numerous connections between area 24 and areas 9 and 10 as well as connections to areas 6 and 8. Area 24 through its many connections regulates many cortical and subcortical areas. It has efferent fibers to the striatum, hypothalamus and tegmental subcortical regions.[348]

What happens in the brain when inhibiting a perceptual process in order to activate a logical reasoning process? Subjects were asked to perform a deductive logic task twice, first with a perceptual bias and then with a logical response following bias-inhibition training. The main finding is a striking shift in the cortical activity of reasoning from the posterior part of the brain (the ventral and dorsal pathway) to a left-prefrontal

[345] Parsons L.M., Osherson D., *New Evidence for Distinct Right and Left Brain Systems for Deductive and Probabilistic Reasoning.*, Cereb Cortex. 2001 Oct;11(10):954-65.
[346] McGuire P.K., Paulesu E., Frackowiak R.S. Frith C.D., *Brain activity during stimulus independent thought.* Neuroreprt. 1996 Sep 2;7(13):2095-9.
[347] Wyland C.L., Kelley W.M., Macrae C.N. Gordon H.L., Hetherton T.F., *Neural Correlates of Thought Suppression.* Neuropsychologia. 2003;41(14):1863-7.
[348] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

area, including the middle frontal gyrus (area 46), Broca's area (areas 44 and 45), the anterior insula and the pre-supplementary motor area (area 6).[349]

Perception is the creation of a modality-specific (i.e., it can be heard) internal representation of a stimulus viewed by a subject. Action is a direct transformation of the visual stimulus into motor commands. The dorsal cortico-cortical pathway (also known as the where pathway) is involved during purely perceptual activities. The dorsal pathway is responsible for visuomotor transformations used for mapping sensory events into movements. The ventral pathway (also known as the what pathway) is a cognitive pathway, enabling the subject to respond to questions concerning sensory events and to activate attention. Visual imagery activates cortical areas closely related to visual perception. According to Kosslyn et al (1993), imagery tasks (e.g., mentally representing letters) activate not only primary visual cortex and middle and inferior temporal gyri (areas 20and 21), but also the angular gyrus (area 39) and areas in the superior and inferior parietal lobules (attentional areas 7 and 40) on both sides.[350]

This seems to indicate that while the attentional systems (somatosensory, hearing and visual, areas 7 and 40) are automatically activated when subjects are asked to perform a task, and after "bias-inhibition training," only the logical reasoning areas (areas 44, 45 and 46) are visibly active.

When using PET scans to compare perceptual and conceptual word priming, a specific blood flow decrease was found in the left inferior temporal (area 20) cortex in the perceptual word priming condition, and in the left superior temporal/inferior parietal cortex (area 22/44) in the perceptual word priming condition.[351]

Using PET scans in an effort to establish if capacity for access to deductive logic depends on emotions, two groups of subjects, who were either able or not able to shift from errors to logical responses in a deductive reasoning task, were compared. They were scanned twice while performing the same task, before and after a training session. The error-to-logical shift occurred in a group that underwent logicoemotional training but not the other group. The results show that deductive logic involved a right ventromedial prefrontal area (areas 24 and 32) devoted to emotion and feeling.[352]

Thinking happens in many areas all over the cortex as well as the cerebellum and the basal ganglia. The process of thinking, whether it is used for interpreting sensory stimuli, or for deductive reasoning or logic, is a complicated process involving many systems simultaneously: sensory memory systems, attentional systems, spatial imagery systems, language centers, as well as planning and coordinating systems evolved from motor systems.

In general, the left hemisphere communicates its internal states via (thinking in words) linguistic means; what is possible to put into "spoken" thoughts can be expressed

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[349] Houde O. Zago L., Mellet E., Moutier S., Pineau A., Mazoyer B., Tzourio-Mazoyer N., *Shifting from the perceptual brain to the logical brain: the neural impact of cognitive inhibition in training.* J Cogn Neurosci. 2000 Sep;12(5):721-8.

[350] Marc Jeannerod, *A Dichotomous Visual Brain?*,Psyche, 5(25), September 1999.

[351] Yasuno F., Nishikawa T., Tokunaga H. Yoshiyama K., Nakagawa Y., Ikejiri Y., Oku N., Hashikawa K., Tanabe H., Shinozaki K., Sugita Y., Nishimura T., Takeda M., *The neural basis of perceptual and conceptual word priming – a PET study.* Coretx. 2000 Feb; 36(1):59-69.

[352]Houde O. Zago L., Mellet E., Moutier S., Pineau A., Mazoyer B., Tzourio-Mazoyer N., *Access to deductive logic depends on right ventromedial prefrontal area devoted to emotion and feeling: evidence from a training paradigm.* Neuroimage. 2001 Dec;14(6):1486-92

with words. The right hemisphere communicates its internal states via (emotions/feelings) external emotional expressions such as facial gestures, body postures and through the prosody in speech. The two hemispheres are interconnected and modulate each other's activities. Thought can alter emotions, just as emotions can alter thought. The prosodic elements of speech communication such as rhythm, force and tonality, can communicate as much as, or more, especially emotional content, than the words themselves. The two hemispheres, working together, reinforce communications with others.

Are You Smarter Than a Goose?

Geese follow migratory routes that involve thousands of miles without losing their way. Geese are monogamous and pair up for life. These behaviors are part of their success at breeding and rearing their offspring. Are these two behaviors part of deductive reasoning or simply learned behaviors? We humans do not always act as our parents acted, and neither do we necessarily follow in their footsteps in their chosen professions. Yet, if geese show any deductive reasoning or learned behavior, isn't this behavior better deduced or learned than what we humans deduce and learn from our parents? Would it not be easier, as it is a proven successful reproductive strategy, to repeat our parents' actions? In most cases, geese seem to know what is good for them a lot better than we do. They travel thousands of miles every year, nurture and rear their young successfully without governments, schools, hospitals, philosophers or even neurologists! Are we smarter than a goose or is it another illusion produced by our brains to make us feel good?

However, the memory aspects of the cortex, primarily the prediction by remembering are enlarged in the human brain. With a larger cortex comes the capacity to make or learn a more complex representation of the world and make more complex predictions. We see deeper analogies, more structure on structure, than other animals. So I need to say that geese are not more intelligent than humans. They are not capable of creating institutions, or of changing their societies, much less writing books explaining how to accomplish this. Language, written or spoken, is a powerful tool that allows us to accomplish many of these tasks. Language permits the communication of memories and the creation of new juxtapositions of mental experiences between humans.

The development of language requires a large cortex capable of handling the nested structure of syntax and semantics. It also requires a more fully developed motor cortex and musculature to enable us to make sophisticated, highly articulate sounds or gestures. Language allows the transfer of information not only from person to person, but from one generation to another.[353]

Intelligence can be traced through several epochs. The first is through the transmittal of DNA. Behavior and memory could only be stored in this fashion. The second epoch comes when modifiable nervous systems could form memories and learn. The third epoch begins with dinosaurs and mammals, as we will se later, through the creation of emotions and emotional transference through emotional gestures and

[353] Jeff Hawkins, *On Intelligence.*

expressions. The fourth begins with evolution of language. For the first time, the learnings of a lifetime could be effectively communicated to others.

11
Can You Taste the Glass Columns?

The illusions the brain creates to perceive and extract more information from our sensory signals sometimes can be mixed up, mostly with no ill effect. Synesthesia is a rare condition where one sensory modality produces sensations in a different modality. The six senses -- sound, sight, touch, taste, smell and proprioception -- can have different synesthetic pairings. Synesthetic relationships only operate in one direction, meaning that for a particular synesthete, sight may induce touch, but not the other way around. This one-way channel allows thirty permutations of sensory pairings. However, smell has never been reported as a trigger, which leaves us with twenty-five possible sensory pairings.

The one thing that differentiates smell from all other sensory modalities is that the olfactory signals don't pass through the thalamus. Olfactory signals are collected by the olfactory nerve fascicles in the olfactory epithelium in the nose. They are then passed to the bulb and sent through the olfactory tract to several primary olfactory areas: the anterior olfactory nucleus, the amygdala, the olfactory tubercle, the piriform and periamigdaloid cortices and the entorhinal cortex.[354] The connection with the amygdala is important, as smells can elicit strong emotional associations. Consequently a strong emotion could also elicit a smell memory.

There is a hereditary component to synesthesia where instead of the brain sensory modules remaining segregated, they become accidentally cross-wired and results in an intermingling of the senses.

There are some cases where people also see colors when they see numbers. Every time they see the number, say the number five (or a white five on a black page), they would see it tinged in red. Six might be green, seven indigo, eight yellow and so on. This type is the most common synesthesia. The number area and the color area are right next to each other in the same part of the brain. In the case of this type of synesthesia, even when a number is hidden (for normal people – suppose that "5" is presented to one side and flaked by two other numbers, called distractors, it is hard to discern the middle number, an effect called crowding), it still stands out because it evokes a color; say the number 5 evokes red. A synesthete, unable to discern the number itself, will still identify a 5 "because it looks red."

Interestingly, when these synesthetes were tested with Roman numbers V and VI instead of Arabic numbers 5 and 6, they knew it was a five or six, but saw no color. This demonstrates that it is not the numerical concept that drives the color but the visual appearance of the number. The fusiform gyrus is the area that represents the visual appearance of numbers and letters, not the abstract concept of sequence or ordinality.

[354] John H. Martin, *Neuroanatomy.*

We don't know where in the brain the abstract idea of number is represented, but a good guess is the angular gyrus in the left hemisphere. When that area is damaged, patients can no longer do arithmetic even thought they could see and identify numbers correctly.

For other synesthetes, not merely numbers but even days of the week and even months of the year evoke colors: Monday is red, December is yellow. What days, months and numbers have in common is the abstract idea of sequence or ordinality, which might be represented higher up in the temporal parietal occipital (TPO) junction (visual attentional area 40), in the vicinity of the angular gyrus. The next color area in the color processing hierarchy is higher up in the general vicinity of the TPO junction, not far from the angular gyrus. It is probable that for people that see colors in the days and months, the cross-wiring happens higher up. These synesthetes, V.S. Ramachandran calls higher synesthetes. If the cross-wiring were in the earlier stage of processing (the visual appearance) they would be called lower synesthetes. If the synesthesia is driven by numerical concept (higher up the processing) then they are higher synesthetes. One in two hundred people have this useless peculiarity of seeing colored numbers. However, among artists, poets and novelists this type of synesthesia is seven times more prevalent. It could be possible that their ability to see the world differently makes them more skillful at using metaphors.[355]

Colored hearing, where particular sounds produce the sensation of seeing colors or shapes, is the most common form of synesthesia, according to Richard E. Cytowic. The least common of synesthetic pairings are: geometric taste, where taste produces vivid sensations of touching geometric shapes with various textures; colored taste; and audiomotor synesthesia, in which, different postures are assumed according to different sounds. Sound and sight are the most common senses involved in synesthesia. Some synesthetic pairings have never been reported.

Richard E. Cytowic in his book *The man Who Tasted Shapes* describes several types of synesthetes. One synesthete reported seeing lightning bolts, described as blinding red jaggers, when hearing a particular frequency. She reported that sharp, shrill sounds, like ambulance sirens, crashes, screeching tires, sudden sounds, occasionally music, always produce sights, if they are loud enough and high enough in pitch. The sound-sight synesthesia was the most highly developed, but she reported a complex, but less developed synesthesia, also involving pan and smell.

Another synesthete with a highly developed geometric taste reported that Karo syrup tasted perfectly spherical, like hundreds of tiny, perfect spheres at his fingertips. Sugar made things taste rounder, while citrus made food taste more pointed. He felt some shapes, like points, throughout his body. Others, like the spheres of sweet tastes, he only felt in his hands. Many shapes were in between, felt in his face, hands, and shoulders. When tasting something, he felt he could grasp the shape and finger its texture or sense its weight and temperature.

He could best describe the different shapes of different tastes as shapes that could change gradually from spheres to spheres with some flat sides that eventually evolved into cubes. The cubes would then change slowly into pyramids, and then into cones. The pyramids could evolve into a more pointed pyramids and then slowly into round columns. Similarly, the cones could become more pointed and evolve into round columns.

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[355] V.S. Ramachandran, *A Brief Tour of Human Consciousness.*

He described the taste of mint as cool glass columns. He felt a round, curved shape, which he could reach behind, and it was very, very smooth. He inferred it must be made of marble or glass, because of this satiny smoothness. Since he didn't feel ripples, or surface indentations, the shape must be glass, because if it were marble, he would be able to feel the roughness of the stone. It was also cold so it had to be some sort of glass or stone because of the temperature. The absolute smoothness was wonderful. He could run his hand up and down, but he couldn't feel where the top ended. It had to go on forever.

He described the feeling of a complex taste, like Angostura bitters, like touching an organic, living shape or thing, irregular like a ball of dough. It had the springy consistency of a mushroom, almost round, but he could feel bumps and could stick his fingers into little holes in the surface. There were leafy tendril-like things coming out of the holes, about six of them. He could feel them with his hands. The round part came first, with a spongy texture; then the shape developed and he could feel the holes; then the strands, a little thread first, which got bigger, like a rope. If he pulled his hand along one it felt like oily leaves on a short vine. The whole thing, he reported, felt like a scraggly basket of hanging ivy.

With intense flavors, the feeling sweeps down his arm into his hand. He can feel it as if he were actually grasping it. There is nothing to see, but there is a sense of movement. His synesthesiae is usually pleasurable. Rarely does he feel a "slap" or a "burning" on his face or a "pricking" in his fingertips. The shape changes with each moment, just as taste does.

In a test of blood flow in the cortex of this synesthete, the blood flows in the resting state were very variable from place to place. Some areas had very minimum blood flows, whereas in normal individuals it is pretty homogeneous. While experiencing geometric taste, however, the blood flow in the left hemisphere dropped to eighteen percent less than in the resting state. Normally, when the cortex is involved in some activity, blood flows in some areas increase at least ten percent, with twenty to fifty percent increases common.[356]

Cytowic continues: another synesthete reported, "I most often see sound as colors, with a certain sense of pressure on my skin. I am not sure that seeing is the most accurate description. I am seeing, but not with my eyes. I can't imagine being without my colors. One of the things I love about my husband is the colours of his voice and his laugh. It's a wonderful golden brown, with a flavor of crisp cherry and buttery toast."

A multiple synesthete when presented with a tone pitched at 2,000 cycles per second, reported, "It looks something like fireworks tinged with a pink-red hue. The strip of color feels rough and unpleasant, and it has an ugly taste – rather like a briny pickle…you could hurt your hand on this." The synesthesia enabled him to visualize vividly each word or sound that he heard. The thing to be remembered automatically converted, without effort, into a visual image of such durability that he could remember it years after the initial encounter. So specific was his ability that the same stimuli would produce the exact synesthetic response.

Synesthesia definitely has a genetic component: all synesthetes report having this remarkable ability since they were born, and it tends to run in families. It is predominant

[356] Richard Cytowic, *The Man Who Tasted Shapes.*

in females by at least 2 to 1, and is more common in left-handers.[357] Synesthesia is as common as *situs inversus*, a condition when the internal disposition of the organs is reversed (e.g., the heart is on the right, etc.), roughly one in ten thousand.[358]

The triggering stimuli are highly individualized and vary tremendously from person to person. For example, a woman reported that with a specific type of music, she saw shiny white isosceles triangles, like shards of broken glass. She also reported that colors had specific shapes: blue had lines and triangles; green had curves. She feels the space above her eyes is a big screen where this scene is playing.

At the other extreme, stimulation of any one sense causes synesthesia in the other senses. For example; a synesthete reported: I heard a bell ringing…a small round object rolled before my eyes…my fingers sensed something like a rope…I experienced a taste of salt water…and something white.[359]

When various synesthetes were tested hundreds of times with a wide range of flavors or sounds, plotting how often a certain shape or color was associated with each stimulus, a pattern emerged. The frequency patterns showed that synesthetic associations were invariant in one part of the test range, but contextual when the entire range was explored.

Synesthesia resembles a number of other experiences. It is partly like a sensation and partly like a memory, but it is unlike either, and has its own qualities.

There are several features of synesthesia:

a) It is involuntary but must be elicited. Synesthesia is insuppressible and cannot be conjured at will. Some synesthetes will respond only to a handful of stimuli, whereas others are sensitive to a much wider range of triggers.

b) The parallel sense that is triggered is projected outside the body. If visual, synesthesia is experienced close to the face. In other modes of sensation it is sensed in the space immediately surrounding the body.

c) The associations of an individual synesthete endure for a lifetime. Particular sensations have a unique feeling. They are always unembellished percepts like blobs, lines, spirals and lattice shapes with smooth or rough textures, agreeable or disagreeable tastes. Synesthetes do not see or feel complicated scenes, like the valley below or taste something like another previous taste, or touch a basketball.

d) The parallel sensations are easily and vividly remembered, often in preference to the stimulus that triggered them.

e) Synesthetes have an unshakable conviction that what they perceive is real.[360]

In the case of synesthesia, following the principle that neurons that fire together stay together and remain connected, a region of the cortex that normally would be devoted to one sense fires in synchrony with an area devoted to another sense, but not the other way around. In this way handshakes are established, ensuring that a particular stimulus that activates one region will also activate the other. Also, the former area sends its own echoes, while the latter sends some of the same echoes as the former as well as its own echoes. The identical echoes, thus established, are sent to the thalamus by two different sensory cortical areas and direct the stimulus to be mirrored to these two areas,

[357] http://wearcam.org/synesthesia/synesthesia_long.html
[358] Chris McManus, *Right Hand, Left Hand.*
[359] Richard E. Cytowic, *The Man Who Tasted Shapes.*
[360]Ibid..

instead of only one. For example, the secondary somatic sensory cortex fires together with the cortical gustatory area, or slices of the secondary visual areas fire the same echoes as parts of the secondary auditory cortices.

In the case of colored hearing we have to search for a mechanism where two different sensory areas send the same echoes: one associated with hearing, the other associated with seeing, and/or establish a distinct handshake between these areas that activates both simultaneously.

The inner ear transductive machinery is located within the temporal bone in a coiled structure called the cochlea. This is the location of the auditory receptors, termed hair cells. Each auditory receptor is sensitive to a limited frequency range of sounds. A topographical relationship exists between the location of a hair cell and the sound frequency to which the receptor is most sensitive. This differential frequency sensitivity of the cochlea is the basis of the tonotopic organization of the auditory receptive sheet.

Many of the components of the auditory system have a tonotopic organization. The topographic relationship between the receptor sheet and the central nervous system is similar to that of the somatic sensory and visual systems, where the subcortical nuclei and cortical areas have a somatotopic or retinotopic organization. In each of these cases, the topographic organization of the central representations is determined by the spatial organization of the peripheral receptive sheet. However, there is an important difference. The receptor sheets of the somatic and visual systems are spatial maps representing stimulus location (e.g., hand versus foot, macular versus peripheral). The cochlea represents the frequency of sounds. Source sound localization is computed by central nervous system's auditory neurons. The cochlear nuclei give rise to parallel auditory pathways that serve different aspects of hearing. In this way horizontal localization and source elevation of sound are determined. The signals eventually reach the medial geniculate nucleus, the thalamic auditory relay, which mirrors the signals to the cortex.

The primary auditory cortex contains multiple tonotopically-organized territories. Many secondary auditory areas surround it. Neurons in the primary area are activated by simple tones, whereas those in the secondary areas are better activated by complex sounds. In some animals, neurons in the secondary areas are activated by species-specific calls.[361]

Similar to the hierarchical structure of vision, the auditory cortex also processes hierarchically. Representations of simple objects at the bottom of the hierarchy can be reused over and over for different high-level sequences. For instance we don't have to use one set of words for the Gettysburg Address and a different set for Martin Luther King's "I Have a Dream" speech, even though both might contain some of the same words. A hierarchy of nested sequences allows the sharing and reuse of lower-level objects, letters, phonemes and words being but a few examples.[362]

The primary auditory cortex (area 41) is located in the middle top of the superior temporal gyrus, almost in the exact opposition of the secondary somatic sensory area, separated by the lateral sulcus. Surrounding the primary auditory cortex on the temporal lobe is the auditory integration area[363] (area 42, also known as secondary auditory area). They receive strong projections from the medial geniculate nucleus that mirrored the

[361] John H. Martin, *Neuroanatomy.*
[362] Jeff Hawkins, *On Intelligence.*
[363] Jean Talairach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

auditory signals arriving from the ears to these areas. These areas are interconnected by commissural fibers and have strong projections and afferents to and from various areas of the cortex: a) the area of visual integration (area 18) and area 19 (also known as V3, V4 and V5), which in turn is interconnected with adjacent areas and contralaterally to area 19 via callosal radiations; b) to the inferior portion of the postcentral convolution, which controls sensation from the teeth, gums, jaw, tongue, pharynx and intra-abdominal; c) to the insular cortex, comprised of the gustatory and the secondary somatic sensory area, across the lateral sulcus from the area of Broca (motor speech), the primary motor cortex, which controls the face, mouth and the pharynx, and most interestingly, area 40 that controls the auditory and visual attentional systems; and d) to the oculomotor fields (area 8).[364]

The auditory memories send handshakes to the visual areas to activate "visuals" related to the sounds. In this way, what we hear has more meaning and is better understood.

The primary auditory cortex and the auditory integration area send echoes to the medial geniculate nucleus of the thalamus to help direct the traffic of auditory impulses. The medial nuclei are adjacent to the midline nuclei, which are diffuse projecting nuclei (as opposed to single functional cortical areas), sometimes described as regional, because they cross functional boundaries in the cortex. The reticular nucleus is a layer that covers the thalamus and does not project to the cortex. Rather it sends axons to other thalamic nuclei and helps coordinate the activity of neurons within the thalamus.[365]

In synesthetes, the midline nuclei might be responsible for mirroring auditory signals to the visual cortex, as it receives identical echoes from the two regions. There are two possible mechanisms at work here. One is "cross wiring" at the thalamic level; and two, when the reticular nucleus detects two identical echoes, it coordinates incoming signals to be mirrored to these two locations.

The lateral geniculate nucleus is adjacent to the medial geniculate nucleus. Both are lodged inside the pulvinar nucleus. Typically, the signals from the eyes reach the lateral geniculate nucleus and are mirrored to the visual areas (18 and 19). The pulvinar nucleus has extensive connections, as well, with the visual auditory integration area (area 37), with the visual and hearing attentional systems (area 40 and 39), and with the somatosensory attentional system (area 7).[366]

Using functional magnetic resonance imaging (fMRI) in synesthetes that report colored hearing, speech activates, as expected, language areas of the superior temporal gyrus bilaterally, the left inferior frontal gyrus, and region V4 (in area 19) in the left hemisphere only, a color-selective region. Besides V4, there was activation in the left anterior fusiform gyrus (V4alfa, also in area 19), perhaps reflecting experience of colored percept with shape or object related properties. Interestingly, no activity was detected in area 17 (V1) or 18 (V2). Control subjects showed no activity in V4 when asked to imagine colors in response to hearing particular words.

Given the left lateralization of cortical language systems, the activation of left V4 might reflect the elicitation by speech-like sounds, rather than sounds in general, of synesthetic color experiences. More probably, because of this lateralization, the echoes in

[364] Ibid.
[365] John H. Martin, *Neuroanatomy.*
[366] Jean Talairach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

the left hemisphere are signaling the left thalamus to relay the signals to the left V4 area. Considering that area 19 (V3+V4+V5) is contralaterally connected, it is not surprising that despite this left lateralization, synesthetes did not report color experiences confined to the right visual field.[367]

Activation of the right claustrum in synesthetes alone is consistent with proposals that this region functions as a multimodal convergence area.[368] The claustrum is a telencephalic nucleus located beneath the insular cortex. The claustrum is a thin sheet of neurons connected reciprocally and topographically with the cortex. Selective activation in synesthetes has been observed in the left posterior cingulate (area 23 and 31). Strong, emotionally meaningful experiences have been associated with left posterior cingulate activity.[369] Since synesthesia is memorable and emotional, this is compatible with enhancement of activation in the posterior cingulate relative controls.

In almost all individuals, each sense will establish its own set of echoes. However, there is enough genetic drift that occasionally, under certain conditions, two different sensory areas will set up the same echoes and tags. If the thalamic relays of these senses are in close proximity, the possibility of producing a synesthetic experience is increased.

Sudden, loud sounds produce colored hearing more frequently than soft sounds or music. This suggests that signals from the pulvinar nucleus that activate the hearing attentional system, which normally sends handshakes to activate relevant memory systems to interpret the sound, also sends out other handshakes that activate visual areas to send the same echo as the sound to the thalamus, thus directing the signal to be mirrored to the visual areas as well. This kind of synesthesia should be labeled thalamic synesthesia. The firing synchronicity of neurons in some visual areas and some hearing areas will strengthen the handshakes established between them, ensuring that the echoes generated are identical; thus, the synesthetic experience is stable and recurrent. In such a case, only very specific sounds will elicit colors or visions.

The secondary visual areas (areas 18 and 19) are connected with the secondary auditory areas (areas 42 and 22). In a few individuals, in addition, parts of area 18 or 19 will establish a synchronous signal with portions of area 42 or 22 through these connections. These synchronous signals will establish the same echoes and tags to the thalamus. For the most part, areas 18 and 19 will set up their own set of echo signals to direct the traffic of visual signals through the lateral geniculate nucleus, but a few echoes will be identical to the echoes sent from the auditory areas. In this way, a wider range of frequencies of sounds can produce a synesthetic experience.

When a particular sound or frequency arrives at the thalamus, the identical echoes, arriving at the medial geniculate and lateral geniculate nucleus, will determine the signal to be mirrored to both the hearing and visual areas, respectively, that produced the echo. When the auditory signal arrives in the visual area, the sequence of action potentials that would be interpreted as a particular sound in the hearing area is interpreted

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[367] J.A. Nunn, L.J. Gregory, M. Brammer, S.C.R. Willimas, D.M. Parslow, M.J. Morgan, R.G. Morris, E.T. Bullmore, S. Baron-Cohen and J.A. Gray, *Functional Magnetic Resonance Imagining of Synesthesia: Activation of V4/V8 by Spoken Words.*

[368] Hadjikhani, N. & Roland, P. *Cross-modal Transfer of Information Between the Tactile and the Visual Representations in the Human Brain: a Positron Emission Tomographic Study.*

[369] J.A. Nunn, L.J. Gregory, M. Brammer, S.C.R. Willimas, D.M. Parslow, M.J. Morgan, R.G. Morris, E.T. Bullmore, S. Baron-Cohen and J.A. Gray, *Functional Magnetic Resonance Imagining of Synesthesia: Activation of V4/V8 by Spoken Words.*

in the visual area as a color, a shape, or both. For groups of neurons, a sequence of action potentials is a sequence of action potentials, but thanks to the echoes, these sequences acquire specific meaning as soon as they arrive. The colors thus perceived are as real as the sensation of phantom limbs.

In the case of phantom limbs, when an area that no longer receives sensory inputs from the missing limb starts receiving inputs from adjacent areas (e.g., other parts of the body), it mistakenly creates the very real illusion of the missing limb. Similarly, when auditory sensory inputs from the thalamus reach the visual areas, they are interpreted as very real sights.

The visions that are produced by sounds are highly individualized and particular for each synesthete according to the particular echoes established in his or her brain. When the synesthete feels a synesthetic sensation, the original emotional experiences that accompanied the trigger sensory signal are also similarly experienced. This emotional experience is what makes the synesthetic experience so memorable. The emotion is reinforced by each sense in relation to the sensation. Doubling the pleasure doubles the emotional response.

The fusiform gyrus, where color information is analyzed, also contains the area that represents visual graphemes of numbers. There are synesthetes that visually perceive numbers as particular colors: 5 might be seen as red, 6 as green, 7 as blue, 8 as yellow and so on. It seems likely that, just as amputation can produce cross-wiring between the face and the hand, synesthesia is caused by cross-wiring between the number and color areas in the fusiform gyrus due to an inherited abnormality. When these kinds of synesthetes are shown numbers in black and white there is activation of the fusiform gyrus (where color information is analyzed). In normal people the color area is activated only if they are shown colored numbers.[370]

Other synesthetic experiences can be explained in a similar fashion, or another sense might be added to the original synesthetic pair.

Other cases of synesthesia are less common because the visual and hearing attentional subsystems are not involved. These arise only when certain, separate sensory cortical areas fire in synchronicity and establish the same echo patterns with neighboring thalamic nuclei. For example, part of the secondary somatic sensory cortex is found in the insular cortex and the parietal operculum, and wraps around the lateral sulcus to a small area on the temporal lobe. The gustatory area is located in the frontal operculum and insular cortex. These two areas are practically overlapping.

The somatic sensory thalamocortical projections are somatotopically organized: neurons receiving input from the leg and the arm are located in the lateral division of the nucleus, whereas neurons receiving input from the face are located in the medial division. Similar to the primary area, the secondary somatic sensory area is somatotopically organized. This part of the cortex sends handshakes starting a sequence of somatic sensory projections to insular cortical areas and the temporal lobe that are important for object recognition by touch and position sense.

Taste is mediated by the facial, glosopharyngeal and vagus nerves. Taste receptor cells are clustered in the taste buds. Chemicals from food either bind to surface membrane receptors or pass directly through membrane channels to activate the taste cells. The distal branches of the primary afferent fibers of the three nerves mentioned

[370] V.S. Ramachandran. *A Brief Tour of Human Consciousness.*

innervate taste cells. These afferent fibers have a pseudounipolar morphology, similar to that of the dorsal root ganglion neurons. In contrast to the nerves of the skin, where generally the terminal portion of the afferent fiber is sensitive to stimulus energy, taste cells are separate from the primary afferent fibers. For taste, the role of the primary afferent fiber is to transmit sensory information encoded as a sequence of action potentials. The signal travels to the solitary nucleus in the brain stem and through the central tegmental tract arrives at the ventral posterior medial nucleus. Normally, the echoes received by the thalamus would help mirror the signal to the gustatory area in the insular cortex.

On the other hand, the somatic sensory pathways reach the ventral posterior lateral nucleus in the thalamus, adjacent to the ventral posterior medial nucleus, and from there, normally, signals are relayed to the primary somatic sensory cortex.[371]

In the case of geometric taste, parts of the secondary somatic sensory area fire in synchronicity with the gustatory area, probably because of proximity connections between the two adjacent areas. The result of this synchronicity is setting the same echoes from the secondary somatic sensory area as the gustatory area. As a result, the thalamus relays the gustatory signals to both areas. When they arrive at the gustatory area, they are interpreted as taste. When they arrive at the secondary somatosensory area, depending on the nature of the gustatory signals, the signals will be interpreted as different shapes. The secondary somatic area sends out handshakes that are interpreted as position sense signals. The varying sequences of taste action potentials will be interpreted as being felt on various parts of the body.

Most tastes will be felt on the face and hands, which not only are adjacent, but also use up almost half of the primary somatosensory area. The more intense the gustatory signal, the more the likelihood that the shapes will be felt with more parts of the body. The perception of shapes on different parts of the body is as real as the sense of taste, and in some cases, even more so. Or put in other words, the illusions created by the brain's processing of the various senses are perceived with more or less equal intensity.

The tendency for synesthetes to establish firing synchronicity between different areas of the cortex also means that interneurons in these areas will be firing synchronously and as a result, neighboring areas will be receiving more inhibitory signals. Instead of showing homogeneous activity throughout the cortex, this produces variable blood flow patterns in the cortex, showing synchronized areas with higher activity than normal, and areas that are inhibited with less activity than normal. These patterns, however, don't seem to affect most other neurological functions.

12
What Are You Feeling?

Inevitably, to understand the brain, we must understand emotions and their role. Building on previous ideas, I am deeply indebted to the coherent and logical presentations of Antonio Damasio in his books *The Feeling of What Happens* and

[371] John H. Martin, *Neuroanatomy.*

Looking for Spinoza. I want to emphasize that any modifications I have made in the ideas of this author or anyone else are solely my responsibility, especially when I introduce new concepts.

Emotions occur in two types of circumstances: when an organism processes certain objects or situations with one of its sensory systems (i.e., sees a familiar place), or when the organism imagines a certain object or situation (i.e., remembers someone who died). A range of stimuli can induce certain classes of emotions. Personal experience and culture certainly influence the genetically preset manifestations of emotion; experience and culture shape what can induce an emotion, and shape some aspects of the expression of the emotion, as well as the cognition and behavior that follow the deployment of an emotion.

Emotions can be induced indirectly. The inducer stimulus can produce its result in a negative fashion by blocking the progress of an ongoing emotion. In the presence of a source of food or sex, an organism develops approach behavior and exhibits features of the emotion happiness; if blocked and prevented from its goal, the organism will experience frustration and even anger, very different emotions from happiness.

As organisms develop and interact with the environment, they gain factual and emotional experience with different objects and situations, and thus associate many objects and situations, which would have been emotionally neutral, with the objects and situations that are naturally prescribed to cause emotions.[372]

From personal experience, we know that emotions can be varied. Some responses are easily apparent; the muscles of the face producing expressions typical of joy, sorrow or anger, or the skin blanching as a reaction to bad news or flushing in a situation of embarrassment. Consider the body postures that signify joy, defiance, sadness, or discouragement; or the sweaty and clammy hands of apprehension; the racing heart associated with pride or the slowing, near stillness of breathing in terror.[373]

Most animals live, from an emotional point of view, with almost automatic reactions to the emotional stimulus. In humans, where we can more easily switch from automatic reactions to willful control, the advantages come from pairing the emotional to the cognitive functions. This allows a shift away from reaction to action or even choosing from several alternate actions. We have also mentioned how thinking can affect emotions, or vice versa, how emotions are activated to suppress particular thoughts.

The hypothalamus, basal forebrain and brain stem release chemicals to initiate emotions and their presence temporarily changes the working of many neural circuits. Emotions trigger myriad chemical changes; hormones are released into the bloodstream and produce a series of changes in the organs, body and brain. Neurotransmitters, such as monoamines, norepinephrine, serotonin and dopamine, are released. As a result of the raising or diminishing concentrations of these neurotransmitters, a feeling of thoughts speeding up or slowing down, as well as a sensation of pleasure or unpleasantness, is produced.

The changes are controlled by two different channels: the bloodstream, where chemical molecules act on receptors in the cells that constitute body tissues; and, neural pathways where electrochemical signals are sent to other neurons, muscular fibers or organs (such as the adrenal gland), which in turn can release chemicals of their own into

[372] Antonio Damasio, *The Feeling of What Happens.*
[373] Antonio Damasio, *Looking For Spinoza*.

the bloodstream.[374] Peptides and their receptors are richest in the parts of the brain implicated in the expression of emotions. Drugs that mimic the brain's endorphins, like heroin, opium, PCP, lithium and Valium clearly affects the emotional state of the person that takes them, making him or her, happy, sad, relaxed or anxious.[375]

The result of this coordinated chemical and neural change is a modification in the state of the organism. This includes changes in the body and the brain itself. The release of substances, such as monoamines and peptides from regions in the brain stem and basal forebrain, alters the mode of processing of numerous other brain circuits, triggering certain specific behaviors (e.g., motivating bonding, playing or crying, fleeing or fighting), and modifies the signaling of body states to the brain.[376] Peptide juices are released from brain glands and brain cells and they bind with specific receptors that enable them to act at sites far from where they originated. However, immune cells also make the same chemicals that control mood in the brain. So the immune cells not only control the tissue integrity of the body, but they also manufacture information chemicals (peptides) that can regulate mood or emotion.[377]

Positive and negative emotions are mediated by different circuits but can use the same area; for example, the area used for face recognition, will be used to identify friend and foe, with differing emotional responses. Neuroimaging data demonstrate that the neural activation pattern of happiness is remarkably distinct from sadness.

Pain and pleasure are two different regulatory modes. Pain is related to punishment. Under most conditions, punishment causes organisms to close themselves in, freezing and withdrawing from their surroundings. Pleasure, on the other hand, generally, is related to reward and is associated with behaviors such as seeking and approaching. Reward causes organisms to open themselves up and out to the environment, approaching it, exploring it, thus increasing both their opportunity for survival and their vulnerability.

Different emotions are produced by different brain systems. Yet, the brain induces emotions from a remarkably small number of brain sites, most of them subcortical. The main subcortical ones are in the brain stem region, hypothalamus and basal forebrain. One example is the periaqueductal gray, which is a major coordinator of emotional responses. The periaqueductal gray acts via motor nuclei of the reticular formation and via the nuclei of cranial nerves. Another very important subcortical site is the amygdala. The induction sites in the cortex include areas of the anterior cingulate region and the ventromedial prefrontal region.

There have been many attempts at classifying emotions, most of which have been manifestly inadequate. Antonio Damasio in his book *The Feeling of What Happens* classifies emotions in three tiers: primary emotions, background emotions and social emotions.

Primary emotions are the easiest to define because there are certain prominent emotions in this group. The frequent list includes fear, anger, disgust, surprise, sadness and happiness. These emotions are universal across cultures and in non-human species as well. The circumstances that cause the emotions and pattern of behavior that define them are also quite consistent across cultures and species.

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[374] Antonio Damasio, *The Feeling of What Happens.*
[375] Candace Pert, *Molecules of Emotion.*
[376] Antonio Damasio, *The Feeling of What Happens.*
[377] Candace Pert. *Molecules of Emotion.*

Background emotions are very subtle but remarkably important. These can be subtle, like malaise or excitement, edginess or tranquility, energy or enthusiasm. Some individuals are very good in detecting them in others through facial expressions and body movement. Background emotions are the consequence of deploying certain combinations of simple regulatory reactions (e.g., basic homeostatic processes, pain and pleasure behaviors, and appetites). They are the result of largely unpredictable combinations of several concurrent regulatory processes engaged as reactions to whatever internal metabolic adjustments are needed, and coordinated with whatever external situations are being handled by other emotions, appetites or intellectual calculations.

Background emotions can be distinguished from moods, which refer to sustaining a given emotion over long periods of times, lasting hours or days. Mood is a term that can be applied to the frequently repeated or prolonged engagement of the same emotion.

The social emotions include sympathy, embarrassment, shame, guilt, pride, jealousy, envy, gratitude, admiration, indignation and contempt. Simon Baron-Cohen has come up with four-hundred-and-twelve different emotions.[378] A whole retinue of regulatory reactions along with elements present in primary emotions can be identified as subcomponents of social emotions in varied combinations. The nested incorporation of components from lower tiers is apparent. Think of how the social emotion "contempt" borrows facial expressions of "disgust," a primary emotion that evolved in association with the automatic and beneficial rejection of potentially toxic food.[379]

Robert Plutchick, a psychology professor at Hofstra University proposed a theory of eight primary emotions – sadness, disgust, anger, fear, anticipation, joy, acceptance and surprise—which, metaphorically speaking, like primary colors could be mixed to produce secondary (or social) emotions.[380] Whether one emotion is a mixture of other emotions might be hard to discern, yet each emotion is a particular state. We will later look into the possibility of the brain "learning" to generate "new" recurring emotional states based on particular triggers.

The ever-changing result of this cauldron of interactions is our "state of being": good, bad, or in-between. When asked, "How we feel," we consult this "state of being" and answer accordingly.

Each emotion helps the brain monitor the state of the body and indicates a slightly different state. When the brain detects an emotion, it is experienced as a feeling. This feeling will be specific to each emotion. We speak of the thrill of surprise; the tingling sensation that goes down the back when something extraordinary happens; twinges of guilt; throbs of passion; pangs of sadness; gnawing grief; butterflies in our stomach; clammy hands. Our language reflects a changing physiology as feelings shift. These subtle changes in physiology also affect the brain. Memories of past experiences and emotions are intimately woven and trigger each other. Particular tastes and smells, not surprisingly, have strong links to memories and feelings.[381]

Various neuropeptides act as ligands in different emotional states and activate particular neural circuits, both in the brain and the body, which generates a behavior involving the whole organism, along with all the required physiological changes. It is

[378] Steven Johnson, *Mind Wide Open.*
[379] Antonio Damasio, *The Feeling of What Happens.*
[380] Candace B. Pert, *Molecules of Emotion.*
[381] Antonio Damasio, *The Feeling of What Happens.*

becoming apparent that the role of peptides is not limited to eliciting simple and singular actions from individual cells and organ systems. Instead, peptides serve to integrate the body's organs and systems into a single system that reacts subtly to external and internal stimuli.[382]

In some instances, emotional responses are innate; in others they may require learning from an appropriate exposure to the environment. In other cases it is a combination of both. It has been shown that a monkey's innate fear of snakes requires not just the exposure to the snake but to the mother's expression of fear of the snake. Once is enough to engage the proper behavior, but without the once, the innate behavior is not triggered.

Moreover, it is important to understand that emotions are triggered as reactions to stimuli from the environment. Just like the brain integrates the extrapersonal with the intrapersonal space to produce a seamless map to navigate through the environment, the brain tries to create a seamless interface between the outside stimuli and the internal emotional landscape in such a way as to produce the correct responses to the changing environment. Emotions are always a reaction to the rich patterns that the senses are conveying (echo matched to stimulus), either genetically wired or learned as emotional competent stimuli.

The echoes generated at low hierarchical levels in the sensory areas do not generate echoes capable of triggering an emotion; neither do the cortical areas associated with constructing a spatial map of the environment. The echoes capable of triggering emotions will come from higher levels where abstract interpretations of what we see or remember are created; this happens at the level of naming objects or higher. However, we need to keep in mind that higher level representations (or memories) are created from the lower level sensory signals, and that the feedback handshakes send echoes from layer V (mirroring forward) keep a whole array of levels active simultaneously. With this in mind, the color green might have a "calming" effect because of the myriad associations to it, or the color "red" might have an "unsettling" effect for the same reasons. Yet, a green Ferrari might be less appealing than a red one, because of a completely different set of associations.

Organisms can produce advantageous reactions (emotions) that lead to good results without deciding to produce those reactions, even without feeling the unfolding of those reactions. These reactions are passed on genetically as preprogrammed emotions that will be triggered in the presence of particular types of stimuli. Then, the organism moves for a certain period toward states of greater or lesser physiological balance. These automated reactions create conditions in the human organism that, once mapped in the nervous system, can be represented as pleasurable or painful and eventually known as feelings. We humans, conscious of the relation between certain objectives and certain emotions, can, to some extent, willfully strive to control our emotions.

Damasio offers the following working hypotheses of emotion-proper in the form of the following definition:

1. - An emotion proper, such as happiness, embarrassment or sympathy, is a complex collection of chemical and neural responses forming a distinctive pattern.
2. - The brain produces the responses when it detects an emotional competent stimulus (ECS), the object or event whose presence, actual or in mental recall, triggers the

[382] Candace B. Pert, *Molecules of Emotion.*

emotion. The responses are automatic. *The ECS is set in memory and produces an echo signal with a respective tag.*[383]
3. - The brain is prepared by evolution to respond to certain ECSs with specific actions. But these can include many that are learned in a lifetime of experience. *New memories set new echoes.*
4. - The immediate result of these responses is a temporary change in the state of the body proper and in the state of the brain structures that map the body and support thinking.
5. - The ultimate result of the responses is the placement of the organism in circumstances conducive to survival and well-being.

The process starts with an appraisal-evaluation phase, starting with the detection of the ECS. *The thalamus matches the stimulus to an ECS echo.*

To store an ECS echo in the cortex requires a higher level area, probably four or more levels up, so that the convergence of many signals from the lower areas generate a stable pattern. This stable pattern activates the echo, and as the combinatorial sensory signals match the convergent signals that produced the ECS echo, the thalamus triggers the appropriate emotional response. However, a partial match of the sensory signals to the ECS echo can trigger the emotion, similar to the auto-associative memories where part of a pattern or sequence is enough to activate the memory.

Wilder Penfield and others found that stimulation of most areas of the cortex produced no reportable sensations, movements or feelings. The excitable areas that produce responses are limited the to the primary sensory areas for bodily and somatic sensations, the visual area (in the occipital lobes) and the auditory cortex. He also observed psychic reports of hallucinations, memories and so on when he stimulated some areas of the temporal lobe. Benjamin Libet and others have shown that stimulation of the "silent" areas produces considerable responsiveness by local nerve cells, but no subjective response. On the other hand, electrical stimulation of the silent areas in animals has been shown (By Robert Doty and others)[384] to participate as part of a conditioned reflex (CR). In an ordinary CR, an effective unconditioned stimulus (US) produces a natural response that requires no learning (withdrawing a paw when a mild shock is applied). If an unrelated conditional stimulus (CS) is applied less than 1 sec before the US, the animal learns to withdraw the paw when the CS (an auditory tone) is applied alone. An electrical stimulus to silent cortex can act like a more conventional CS, equivalent to a sounding tone. That is the animal can learn to withdraw its paw when the electrical stimulus is given alone.[385] The electrical stimulus to the cortex can act as a match between stimulus and echo, activating the related handshakes that cascade to produce the CR.

As we develop, most objects that surround us can trigger some form of emotion, weak or strong, good or bad, and can do so whether we feel (are conscious of) the emotion or not. Some of these triggers were set by evolution, but our brains associate some with emotionally competent objects by virtue of our experience.

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[383]Words in italics added by author.
[384] Robert W. Doty, *Electrical Stimulation of the Brain in Behavioral Cortex.* Annual Reviews of Physiology 20:289-320.
[385] Benjamin Libet, *Mind Time.* 2004

In neural terms, images or sounds related to the emotionally competent object must be represented in one or more of the brain's sensory processing systems, such as the visual or auditory regions. This image is made available to emotion-triggering sites in the form of an echo signal with a tag so the thalamus can trigger the emotion.

The thalamus will try to match the incoming sensory signals with the continuous echo signals arriving from the cortex searching for one that matches an ECS. If a match is found, a number of emotion-execution sites will be activated elsewhere in the brain. These sites are the immediate cause of the modified emotional state in the body and the brain regions that support the emotion-feeling process. The process can reverberate and amplify itself or shrivel, dampen and close down.[386]

Primary emotions are triggered automatically by the thalamus when an echo representing the emotionally competent stimulus matches a corresponding stimulus. This automatic trigger is done without any further cortical processing of the stimulus. This process begins when neural signals of a certain configuration, originating in the visual cortices that are holding patterns corresponding to the threatening object (the echoes and handshakes that help signal that the object is dangerous), are relayed in parallel along several pathways to several brain structures. When the thalamus finds a match between stimulus and the echoes, the amygdala will be activated immediately and will send signals to other brain regions, thus producing the cascade of events that will become an emotion. These chemical and electrical messages that produce changes in the state of the body and the brain are called emotions. When the brain detects these specific changes, that particular emotion is experienced as a feeling.

The thalamus relays the stimulus to the cortex for further evaluation. After reaching the appropriate areas in the cortex, a series of handshakes are activated to interpret the stimulus in greater detail. Complex patterns of handshakes will represent differing degrees of positive or negative affective valence, particularly in the case of competent social emotion stimuli. When the orbitofrontal area detects these complex patterns of handshakes, it feeds back signals to the hypothalamus, amygdala and reticular formation. The orbitofrontal area sends echoes matching the incoming stimuli, and the subcortical structures will increase or decrease the emotional reaction accordingly. The reticular formation is involved in arousal and it is the most basic level of regulatory process. The connections to the hypothalamus, the head ganglion of the autonomic nervous system, controls visceral-somatic emotional reactions. The amygdala is involved in processing fear and anger, having to do mostly with primary emotions.[387]

The first expressions of emotion are genetically wired. Most mammals and birds, very early in their development, emit sounds to express these first emotions, mostly background emotions related with maintaining homeostatic balance (i.e., hunger, discomfort, pain). In the presence of certain hormones, the parents are imprinted by these sounds, which in turn activates certain nourishing and protective behaviors. These initial interactions between parents and offspring, generally olfactory-gustatory and tactile-thermal sensory modalities, help reinforce the brain's circuits involved in homeostatic regulation. Similarly, at slightly later stages other cognitive signals, generally auditory-visual or auditory-olfactory, become capable of triggering emotions. Through experience, an assortment of objects and events become emotionally competent stimuli to trigger the

[386] Antonio Damasio, *The Feeling of What Happens.*
[387] Allan Schore, *Affect Dysregulation.*

primary and social emotions. Some of these and their expressions are commonly learned from his or her parents.

In humans, initially, the bonding between infant and mother is patterned by an infant-leads-mother-follows sequence of interactions. This highly organized nonverbal dialogue of auditory and visual signals is transacted within milliseconds, consisting in cyclic oscillations between attentive and inattentive states.[388] The quick changes of visual and auditory stimuli, provided by the mother's facial gestures and voice, automatically engage and disengage the attentional systems controlled by the thalamus. The infant's developing regulatory systems, through these continuous changes of state produce spontaneous physiological rhythms manifested as fluctuating emotional states. As each sensory modality matures by adding more memories and discriminates better among stimuli, a greater repertoire of memories related to each emotion is stored.

Face-to face interactions begin at about two months in the context of social play. A little before one year, the child can read the mother's face for emotional information about the physical environment by following her gaze. The mother's facially expressed emotional communications provide the infant with appraisals of objects and events. In social contexts this process of "emotional vision" directly influences the infant's learning of "how to feel," "how much to feel," and "whether to feel" about objects or events in the environment. This very efficient system of emotional exchanges is entirely nonverbal, and it continues throughout life, particularly used in intimate relationships.

The orbital cortex matures in the middle of the second year, a time when the right hemisphere ends a growth phase and the left hemisphere begins one. The orbitofrontal cortex is involved in evaluating the emotional significance of events. It is at this time that individuals begin to impute mental states to self and others and predict behavior on the basis of such states. Indeed there is evidence that the capacity of empathizing and inferring the states of others is mediated by the orbital frontolimbic system. Also, at this time, limbic areas show anatomical maturation, suggesting that corticolimbic functional activity relating emotions and memory are active by this time.[389]

The Caudate Nucleus

The importance of the interrelation of emotions and memories cannot be stressed enough. The caudate nucleus surrounds the globus pallidus, which is lateral to the thalamus. It is composed of a head, directly above the globus pallidus, a body that curls around it and a tail that bends forward in a C-shape and ends at the amygdala.

The caudate nucleus and the putamen, which develop from the corpus striatum, are incompletely separated by axons of the internal capsule. This partial separation is reflected in thin cell bridges that link these two structures. The internal capsule, shaped like an arrowhead, contains ascending thalamocortical and descending cortical fibers. The caudate nucleus is medial to the internal capsule and the putamen and nucleus accumbens are lateral.[390] The putamen is part of the circuit that integrates the extrapersonal and intrapersonal space and is important in the control of movement. These connections quickly activate the initiation of movement when a response is necessary.

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[388] Ibid.
[389] Ibid.
[390] John Martin, *Neuroanatomy.*

The caudate nucleus has numerous afferent connections from the thalamus and through it efferent connections to the premotor and motor areas. These afferent fibers come into the matrisomes. Matrisomes are clumps of axon terminals that are also receiving signals from the lateral prefrontal cortex, the orbital frontal cortex and the anterior cingulate gyrus. There are strong efferent projections to the basal ganglia outputs, which are feeding back to the thalamus as well as to the medial and lateral globus pallidus and subthalamic nuclei.

Striosomes are clumps of axons receiving signals from the amygdala and the orbital frontal cortex. They are connected to the matrisomes via special neurons called tonically active neurons (TANs). The TANs fire with characteristic patterns when the brain senses something with positive or negative emotional meaning. The characteristics of these signals determine the patterns. These various patterns, representing emotionally competent stimuli, elicit different behavioral and cognitive responses as TANs shift the output flow to the striatum (putamen and globus pallidus). In this way, TANs could serve as the foundation for the development of new patterns of activity in the striatum. More important, TANs could be crucial for the acquisition of new behavioral skills.[391]

The caudate body is part of the oculomotor loop, which aids control of eye movement through its connections with the various cortical areas (the frontal eye and supplementary field (area 8) and with the visual areas 18 and 19).

The caudate head is part of the prefrontal loop, which aids in controlling movement by providing the premotor cortical areas with information about the body integrated with extrapersonal.

The caudate nucleus is ideally situated, with its rich connections to the cingulate girus, the cortex, the striatum and the thalamus, to activate memories, experiences, modes of thinking and behaviors associated with particular emotions. When the organism is presented with stimuli that set off an emotion, the brain activates only relevant information instead of wasting time sifting through all past experiences. In most cases action is of the essence. There is no time to ponder at length; it doesn't do any good to be mauled by a predator and recognize that it was a tiger half an hour after the fact.

Once the caudate nucleus detects an emotion it sends signals to activate specific memories related to the emotion. The echoes of the memories along with signals from the amygdala and thalamus guide the hippocampus to put the emotion into the context of the stimulus and activate only memories that are related to this context. The combination of chemical changes in the body and brain and the activity of the caudate are the mechanisms through which memories and experiences related to the emotion in a particular context are quickly activated. The reverse is also possible: certain memories can trigger related emotions.

The Regulation of Emotions

Emotions are a direct expression of bio-regulation. Some of the structures or regions in the brain identified as emotion-triggering sites are the amygdala, the hypothalamus, a part of the frontal lobe known as the ventromedial prefrontal cortex

[391] Jeffrey M. Schwartz, *The Mind and the Brain*.

(areas 10 and 11) and another frontal region, the supplementary motor area (area 6), and the cingulate (area 24) among others.[392]

The orbital frontal cortex, adaptively modulates lower structures, inhibits drives and regulates arousal. Alexandr Luria showed that disturbances of the orbital frontal regions elicit changes in affective process, such as, lack of self control, emotional outburst, generalized disinhibition, and disorganization of personality.[393]

The amygdala is an important interface between visual and auditory ECS and the triggering of emotions, in particular, but not exclusively, fear and anger. When the amygdala is damaged, fear and anger are not possible. Activation of the amygdala shows a linear relationship with decreasing intensity of happiness and increasing intensity of fear.

Emotionally competent stimuli are detected very quickly, ahead of selective attention. This is accomplished by setting up an echo signal with a tag that, when a (sensory) stimulus is matched by the thalamus, automatically triggers an emotional response even before the stimulus is further processed cognitively.

When there are lesions of the occipital lobe or parietal lobe that cause a blind field of vision (certain categories of objects can't be "seen", called blindsight), ECS (e.g., angry or happy faces) nevertheless "break through" the barrier of blindness and are indeed detected. The triggering emotional machinery captures these stimuli because they bypass the normal channels – channels that might have led to cognitive appraisal but simply could not do so because of blindness.[394] In the thalamus, echoes are matched to the stimulus, the appropriate emotion is thus triggered and handshakes are activated in spite of the blindness. The handshakes, in turn, activate other areas that interpret the emotional significance of the stimulus without interpreting the spatial-visual aspects of it.

The ventromedial frontal area (areas 10 and 11) and especially the orbitofrontal cortex (areas 11 and 47) are tuned to detecting the emotional significance of more complex stimuli, for example objects and situations, natural and learned.

The orbito-frontal circuit is responsive to events in the external environment, especially the social environment. It has also been shown that it is active in response to the emotional expressions of human faces, is involved in attachment processes and in the pleasurable qualities of social interaction. Orbitofrontal areas also subserve memory and cognitive-emotional interactions and are activated during the mental generation of images of faces. These areas are participate in the encoding of high-level, psychological representation of other individuals. This system thus contains the capacity to generate internalized object relation; that is, a self-representation, and object representation, and a linking affect state.[395]

Social emotions are triggered by complex and specific patterns of handshakes from the sensory and other cortex areas that, when presented together, are recognized by the frontal lobes as emotional competent stimuli (ECS) through genetic and learned responses in our childhood. Once the ECS is recognized, represented by complicated neural patterns, echo signals from the ventromedial frontal area and the orbital cortex that represent the ECS are sent to the thalamus and the caudate nucleus, automatically

[392] Ibid.
[393] Shore, A.N. *Affect Regulation and the Repair of the Self.* 2003.
[394] Ibid.
[395] Shore, A.N. *Affect Regulation and the Repair of the Self.* 2003.

triggering the appropriate social emotion. Social emotions differ slightly from primary emotions. In primary emotions, the thalamus detects an exact match between incoming sensory signals and the echoes from the cortex representing the primary ECS and the emotion is triggered automatically. In social emotions, the ventromedial and orbital frontal areas detect complicated patterns of handshakes representing the social ECS. Depending on the handshakes' qualities, echoes are sent to the limbic system and the thalamus and automatically signals are sent to initiate the proper social emotion by initiating the appropriate chemical and neural responses without further matching with sensory signals.

The orbitofrontal areas also signal the amygdala, the hypothalamus and the reticular formation and through dopaminergic or noradrenergic activity increase or decrease emotional responses. It has been demonstrated that damage to this region alters the ability to emote when the ECS is social in nature, especially when the appropriate response is a social emotion such as embarrassment, guilt or despair. Impairments of this sort compromise normal social behavior.

The frontolimbic system provides a high-level coding that flexibly coordinates sensory and somatosensory information and functions to correct responses as the conditions change, processes feedback information, and therefore monitors and adjusts emotional responses and modulates control of goal-directed behavior.

The orbitofrontal cortex is known to functions as an appraisal mechanism using cognitive as well as emotional components. It acts to integrate and assign emotional-motivational significance to cognitive impressions; it associates emotion with ideas and thought. The orbitofrontal system is also deeply connected into the autonomic nervous system and the arousal-generating reticular formation, and due to the fact that it is the only cortical structure with such direct connections, it can regulate autonomic responses to social stimuli[396] and thus fine-tune social emotions.

The ventromedial frontal areas also send signals directly to the amygdala, in this way help to regulate the emotional responses more finely by dampening or increasing the response.

The primary role for the right ventromedial prefrontal cortex may be the integration of internal physiological states with important environmental cues, to guide behavior in an optimally cautious or adaptive manner in situations of perceived threat (Sullivan & Gratton, 2002),[397] or other emotionally competent stimuli.

These prefrontal circuits are expanded in the right hemisphere. They regulate psychobiological states and organismic energy balance in a nonlinear way and enable the organism to cope passively and actively with stress. The right hemisphere plays a superior role in the control of vital functions supporting survival and coping with external challenges. Indeed, the right brain is thought to contain the essential elements of the self-system.

The orbital prefrontal cortex is especially expanded in the right hemisphere, which is responsible for regulating homeostasis and modulating physiological state in response to both internal (i.e., visceral) and external (i.e., environmental) feedback. Because the right (more so than the left) cortical hemisphere has extensive reciprocal

[396] Allan Schore, *Affect Dysregulation.*
[397] Allan Schore, *Affect Regulation and the Repair of the Self.*

connections with limbic and subcortical regions, it is dominant for the processing, expression and regulation of emotional information.[398]

Using concepts from physics is useful to begin to understand how this is possible. In dynamic systems theory when an open system is openly exchanging energy and matter with the environment it uses free energy for matter-energy transformations and exports it in degraded form. As a result, the system moves away from equilibrium and remains for periods of time in disequilibrium, one that exhibits negative entropy. In this manner the flow of energy through the system creates conditions for strong deviations from thermodynamic equilibrium, and this results in the phenomenon of self-organization. Energy is continuously dissipated when a system is far from equilibrium. This process binds the elements of the system together by behaving in a synchronous fashion with ongoing feedback and to act together rather than as independent entities.

As the patterns of the signals among the elements of a self-organizing system become more increasingly interconnected and well ordered, it is more capable of maintaining a coherent organization in relation to variations in the environment.[399] In other words, the brain is attempting to maintain at all times a one-to-one internal emotional landscape in relation to the external conditions to produce the best response. This depends on the brain creating and maintaining a dynamic model of the external environment and generating a new internal emotional representation in response.

In chaos theory vernacular, emotions represent desired attractors that maintain self-organization by perpetuating emotional equilibrium and resolving emotional disequilibrium. Chaotic variability in self-regulatory activity is thus necessary for flexibility and adaptability in a changing environment. Further research has indicated that the orbitofrontal circuits are specialized for cognitive-emotional interactions, and that neurons in the right prefrontal cortex with balanced excitatory and inhibitory signals show chaotic behavior.[400]

Neurons in the ventromedial prefrontal region respond rapidly and differently to the pleasant or unpleasant emotional content of pictures. Unpleasant emotions activate the right side more.[401] This suggests a certain asymmetry in which the right side is more involved with negative emotions than the left. More likely, more activity on the right side, relative to the left, is perceived as a negative emotion.

The hippocampus is connected to the amygdala through the basolateral nucleus and provides it with information about the context of the present emotion. The basolateral nucleus communicates with the central nucleus and the basal nucleus. The basal nucleus sends signals to the hypothalamus, midbrain, pons and medulla, and thus helps control the emotion reactions according to the context. The basal nucleus projects to the periaqueductal gray matter and, in this way, the extent of an emotional reaction (gestures and motor actions) can be carefully adjusted depending on the specifics of a particular situation.

The emotion-execution sites include the hypothalamus, the basal forebrain and some nuclei in the brain stem tegmentum. The hypothalamus is the master executor of many chemical responses that are part of our emotions. It releases into the bloodstream,

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[398] Ibid.
[399] Allan Schore, *Affect Dysregulation.*
[400] Ibid.
[401] Jeffrey M. Schwartz, *The Mind and the Brain*.

directly or via the pituitary gland, chemical molecules that alter the internal milieu, the function of viscera, and the function of the nervous system. Oxytocin and vasopressin, both peptides, are examples of molecules released under the control of the hypothalamic nucleus with the help of the posterior pituitary gland.[402]

Many emotional behaviors (like attachment and nurturing) depend on the timely availability of these hormones within the brain structures that command the execution of these behaviors. It is crucial to have the right responses at the right times. Attempting to have sex with a predator could be lethal under the best of conditions.

Likewise, the local availability of molecules, which modulate neural activity, like dopamine and serotonin, causes certain behaviors to occur. The sort of behaviors experienced as rewarding or pleasurable appear to depend on the release of dopamine from one particular area (the ventrotegmental area in the brain stem) and its availability in yet another area (the nucleus accumbens in the basal forebrain).

In short, the basal forebrain and hypothalamic nuclei, some nuclei in the brain stem tegmentum, and the brain stem nuclei that control the movement of the face, tongue, pharynx and larynx are the ultimate executors of many behaviors, simple and complex, that define emotions, from gestures and body postures, to courting or fleeing, to laughing or crying and fighting. It makes sense that the controlled movements of vocalizations (screaming or shouting), or facial gestures (laughing or smiling), or body postures (leaning forwards or slumping) are intimately linked to communicating the different emotional responses. Facial expressions, vocalizations, body postures and specific patterns of behavior (e.g., running, freezing, parenting and so on) are thus enacted. The body chemistries as well as the viscera, such as heart and lungs, help along. Emotion is all about transition and commotion, sometimes real body upheaval. In a parallel set of commands the brain structures that support image-production and attention change as well. Depending on the chemistry of each emotion, some areas of the cortex become less active while others become particularly active.

Emotions elicit particular memories to initiate certain behaviors in response to specific stimuli. They manage this in three ways: (1) the chemistry of the emotional state activates all memories related to the emotion, as this chemistry is specific to the memories; (2) they intrude on the attentional systems; and (3) they initiate certain behaviors (motivations or modes of thinking) like fleeing or approaching the stimulus. Motivation is used here as a term that refers to neural activity that guides us to a goal, outcomes that are desirable and for which we will exert effort, or to the opposite, an outcome that we dread and will exert effort to prevent, escape from or avoid.

Goals direct action. They can be a specific stimulus (food) or an abstract belief or idea (it is worth dying defending freedom). Some of our beliefs are obtained early in childhood by conditioning (families should or should not stay together) or by observational learning (we learn to parent as young children and we learn to hunt by playing games) or even by force of imagination (God is on my side).

Not all motivations are induced by emotions, but emotions are powerful motivators to action. Motivations can be modified by past experience. The purpose of these beliefs is to push the brain into a state that more likely will produce an instrumental response. The nucleus accumbens might be part of the interface between emotion and movement; dopamine release in this region might play a role in goal-directed behavior.

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[402]Ibid.

This is based on the following: (1) the nucleus accumbens receives massive dopamine inputs from the tegmentum, (2) injection of amphetamine or cocaine (they mimic dopamine) into the nucleus accumbens leads to behavioral activation, (3) the nucleus accumbens receives inputs from the amygdala and other emotional related areas, and (4) the nucleus accumbens sends output to areas involved in the control of movement (such as the pallidum, an area that connects with the movement control areas in the brain stem and cortex).

In the presence of an emotionally arousing stimulus, the brain is placed in a state, sometimes called a motive state, which leads to coordinated information processing within and across areas, and results in invigoration and guidance of behavior towards positive goals and away from aversive ones. When the pallidum receives more input from the nucleus accumbens, the motor regions are strongly activated and movement is initiated. Behavior can be potentially invigorated by anything that activates tegmental cells and causes them to release dopamine in the accumbens. Novel stimuli are a prime example of invigorating stimuli. But invigoration alone is not enough; behavior also needs to be guided. The amygdala through the basal nucleus will signal the accumbens if it detects a positive outcome and increases the dopamine release and reinforces the signal to the pallidum.

Once an emotional habit is well learned, the brain system involved in expressing it becomes simpler. Once learned, the procedure might be transferred from the accumbens to the cortex. With an expanded cortex, more habits can be stored and enacted. This is similar to explicit learning: initially, both the hippocampus and cortex are involved, but once the hippocampus has slowly "taught" the cortex the memory, the memory persists without the aid of the hippocampus. The hippocampus participates by way of its connections to the amygdala and nucleus accumbens, and may well be involved in the guidance of behavior on the basis of spatial and other kinds of relational or emotional cues in the environment. In order to find good things and avoid bad ones, you need to know where you are, where you need to go, and how to get there from here, as well as activating all the memories that might be useful to guide you on the way. The hippocampus contextualizes emotions, and if the context is appropriate, reinforces the emotion; conversely if the context is inappropriate, the hippocampus defuses the emotion.

There are two main dopaminergic systems: 1) The nirgrostriatal dopaminergic system, originating in the substantia nigra pars compacta and projecting primarily to the caudate and putamen, and less so to the nucleus accumbens. The caudate participates in eye movement and cognition; the putamen participates in control of trunk and limb movements; and the nucleus accumbens participates in emotions. The caudate, the putamen and the globus pallidus integrate the body and the environment into a seamless map. Dysfunction of the nigrostriatal systems is associated with Parkinson disease; and 2) The mesocorticolimbic dopaminergic system originates from the ventral tegmental area and provides the principal dopaminergic innervation of the nucleus accumbens, the amygdala and various parts of the cortex, especially the prefrontal cortex. Dysfunction of the mesocorticolimbic system is implicated in schizophrenia and depression.[403]

Goal directed behavior is best thought of in functional terms. Normally we try to escape or avoid harmful stimuli, but in some cases, we have to actively engage something dangerous in order to achieve protection. Hunting is a good example. Sometimes,

[403] John H. Martin, *Neuroanatomy.*

fighting is a better alternative to fleeing or the only alternative. Decision-making compresses trial and error learning experiences into an instantaneous mental evaluation about what the consequence of a particular action will be for a given situation. Various echoes continually produce subtle emotional responses that produce a gut feeling. The decision-making requires integrating information from various sources: perceptual information, relevant facts and experiences, feedback from the emotional systems and the physiological consequences of the emotional arousal, expectations of results of various possible actions and so on. All these related memories and their echoes contribute to the general feeling that motivates a response (or lack of).

We have to be careful not to fall into the illusion that all executive functions happen in the prefrontal cortex. The different attentional systems are generally involved. For example, recent studies point to contributions from the parietal regions to the decision making process of what eye movements to control. The executive functions are a process that happens in many areas working in unison.

For example, the anterior cingulate cortex (area 24) receives inputs from the dopamine cells in the tegmentum as well as from the basal amygdala, ventral pallidum and the hippocampus. In addition it sends outputs to the accumbens and the motor cortex. It is in an excellent position to receive information about behavioral arousal (dopamine from the tegmentum) and about motivations and their amplifications (dopamine coming from the amygdala and pallidum). It can then integrate this with long-term memory (connections to the hippocampus) and with working memory (connections to the prefrontal area) in the process of controlling movement (connections to the motor area). The orbital cortex (areas 10 and 11) is also connected to the anterior cingulate (area 24) and is implicated in processing rewards and punishments and evaluating emotions; it, is therefore, essential to motivation and decision processes. The orbital cortex is part of the dopaminergic circuit. The orbital cortex also receives information from the amygdala and the hippocampus. It seems to be evaluating events and determining if they are good or bad. The thalamus, according to signals (produced by the echoes and handshakes corresponding to matches to external or internal stimuli) from the orbital cortex, will generate a degree of calmness or anxiety indicative of how positive or negative the event is. The medial dorsal nucleus of the thalamus links the basolateral amygdala indirectly with the prefrontal and orbitofrontal cortical areas. These help regulate the activity of the amygdala, reflecting the degree of anxiety or calmness, and accordingly, will control release of dopamine to the nucleus accumbens. The levels of dopamine, in part, will then determine the degree of pleasure or desirability.

The brain communicates its internal emotional state to other brains using specific universally recognizable facial movements, gestures, body postures and the prosody of speech. In social animals this is of extreme importance.

Paul Ekman and W.W. Friesen identified every distinct muscular movement the face could make. There were forty-three such movements, which they called units. By mixing combinations of three muscles more than four thousand visible facial configurations are possible; with five muscles more than ten thousand. Of course, most of those facial expressions don’t mean anything, more like children making faces. However, Ekman and Friesen identified about three thousand combinations that seem to mean something, essentially cataloguing the repertoire of human facial displays of emotion. The various expressions were numbered. Fear is action unit one, two and four, or, more

fully, one, two, four, five and twenty, with or without action units twenty five, twenty six, or twenty seven. Disgust is mostly action unit nine, the wrinkling of the nose (levator labii superioris alaeque nasi), but it can sometimes be ten, and in either case it may be combined with action unit fifteen or sixteen or seventeen.

Ekman and Friesen put together the rules for reading and interpreting the emotional displays in the Facial Action Coding System in a five hundred plus page document.[404] The emotional displays reflect in very subtle ways the emotional states of the brain; and an emotional transfer is achieved when properly read. And more interestingly, producing the exact facial expression of an emotion generates the actual emotion. This has tremendous therapeutic potential.

If you do action unit one, raising the inner eyebrows, and six, raising the cheeks, and fifteen, the lowering of the corner of the lips, it will be sufficient to create marked changes in the autonomic system. This generates sadness and anguish. If you do action unit four, lower the brows, and five, raise the upper eyelid, and seven, narrow the eyelids, and twenty-four, press the lips together, you generate anger. The heartbeat will go up ten to twelve beats and the hands will get hot. By simply learning how to create the facial expressions that correspond to stressful emotions as anger, sadness and fear produce the corresponding physiological changes.[405]

In humans, over the course of the first year, limbic circuits emerge in a sequential progression, from amygdala to anterior cingulate to insula and finally to orbitofrontal. Through attachment experiences, these circuits enter a critical period of maturation in the last quarter of the first year.

The orbital prefrontal cortex is positioned as a convergence zone where the cortex and the subcortex meet. It is the only cortical structure with direct connections to the hypothalamus, the amygdala, and the reticular formation in the brain stem that regulates arousal.[406] Other areas of the cortex, through extensive handshakes to the orbital prefrontal regions activate neurons that process facial gestures and prosody. These handshake signals can also activate clusters capable of appraising changes in the social environment, especially social interactions.

Mirror neurons in the parietal and frontal lobes that fire when you move your hand as well as when you just watch someone else move their hand, also have counterparts that not only fire when you stick your tongue out or purse your lips, but also when you see someone else do it, even though you have never seen your own lips or tongue.[407] The mirror neurons guide imaginary replication of other's expressions, and through the association of emotion to motor commands linked to emotional expressions, trigger subtle emotional reactions.

Emotions do not only elicit specific, related memories and behaviors, but also, through the external expression of these emotions, communicate these emotional changes to other brains. What is known in psychotherapy as transference and countertransference is a continuous process of emotional information transfer between individuals. Species-specific, emotional, expressive displays in the sender activate the attentional systems of the receiver, thus becoming emotionally competent stimulus. As such, the expressive

[404] Malcolm Gladwell, *Blink.*
[405] Ibid.
[406] Allan Schore, *Affect Regulation.*
[407] V. S. Ramachandran, *A brief Tour of Human Consciousness.*

displays automatically trigger the same emotion in the receiver. When the brain of the receiver perceives the emotion, the meaning of the emotional display is felt directly. The attentional systems hover, shifting from the external sensory stimuli (the expressive displays) to the internal emerging bodily sensations (the emotions generated as an automatic response). Thus the emotional communication achieves a somatic transference.

When emotionally competent visual and auditory stimuli emanating from a face are detected (by matching facial and prosodic echoes), handshakes are sent to the orbitofrontal cortex. These handshakes are interpreted as particular ECSs by the orbitofrontal cortex. Due to its unique connections, concurrent changes in the emotional or body state can be enacted as a response to the external emotional information. Fleeting exchanges of facial expressions are acknowledgements of fast emotional transfers. These exchanges are primarily appraised from movements occurring mostly in the regions around the eyes and from prosodic expressions from the mouth (Fridlund, 1991). Human vocal affect expressions of anger elicit detectable changes in the receiver's facial affect expressions (Hietanen, Surakka & Linnankoski, 1998) and hence the receiver's face briefly mimics the state changes induced by the sender's emotional communication.[408] This reciprocal process reflects the changes in internal states. This transfer of emotional information begins in early development between child and mother, and continues throughout life in social interactions.

The emotional information transfer between two or more people is achieved in a variety of ways. The transference of emotional information is based on recognizing the affective expressive qualities using various sensory signals (visual, auditory, tactile, kinesthetic and olfactory). Facial expressions are, on occasion, automatically mimicked. When we do so, our sequence of facial movements can trigger the same emotion that generated the facial expression. The emotional transfer is achieved by generating internally the same emotion, generally at a less intense level. We "recognize" emotions from visually presented facial expressions by reproducing internally the emotion that would generate the same facial expression. This non-verbal process allows us to feel what others are feeling. It is what Damasio calls our gut feelings. This is how empathy works. It is a process where one brain attunes to another, and then, resonates emotionally with the emotional expressions of the other. Fast acting co-constructions occur within moment-to-moment interactions transferring and producing dynamic changes in the internal emotional state.

A gaze between one individual and another also acts as a strong channel for transmission of emotional states. It has been observed that the pupil of the eye acts as a nonverbal communication device.[409]

Giaccomo Rizzollati showed that parts of the frontal lobes (in monkeys) fire when a monkey performs a certain motion. Yet the same cell also fires when it sees another monkey perform that same motion. Rizzollati called these mirror neurons [not to be confused with mirror signals, which are unrelated]. So mirror neurons have important implications for understanding many aspects of human nature, such as interpreting somebody else's actions and intentions.[410] As mentioned, the orbital prefrontal cortex is the only cortical structure with direct connections to the hypothalamus, the amygdala, and

[408] Ibid.
[409] Hess, E.H., *The role of pupil size in communication.*
[410] V.S. Ramachandran, *A brief Tour of Human Consciousness.*

the reticular formation in the brain stem that regulates arousal. It is possible that the mirror neurons and these prefrontal connections serve to mimic an emotional state in others by subtly activating the same emotion by mimicking the facial gestures and body posture of an emotional expression.

In the case of facial oral apraxia it may occur with lesions that undercut the left supramarginal gyrus or the left motor association cortex. Such patients are unable to carry out facial movements to command (lick the lips, blow out a match, etc.), although they may do better when asked to imitate the examiner.[411]

The mirror neurons might have a role in learning movements to hunt and flee (as well as mating, sports and dance) by imagining and then participating in making the movements, as well as triggering (by imitating emotional expressions) subtle emotional responses to emotional expressions.

Under normal conditions, every transference of emotional information elicits a countertransference that confirms the emotional communication. These reactions are very fast, occurring in microseconds, reflecting the somatic emotional changes. Transference of emotional positive changes generate positive changes in the receiver, just as transference of negative emotional changes produce negative changes in the receiver. These reciprocal transactions amplify the autonomic internal state. These transferences are very valuable in a social environment to: a) quickly spread information about how good or bad an event is; b) to ease coordination of actions among a group as a response to an outside threat or opportunity; and c) to facilitate adaptive behaviors such as attachment, bonding, fleeing or attacking. The somatic changes reflect what Damasio calls “gut” feelings that are experienced in response to various stimuli. These are a bodily-based perception of meaning. The feelings are a viscero-sensation that serves to evaluate if an event is “good” or “bad” in proportion to the feeling generated. Thus sensory inputs alter the internal environment to heighten or dull the perception of the external world and elicit a behavioral response.

Not surprisingly, since the memories to identify faces and prosody are on the right side, recent studies have shown that the right hemisphere is faster than the left hemisphere in processing emotional content from facial expressions and spoken language.

The right hemisphere is, more so than the left, deeply connected into not only the limbic system but also the sympathetic and parasympathetic branches of the autonomic nervous system that controls the somatic expressions of all emotional states. Because the hypothalamo-pituitary-adrenocortical axis and the sympathetic-adrenomedullary axis are both under the main control of the right cortex,[412] the right side is responsible to a greater degree to mediate adaptive functions by generating the appropriate emotions. Basic emotions – excitement, fear, elation, rage, disgust, and shame – produce differentiable autonomic activity. The intensity of the feelings, positive or negative, elicited by the emotional reactions, produces non-verbal evaluations of events; we “know in our guts” if it is good or bad. The automatic and fleeting emotional expressions produce an emotional reaction in the receiver. This resonating process is interactively regulated, amplified, and can be held in short term memory long enough to be felt and recognized. At this point the

[411] Allan Roper and Robert Brown, *Adams and Victor’s Principles of Neurology*.
[412] Allan Schore, *Affect Regulation*.

right-brain "gut" knowledge becomes available to the verbal (thinking) left hemisphere for further processing.

The right orbitofrontal areas are associated with emotional changes, whereas the left orbitofrontal areas are involved in "semantic implicit retrieval that does not depend upon intentional recollection" (Demb et al, 1995). Connections between the right and left orbital areas may thus allow for left hemisphere retrieval from implicit-procedural memory and semantic encoding of right-hemispheric emotional states.[413]

The ability to communicate to others and, read in others, these subtle emotional states, varies from individual to individual (and from species to species).

Brothers (1995, 1997) described a limbic circuit of orbitofrontal cortex, anterior cingulate gyrus, amygdala, and temporal pole that is "specialized for processing others' social intentions" by appraising "significant gestures and expressions."

The right hemisphere is specialized for implicit learning and performs rapid, in the order of 80 milliseconds, valence-dependent, automatic appraisals of facial expressions. The detection and complex processing of the smallest change within a human face occurs within 100 milliseconds (Lehky, 2000) and such facially expressed state changes are mirrored (Dimberg & Ohman, 1996) and synchronously matched by an observer's right hemisphere within 300-400 milliseconds (Stenberg, Wiking, & Dahl, 1998). It has been established that positive and negative emotional expressions elicit equivalent emotional facial gestures and that the right hemisphere is dominant for control of spontaneously evoked emotional reactions (Dimberg & Petterson, 2000; Dimberg, Thunberg, & Elmehead, 2000).[414] The right hemisphere recognizes an emotional display by recreating, as close as possible, a somatosensory, bodily-based representation of the emotional display, thus, actually feeling how another feels when producing a particular emotional expression. When the sensory (emotional display) stimulus is matched by an echo representing the same emotional display, the emotion is automatically triggered.

After the brain's perception of the emotion, the non-verbal emotional experience in the right hemisphere must be transferred to the left hemisphere for linguistic expression of the feeling. The bodily sensations produced by the emotion are perceived as feelings and eventually the feeling can be verbally articulated. This allows for a linkage of the non-verbal implicit and verbal explicit memories through emotions. The transfer of information from the non-verbal to the verbal and back reflects a bi-directional flow of information from implicit and explicit processing. According to Bornstein, "When an implicit memory is made explicit, the origin of that memory is also made explicit [and it becomes easier to gain insight of], which is to say the causal chain of events that led from past experience to present functioning" (1993, p 341).[415]

When a stimulus generates an emotion, the emotion gives rise to a bodily felt sensation, which is the implicit knowledge. It is knowing without words. The explicit knowledge emerges at another level. It is formed from pre-conceptual, implicit, and incomplete information through the interaction of feelings and symbols (words or thoughts). The explicit knowledge is not a previously hidden one that now becomes

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[413] Ibid.
[414] Ibid.
[415] Bornstein, R.F., *Implicit perception. Implicit memory. And the recovery of unconscious material in psychotherapy.* From Allan Schore's *Affect Regulation.*

clear, but one that is formed by putting feelings into words. This process, the verbalization of emotions, is not always possible.

The right hemisphere uses the expanded attentional system that focuses on global features, while the left focuses on local detail (Derryberry & Tucker, 1994).

Transferential events clearly happen during emotional arousal. Attention is altered during emotional arousal such that there is an increased sensitivity to cues relating to the current emotional state. According to Gilboa & Revelle (1994, p.135), "The longer the period during which a person is influenced by physiological and cognitive processes activated by the emotion the higher the probability that this experience will be perceived as important and meaningful.[416]

There are several emotional regulation modes: one is an interactive regulation via two or more emotionally interacting individuals, the emotional information transfer and counter-transfer; another, is an interactive regulation triggered by the external changing conditions that change the internal emotional state; and lastly, is a self-regulatory process, based on feedback and automatic tendencies to reach a neutral state of calmness.

The Isorropic Circuit

This elegant system, comprised of the habenula and the medial and lateral septal nuclei (including the diagonal band of Broca), receives its major inputs from the thalamus and the hippocampus respectively and is continuously adjusting (adapting) the internal emotional state to the external, ever-changing environment, attempting to produce, at all times, the adequate response. This system, through the signals it sends to the reticular formation, is an emotional arousal and, balancing and tuning system. It summarizes the activity of the entire brain, taking into account emotions, cognitive signals translated into contexts and meanings, and accordingly, fine-tunes the signals of all neurotransmitter systems in the brain stem.

This arousal system, in a slow gradation of excitability, from less to more, associated with negative and positive emotions, using asymmetries in the brain, detects and generates very fine emotional distinctions covering a whole range: from happy, changing slightly to blissful, playful, grateful, safe, relaxed, undecided, uneasy, frustrated, alert, tense, cautious, anxious, afraid, all the way to panicky; or conversely, starting from lonely, changing to bored, humble, bashful, ashamed, envious, determined, optimistic, joyous, all the way to loved.

The primary function of this circuit is to try to balance activity in both hemispheres, continuously attempting to restore neutral calmness, reflecting its evolutionary path when lateralization was less prevalent in more primitive brains. This habenula-septal circuit is important enough to deserve it own name, the isorropic circuit (from the Greek, isorropia=balance). It is worthwhile to see in detail how the isorropic circuit works.

The convergence of signals from the cortex and the output of the basal ganglia (where the integration of external with internal space is accomplished by the basal ganglia loops through a continuous stream of echoes that activate implicit memories and

[416] Allan Schore, *Affect Regulation*.

trigger emotions automatically) to the thalamus as well as the extensive reciprocal connections of the cortex to the hippocampus are the circuits where a variety of cortical signals can be unified and the attentional systems controlled. This unification and control of attention permits the activation of explicit and episodic memories aided by the very subtle activation of the needed emotions.

If we add the hippocampus, the thalamus and the basal ganglia to the isorropic circuit, we have the center where all cortical activities are streamlined into a single unified perception. This perception has a spatial/somatosensory (a body/external space integration), a sensory (from all senses), echoes from all cortical areas (implicit memories) as well as an emotional component, which in turn has the potential to activate handshakes (all explicit memories), and an associated context (activating attention to focus on associative areas – more handshakes). The attentional systems, the somatosensory, the visual and the auditory, focus on one salient stimulus to extract the most possible information. This is as close as possible to a technical definition of consciousness.

Emotions can be labeled positive or negative. In general, situations and events conducive to positive emotions should be promoted; those leading to negative emotions, avoided. Such emotions should not be confused with drives or needs, or with motivations of approaching or withdrawing; both easily found behaviors within the context of experiencing a positive or negative emotion. Approaching or withdrawing behaviors depend on previous knowledge and/or a particular context.

The right hemisphere computes on a moment-by-moment basis the emotional salience of external stimuli. This is equivalent to sending out handshakes with a "valence tag," in which perceptions are given a negative or positive affective value reflecting degrees of pleasure-unpleasure.

Positive emotions are associated with a very slight increase of neural activity in the whole brain, and activation of the left anterior cingulate cortex, relative to the right. Conversely, negative emotions are linked to a slight decrease in neural activity overall and activation of the right anterior cingulate cortex, relative to the left.

Emotions can produce asymmetrical activation, where, for example, anger produces more left frontal activation and fear more right frontal activation.[417] In this case we need to think of anger as a positive emotion and fear as a negative one.

The excitatory limbic circuit termed the ventral tegmental limbic forebrain-midbrain circuit is associated with positively valenced emotions. The inhibitory circuit, including regions in the orbitofrontal cortex that project to the parasympathetic areas in the hypothalamus and to the noradrenergic neurons in the medulla and the vagal complex in the brain stem caudal reticular formation, termed the lateral tegmental limbic forebrain-midbrain circuit is associated with negatively valenced emotions.[418] In this elegant manner, the orbitofrontal circuits alter the brain's basic rates of signaling: the positive states speeding up the rate of signaling and the negative states reducing the overall rates. The job of the isorropic circuit is to restore balance within certain ranges as soon as feasible.

[417] Jan Wacker, Marcus Heldmann, and Gerhard Stemmler, *Separating Emotion and Motivational Direction in Fear and Anger: Effects on Frontal Asymmetry.*
[418] Allan Schore, *Affect Dysregulation.*

As we have mentioned, the output of the TAN neurons in the caudate nucleus is directed to the basal ganglia, whose output in turn is mostly directed to the thalamus.[419] The caudate nucleus is the interface between emotions and memories. The thalami are connected contralaterally (in about 70 per cent of people, in women more than men, and in women more strongly than in men) through the massa intermedia.[420] Could there be some relation between the 30% that do not have a massa intermedia, making it harder to balance activity on both hemispheres, and a tendency to suffer unipolar or bipolar disorder? The thalami project homolaterally, through the stria medullaris (located laterally to the wall of the third ventricle), to the habenula.[421] The stria medullaris is rich in GABA neurons and there is some evidence that dopamine can strongly inhibit their action.[422] The anterior nucleus has many afferent and efferent connections with the cingulate cortex (areas 23, 24, 29 and 32). The stria medullaris thalami are the habenula's major input bundle. The habenula is a small swelling on each side, rostral to the stalk of the pineal gland.

The lateral septal nucleus receives input from the hippocampus via the fornix. The medial septal nucleus is a major target of the lateral septal nucleus, feeds back to the hippocampal formation (the dentate gyrus, the hippocampus and the subicular complex), and projects to the habenula and the periaqueductal gray matter and reticular formation (including the lateral and ventral tegmental) via the medial forebrain bundle. The medial forebrain bundle consists of neurons that contain dopamine, serotonin and noradrenaline. The projection to the habenula is part of a circuit with the midbrain medial dopaminergic and serotonergic systems.[423] The connections from the hippocampus to the medial septal and the diagonal band of Broca are cholinergic,[424]as well as the feedback projection from the band of Broca to the hippocampus. The hippocampus connects contralaterally and also sends projections to the amygdala, the hypothalamus and the ipsilateral olfactory bulb.[425] The hippocampal commissure is rich in m4 muscarinic acetylcholine receptors.[426]

The habenula receives major information from the activity of the thalamus, reflecting total cortical activity from each hemisphere, including information from the amygdala, mirroring the emotional state. There are also direct projections from the frontal cortex to the habenula through the thalamus via the stria medullaris. The connections of the anterior cingulate gyrus (area 24) to the thalamus, as well as efferents to areas 6, 8, 9,

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[419] Jeffrey M. Schwartz, *The Mind and the Brain.*
[420] John H Martin, *Neuroanatomy.*
[421] Ibid.
[422] Gaylord Ellison, *Neural degeneration following chronic stimulant abuse reveals a weak link in brain, fasciculus retroflexus, implying the loss of forebrain control circuitry.* European Neurospychopharmacology. 12 (2002) 287-297.
[423] John H. Martin, *Neuroanatomy.*
[424] Gaykema, R.P., van der Kuil, J., Hersh, L.B., Luiten, P.G., *Patterns of direct projections from the hippocampus to the meidal septum-diagonal band complex: anterograde tracing with Phaseolus vulgaris leucoagglutinin combined with immunohistochemistry of choline acetyltransferase.*, Neuroscience. 1991;43(2-3):349-60.
[425] VanGroen, T., Wyss, J.M., *Extrinsic projections from area CA1 of the rat hippocampus: olfactory, cortical, subcortical, and bilateral hippocampal formation projections.*, J Comp Nerol. 1990 Dec 15;3023):515-28
[426] Levey AI, Edmund SM, Koliatsos V, Wiley RG,Heilman CJ, *Expression of m1-m4 muscarinic acetylcholine receptor proteins in rat hippocampus and regulation by cholinergic innervation.* J Neurosci. 1995 May;15(5 Pt2):4077-92

10 and 29, as well as efferents to the orbitofrontal cortex (areas 11 and 12) have been established.[427] As a minor input, the habenula receives, through the medial septal nucleus, contextual information from the hippocampus.

The habenular commissure is made of a band of fibers of the stria medullaris that pass through the habenula of each side to decussate and terminate in the habenula on the opposite side.[428]

Thus the habenula has efferents from various structures involving different neurotransmitters: acetylcholine, serotonin and dopamine from the septal nucleus and primarily GABA (which can be affected by dopamine) from the thalamus' stria medullaris. The hippocampal and the habenular commissures, more so than the massa intermedia that joins the thalami, assist in maintaining a balance between the activity of the two hemispheres by speeding up or slowing down one hemisphere with respect to the other.

The diagonal band of Broca and the medial septal nucleus act almost as a unit. This region contains GABAergic interneurons, GABAergic projection neurons whose axons innervate the hippocampal formation as well as cholinergic neurons.[429] Additional cholinergic neurons with widespread cortical projections in the brain stem are found near the pedunculopontine nucleus, which is an important target of the output nuclei of the basal ganglia (the caudate nucleus, globus pallidus, the putamen, the ventral pallidum, and the substantia nigra pars reticulata and pars compacta). Many of the neurons in this nucleus are cholinergic, including those projecting to the thalamus. Targets of the cholinergic projections include the entire cortex, including the limbic association cortex, the amygdala and the hippocampal formation. Other cholinergic neurons are dispersed between the lamina of the globus pallidus and putamen and adjacent to the internal capsule.

The basal forebrain cholinergic neurons, including those in the medial septal nucleus, excite their targets primarily through muscarinic receptors; the slower action of acetylcholine may facilitate cortical responses to other inputs. These cholinergic neurons, with their widespread projections to the entire cortex, modulate overall cortical excitability and also, indirectly, link the amygdala with the cortex.[430]

Also, both the GABAergic and cholinergic neurons in the diagonal band of Broca and the medial septal nucleus have a strong presence of potassium channel sub-unit KCNQ2, which suggests that both groups could be excited simultaneously. The small, densely packed cells of the triangular septal nucleus, responsible for the strong purinergic input (ion channels activated by extracellular ATP) to the habenular region, also exhibit strong KCNQ2 channels.[431] This architecture suggests a strong emotional modulatory role for these circuits: when activity in the brain picks up (positive emotions), the GABAergic interneurons of the isorropic circuit slow it down; when activity slows down (negative emotions), the activity of GABAergic interneurons slows down, and brain activity increases. However, the increase or decrease of brain activity modulated by the

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[427] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[428] Dorland's Illustrated Medical Dictionary.
[429] Edward C. Cooper, Emily Harrington, Yuh Nung Jan, & Lily Y. Jan, *M Channel KCNQ2 Subunits Are Localized to Key Sites for Control of Neuronal Network Oscillations and Synchronization in Mouse Brain.*
[430] John H. Martin, *Neuroanatomy.*
[431] Edward C. Cooper, Emily Harrington, Yuh Nung Jan, & Lily Y. Jan, *M Channel KCNQ2 Subunits Are Localized to Key Sites for Control of Neuronal Network Oscillations and Synchronization in Mouse Brain.*

habenula is not a linear function because GABAergic interneurons also slow down or speed up cholinergic activity inversely. Simultaneously, the cholinergic activity increases or decreases the inhibitory action of GABAergic projection neurons, but because the cholinergic excitation is through slow muscarinic receptors, there is a time lag as well.

The habenula can be anatomically divided into the medial and lateral habenula. Underlying each habenula are the habenular nuclei. The left and right habenula are interconnected by the small habenular commissure. The major output bundle of the habenulas, known as the habenulointerpeduncular tract, projects to the interpeduncular nucleus in the reticular formation. The cholinergic neurons of the medial habenula exhibit both KCNQ2 and ChAT (cholinergic) channels, but not the neurons of the lateral habenula, which only exhibit KCNQ2 channels. The fasciculus retroflexus, the projection pathway of myelinated fibers of the medial habenula to the interpeduncular nucleus, is cholinergic.[432]

Indirectly, through the thalamus and the hippocampus, when positive emotions are present the left habenula receives greater excitatory signals than the right habenula – the activity in the left anterior cingulate is greater compared to the right and activity of the cortex as a whole is increased – excitatory (more+) from the whole cortex and excitatory (more+) from the left anterior cingulate through the thalamus. Let's call it (more+)(more+) excitation. Whereas the effect on the right habenula under similar conditions is excitatory (more+) from the whole cortex but less from the right anterior cingulate (less-). Let's call this (more+)(less-) excitation. This will establish a net excitatory effect from the left to the right habenula, attempting to restore a balance by making the signals from both habenulas (left and right) to the reticular formation more similar. This net excitatory effect from left to right through the habenular commissure is perceived by the brain as pleasant. Directly proportional to the pleasantness will be a behavioral response, an impulse to engage stimuli that produce this effect, guiding the organism's behavior.

Adding to the excitatory (or inhibitory) effect is the action of the massa intermedia (when existent) and of the hippocampal commissure, stimulating (or inhibiting) each hippocampus to match each other's activity and through their many glutamate and cholinergic cortical connections increase or decrease each hemisphere's activity as well.

Similarly, when negative emotions are present the left habenula receives less excitatory signals than the right habenula – the activity in the right anterior cingulate is greater compared to the left and the activity of the cortex as a whole is decreased – less excitatory (less-) from the whole cortex and less excitatory (less-) from the left anterior cingulate. The excitation is (less-)(less-). Whereas the effect on the right habenula is less from the whole cortex (less-) but greater from the right anterior cingulate (more+); this produces (less-)(more+) excitation. This is not necessarily the same as (more+)(less-), because the degree of excitation from the whole cortex and the anterior cingulate are not equivalent. In this case, a net excitatory effect is produced from the right to the left habenula. This net excitatory effect from right to left is perceived by the brain as unpleasant. A behavioral avoidance response will be generated in direct proportion to the unpleasantness, motivating the organism to avoid stimuli that produce negative feelings.

[432] Ibid.

The isorropic circuit's main activity is to return the whole brain to a desired neutral state, speeding up or slowing down the activity of each hemisphere or the entire cortex as needed. Dictated by the cytoarchitecture, the isorropic circuit can re-establish a neutral calmness at a faster rate when the emotion is positive than when it is negative.

The contralateral communication between the medial septal nuclei and the habenulas also helps regulate the output of each habenula to the interpeduncular nucleus and the reticular formation. Thus, GABAergic, cholinergic, dopaminergic and serotonergic systems excite a cholinergic output to the reticular formation. The actions of these circuits continuously attempt to establish a balance between the activities of each hemisphere. When the activity of both hemispheres is equal, a preferred state of neutral calmness is achieved.

Primarily, the isorropic circuit achieves five actions: 1) modulate the activity in each hemisphere by dampening or quickening activity as needed through the GABAergic interneurons and projection neurons of the diagonal band of Broca and the medial septal nucleus to the hippocampus and the GABAergic projections of the thalamus to the habenula and the habenular commissure; 2) increase overall activity of the entire cortex through the cholinergic projections to the reticular formation and the periaqueductal gray, and the interpeduncular nucleus from the medial septal nucleus and the habenula respectively; 3) determine the emotional state through the indirect connections from the amygdala; 4) determine the context of the emotion through the connections from the hippocampus; and 5) measure and compare the neural activity in each hemisphere to determine if a positive or negative emotion is present by comparing the activity of the left and right habenulas aided by the signals from the thalami, the amygdalae and the hippocampi. The overall net result of the actions of the isorropic circuit is to naturally drift, at varying rates, towards a neutral state.

When there is relatively more activity in the right cingulate cortex, the emotion is determined to be undesirable (negative, feels unpleasant, and proportionally, everything is done to lessen or rid the organism of it). When the reverse is true, the emotion is determined to be desirable (positive, feels pleasant, and proportionally, everything should be done to increase the outcome).

Slowly, depending on the changing external environment and internal conditions, which produce various responses and behaviors, the isorropic circuit will manage to restore calmness. This is one way of saying that positive and negative emotions are a transitory condition.

Occasionally, an extreme case of neutral calmness is achieved close to death. Once, I almost drowned bodysurfing, "I was jerked around like a ragged doll, I lost all sense of what was up or down: the light seemed the same in all directions. I started to see stars; I was running out of breath; and the ride was showing no signs of abating. I tried to move my arms and swim, only to hit the sandy bottom again. My lungs were burning. My limbs were not responding, memories flashed quickly through my head; fear, more stars in my field of vision. Suddenly, my vision faded, the blackness formed a narrowing tunnel, and in the middle there was a bright light. The bright light got smaller, and as it did, *a tremendous sense of calm and peace overcame me*. I looked at the light; it seemed to be getting smaller, but perhaps closer. But the peace was all encompassing. The triumphal march into nothingness, death, loomed close by. Then suddenly my head broke the surface and air poured into my lungs."

As oxygen levels decrease, the emotional responses shut down first, then the senses. The sensation of complete peace is simply the absence of emotions. The tunnel and the light that many people near death describe is simply what the brain perceives when emotions and sensory input are slowly shut down!

The output of the habenulointerpeduncular tract depends on a comparison of the entire cortical echoes, especially from the cingulate cortex, being sent to the left and right thalami, as well as the output of the medial septal nucleus, which in turn, depends on the output of the left and right hippocampi and amygdalae to the left and right lateral septal nuclei, respectively.

The echoes, in turn, depend on the emotional state as well as all the feedback handshakes generated by the emotion and the context of the emotion. These continuous feedback circuits summarize the totality of brain activity in a compact way. They fine-tune the emotional landscape of the brain by regulating the reticular formation activities, including regulation of arousal, motor control through the integration of internal and external space, and vegetative functions.

Thus, projections from the habenula, through the habenulointerpeduncular tract, to the interpeduncular nucleus in the reticular formation, affect most all the principal neurotransmitter systems:

a) The cholinergic diffuse projection patterns are activated through the basal nucleus of Meynert (to the cortex) and the septal nuclei (to the hippocampal formation). Acetylcholine augments excitability of cortical neurons, especially in the association areas.
b) The dopamine containing neurons of the substantia nigra pars compacta and ventral tegmental area, activate the nigrostriatal dopaminergic system and mesocorticolimbic dopaminergic system through their connections to the striatum and frontal cortex, and prepare the brain for action. This is an activation-excitatory circuit. The dopaminergic systems are important in responding to natural rewarding stimuli, such as feeding and reproduction. However, dopaminergic neurons do not simply signal the hedonic value of events, because novel negative reinforcing stimuli can also activate the dopaminergic systems.
c) The serotonin system through the Raphe nuclei. The actions of this system are diverse because there are many types of serotonin receptors.
d) And the noradrenaline system through the locus ceruleus with projections to the thalamus, amygdala and hippocampal formations as well as medullary projections. This system plays an important role in reacting to stress, and particularly the activation of fear and anger.

Through the various projections mentioned, the isorropic circuit affects and regulates the output of other loops. The amygdala projects from the central nucleus to the brain stem areas that are involved in the control of the heart rate and other autonomic nervous systems that will regulate the body's responses as emotions change. The striatum (consisting of the caudate nucleus, the putamen and the ventral striatum, which includes the nucleus accumbens) is the major recipient of inputs to the basal ganglia from the cortex, thalamus, and through the output of the isorropic circuit, from the brain stem.[433]

[433] Eric R. Kandel, James H. Schwartz, Thomas M. Jessell, *Principles of Neural Science*, Fourth Edition, 2000.

The reticular formation is the core of the brain stem. Neurons of this region regulate the neuronal excitability directly through diffuse projections rostrally and caudally, or indirectly through connections with thalamic nuclei that have diffuse cortical projections: through the ventral posterior lateral nucleus to the primary somatic sensory area, through the medial dorsal nucleus to the cingulate cortex and through the ventral medial posterior nucleus to the insular cortex.[434]

A whole array of chemicals and hormones regulate emotions and motivate behaviors. The hypothalamus and the pituitary gland have a central role in the chemistry of the body. Regulating processes such as breathing and heart rate, they also regulate, to a lesser degree through the limbic system, emotional responses. The hypothalamus is ventral to the thalamus; the third ventricle separates the two halves. The two halves are interconnected by the median eminence and the arcuate nucleus. The functions are organized by projection neurons in small groups of nuclei that interface with effector systems in other parts of the nervous system. These hypothalamic nuclei are arranged into three mediolateral zones: 1) the periventricular zone is the most medial. This zone is important in regulating the release of endocrine hormones from the anterior pituitary gland; 2) the middle zone contains nuclei that release vasopressin and oxytocin from the posterior pituitary gland. It is also a major site for neurons that regulate the autonomic nervous system, including the body's circadian rhythms and aspects of wakefulness control; 3) the lateral zone contains neurons that integrate information from the telencephalic structures engaged in emotions and transmit this information to other parts of the brain as well as to other hypothalamic nuclei. This zone is important in the behavioral expression of emotions.

There is a long list of releasing and release-inhibiting hormones that are regulated by the hypothalamus and the pituitary gland. In addition, there are extrahypothalamic sources of these same hormones. For example, the septal nuclei are a source of gonadotropin-releasing hormone. Many of these neurohormones are also found in hypothalamic neurons and in neurons in other regions of the central nervous system. This widespread distribution of neurohormones indicates that there are neuroactive compounds at these other sites and not just chemicals that regulate the pituitary hormone release.[435]

The right hemisphere is more deeply connected and exerts greater control over the emotional responses mediated by the parasympathetic and sympathetic system. The hypothalamus, the head ganglion of the autonomic nervous system, is right lateralized and the hypothalamic nuclei are considerably larger in the right side. Thus the right side is dominant for the production of corticotropin-releasing factor and cortisol, and the neurohormones that mediate coping responses.[436]

Certain groups of parvocellular neurons may synthesize more than one peptide. The release and/or production of one or another peptide may be regulated by circulating hormones in the blood. This is one way that environmental factors, such as prolonged stress, may alter neurohormonal compositions and alter pituitary hormone release.[437]

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[434] John H. Martin, *Neuroanatomy*.
[435] Ibid.
[436] Allan Schore, *Affect Dysregulation and Disorders of the Self*.
[437] Ibid.

The right brain contains circuits involved in regulating intense emotional-homeostatic processes and modulates negative primary emotions such as fear and disgust and negative social emotions such as shame, as well as positive emotions such as excitement and joy.

When the brain perceives emotions it creates the illusion of feelings. These feelings serve to guide our responses to the ever-changing environment. The ability to adapt depends on the regulatory process to return smoothly to a neutral state of calmness.

The Self

The cholinergic projections of the isorropic circuit, primarily from the medial septal nucleus and the band of Broca to the hippocampal formation, the periaqueductal gray matter and the reticular formation act through muscarinic receptors. The muscarinic receptors are slow acting, consequently their effects occur with a time lag. This time lag, in chaos theory terms, allows the isorropic circuit to wander about a strange attractor, which under normal conditions is the point of neutral calmness.

Under most conditions, this strange attractor is the state (point) towards where the isorropic circuit's actions tend to modulate the cortex's activities (represented by a point). Lets call this attractor the isorropic attractor. The subtle wandering of the isorropic attractor permits the isorropic circuit to generate and regulate a wide spectrum of emotions. Generally, this wandering activity remains within the range of chemical changes that do not affect the homeostatic balance. Potentially, this wandering permits the generation of myriad slightly differing emotions as a response to a vast array of changing internal and external stimuli. When the isorropic attractor is close to neutral calmness a wider spectrum of potential emotional responses is available, positive and negative, and by activating memories associated with the emotions, allows for activation of a greater pool of memories. The speed at which small emotional changes can be generated also allows the search for the greatest potential number of contexts. Thus the brain achieves a state that can generate the maximum variety of behaviors in the quickest time possible as response to the ever-changing environment. This places the organism in a state of maximum adaptability. When the brain detects this healthy state of maximum adaptability of the body/brain (organism) it is perceived (felt) as a sense of self.

Some philosophers have called this state "the center of the self." Others have called it the "true essence." Franz Kafka, the Austrian philosopher and poet, recommended, perhaps as a means to reach neutral calmness, "You need not leave your room. Remain sitting at your table and listen. You need not even listen, simply wait. You need not even wait, just learn to become quiet, and still, and solitary. The world will freely offer itself to you to be unmasked. It has no choice; it will roll in ecstasy at your feet."[438]

The wider the spectrum of emotional responses that can be triggered, the more intense the sense of self is felt. Conversely, the narrower the spectrum, the less intense the sense of self is perceived. This translates into a nonverbal knowledge that many memories can be quickly activated because the brain can flutter, ever so slightly from emotion to emotion, changing from moment to moment the chemical milieu of the body

[438] Deepak Chopra, *The Seven Spiritual Laws of Success.* 1994.

and brain. Normally, the brain is changing, second by second, the emotional internal landscape in subtle ways that are almost imperceptible.

The isorropic circuit interacts in fine ways with numerous other circuits, primarily with the basal ganglia through the brain stem, the thalamus and hippocampus; with the cortex, affecting memory; with the hippocampus affecting context and orientation; with the amygdala and hypothalamus affecting emotions; with the orbitofrontal lobes through the caudate nucleus and the putamen affecting anxiety and fear thresholds.

Individual personality traits are genetically set according to the interaction between the isorropic circuit and the basal ganglia, which do not have direct input or output connections with the spinal cord. The basal ganglia receive major input from the cortex and the thalamus and send their output back to the cortex via the thalamus. In broad terms, the interactions between the isorropic circuit and the basal ganglia are genetically set, whereas the interactions between the cortex and the basal ganglia are learned. The nature versus nurture argument is elegantly separated. The greater the cortex, the greater the level of learned responses.

In chaos theory terms, when the isorropic circuit's attractor is wandering on the positive emotional side, the brain perceives this as a high degree of self-esteem. If it is wandering on the negative emotional side, the degree of self-esteem is low.

When the isorropic circuit is close to neutral calmness, autobiographical memories can be more easily activated because of the continuous wandering of the isorropic attractor; as a result, myriad emotions associated (through handshakes) with all the memories can be quickly triggered.

When the isorropic attractor is far from neutral calm, indicative of a strong emotional state, the emotion affects short term, working and explicit memories, and thalamic control of the attentional systems can be disrupted.

In contrast, semantic, source and procedural memory, because of a small or inexistent relation to emotions can still be activated even when the isorropic attractor is far from neutral calmness. The hippocampus can detect a particular context, independent of an emotion, and send the appropriate signals and activate these types of memories independent of the emotional state.

If environmental or internal stimuli push the isorropic attractor outside the chemical ranges that permit homeostatic balance, the sense of self becomes distorted; the spectrum of emotions that can be potentially generated, thus the memories that can be activated, are greatly diminished and the behavioral responses limited. The limited choice of behaviors, imposed by stressful conditions, under a wide array of circumstances, can still generate a correct response. But the longer the stressful conditions prevail, the smaller the number of responses that can be activated and the less the probability that the correct response will be generated.

In extreme cases, when the isorropic attractor is pushed far enough from the range of homeostatic balance, the brain will no longer be able to perceive a sense of self; the organism can no longer adapt.

The sense of self is an indirect measure of the organism's capacity to adapt.

There are other aspects to the sense of self superimposed on the activity of the isorropic circuit. As we saw in detail at the tennis match, there is a constructive process of the present. Even when there is a referral in time of sensory signals and backward masking, and these signals are processed faster than they can reach awareness, this

constructive process creates a sense of continuity of our experience with an accompanying feeling of past (using attentional systems and different memory systems to remember events) and present (using attentional systems to create it).

When our attentional systems activate biographical memories, in spite of the diversity of sensory signals, memories, beliefs and thoughts, a coherent sense of self emerges. In this way the brain constructs continuity and a unity of the self.

But still, there is more to the self; there exists a sense of embodiment, a feeling that we are bonded to our bodies. The interactions between the isorropic circuit and the basal ganglia, through the thalamus are partly responsible for this feeling. The continuous fusion of the external and internal spaces as created by the somatosensory attentional system, using all pain, pressure, temperature and proprioceptive signals creates this illusion and firmly roots us in our bodies. And beyond this, the self is empowered with a sense of agency or free will, even if it is generated outside awareness, which allows us to feel we can direct our bodies and our actions.

These different aspects of the self are embedded in an ever-changing emotional milieu, which as we have seen activates relevant memories. With the use of mirror neurons, through emotional expressions and emotional transfers, the brain perceives feelings and feelings in others. Ultimately, the activity of the attentional systems permits us to reflect, of becoming aware of our self with all its subtleties. The attentional systems, somatosensory, visual and auditory (perhaps olfactory and gustatory as well), are the circuits that generate the sense of self and our perception of consciousness.

The self has many dimensions to it and as a result any of these different aspects can be individually disturbed. However, given the emotional nature of the self, which activates memories associated to the emotion according to a context, even in the extreme case of split-brain patients whose two hemispheres have been surgically disconnected, the patients don’t exhibit split personalities or a double subjectivity.

The normal functioning of the isorropic circuit and disturbances of the self will determine personality traits. The personality traits will determine the patterns of response to various stimuli. The interaction of the isorropic circuit with the basal ganglia circuits is genetic, whereas the interaction of the cortex and the hippocampus with the basal ganglia is stored as memories and is mostly learned. In a gradation from normal to maladaptive personality traits, nature and nurture will interact to produce individual responses.

The American Psychiatric Association recognizes marked disturbances of personality traits that affect cognition and affectivity. Part of the diagnostic criteria for Personality Disorders is when these patterns cause significant distress or impairment in social or other important areas. These enduring patterns of cognition and affectivity are inflexible, stable and of long duration.[439]

If we lessen the gravity, or reduce the number of symptoms of the diagnostic criteria for the recognized personality disorders, each personality disorder probably sounds like someone we know. Consequently, basic personality traits could be deduced from this list in a gradient: trust/distrust, attach/detach from relationships, cognitive or perceptual distortions, sympathy/empathy, cautious/impulsive, affective distortions of self or others, submissive/dominating and orderliness/disorderliness. In Chapter 22 I will discuss how personality disorders arise.

[439] Diagnostic and Statistical Manual of Mental Disorders. DSM-IV-TR.

13
Don't Be Afraid!

Each of the different emotions has its own echoes, triggering sites, loops and its specific ECS's. In the following section, I will present a more detailed discussion of some of the more studied emotions from a neurological point of view. I take some of the following ideas from Joseph LeDoux's books, *The Emotional Brain* and *Synaptic Self*.

The system used to defend against danger is different from the system used for procreation. The feelings that result from the emotions generated in each case, fear and sexual pleasure, do not have a common origin. Moreover, there is no such thing as the "emotion generator," no single brain system dedicated to create all emotions. We need to focus on classes of emotions. Brain regions have functions because they are part of integrated systems. Mental functions involve many different regions working together; each function requires a unique set of interconnected regions, forming its own system. Many regions might be used by different systems.

The brain can be divided into three divisions along the vertical axis: the hindbrain, midbrain, and forebrain. As you move from the hindbrain to the forebrain, the functions go from psychologically primitive to elaborate. The hypothalamus sits at the base of the forebrain and forms the interface between the sophisticated forebrain and the more primitive lower areas.[440]

The sensory signals are mirrored through the thalamic relays on their way to their specialized cortical areas. These thalamic regions specialize in matching the echoes of the cortex with the inputs from the senses and then mirroring those signals; ear signals are sent to the auditory cortex, skin sensations are routed to the somatosensory cortex, the eye signals are relayed to the visual cortex, and so on.

When appropriate, that is, when a set of signals matches an echo corresponding to en emotional competent stimulus, the thalamus signals the amygdala. The amygdala also receives signals from the various sensory memory systems (auditory, visual and somatosensory) as well as having inputs from the medial temporal memory systems and the medial prefrontal (emotion detecting, area 11) area. In this way the various signals fine-tune the amygdala's responses.[441]

The right amygdala is preferentially activated by briefly presented, subliminal faces (Morris et al, 1998) and specialized for the expression of memory of aversively motivated experiences (Colman-Mensches & McGaugh, 1995). Autonomic changes in the body are evoked when angry facial expressions are subliminally presented to the right and not the left hemisphere (Johnsen & Hugdahl, 1991).[442] It follows from this that the echoes representing ECSs are set in specific areas that specialize in the task at hand. Echoes dealing with faces are on the right side; the echoes of angry faces automatically induce the thalamus to signal the right amygdala more than the left.

The Fear Circuit

[440] Joseph LeDoux, *The Emotional Brain*.
[441] Allan Schore, *Affect Dysregulation*.
[442] Ibid.

In a series of studies with rats, in which different structures or brain regions were purposefully damaged to determine which parts of the auditory system are required for auditory fear conditioning, the following was determined: the signals that reach the ear are transmitted to the auditory brainstem nucleus (cochlear nucleus), then cross to the opposite side to the inferior colliculus of the midbrain. Axons then travel to the auditory thalamic relay nucleus, the medial geniculate.

From the medial geniculate the signal is relayed to the amygdala if the thalamus determines (by matching the stimulus with the appropriate echo from the cortex) it to be a danger signal. The signal is also mirrored (relayed, because of the echo) to the auditory cortex, which in turn is made up of several regions and sub regions. When the thalamus detects a match, the mirrored signal is tagged. When the cortex detects the tag, two things should happen: a) the cortex interprets the signal to be positive or negative; and b) signals the amygdala accordingly. The amygdala will then amplify the emotion or dampen it. The thalamus also projects to three other sub-cortical regions. However, these last three connections have nothing to do with the fear conditioned response.

The amygdala –through the central nucleus – connects to the brain stem areas that are involved in the control of the heart rate and other autonomic nervous systems. The stimulation of the central nucleus elicits freezing responses. Lesions to the central nucleus interfere with every measure of conditioned fear: freezing behavior, autonomic responses, suppression of pain, stress hormone release, and reflex potentiation. Each of these responses is mediated by different outputs of the central nucleus. It should be noted that blood pressure responses were not controlled by the projections of the central nucleus. However, a lesion of the lateral hypothalamus does interfere with the blood pressure response, but not the freezing behavior.[443] Lesions to the third projection (the bed nucleus of the stria terminalis) interfere with the elicitation of stress hormones.[444]

The thalamus also sends the auditory stimulus, because it was matched to a danger echo, to the lateral nucleus of the amygdala. The lateral nucleus seems to receive the conditioned response signals. The central nucleus, together with the hypothalamus controls the activation of the response control systems.

The lateral and central nuclei receive some direct projections from the thalamus, but there are also two other nuclei (the basal and accessory basal) in the amygdala that are interconnected to these two.

In essence, the central nucleus of the amygdala, through different output pathways, controls the fear responses: freezing behavior through the central gray; blood pressure through the lateral hypothalamus; release of stress hormones by the paraventricular thalamus (which receives inputs from the central nucleus and by way of the bed nucleus of the stria terminalis); and the control of the startle reflex by the reticulopontis caudalis.[445]

Neurons that project from the thalamus to the primary auditory cortex are narrowly tuned – they are very particular about what they will respond to. Cells that project to the amygdala respond to a much wider range of stimuli and are said to be broadly tuned. When two similar sounds are used in a conditioning response, the thalamus will send the amygdala essentially the same information, regardless of which

[443] Joseph LeDoux, *The Emotional Brain*.
[444] Allan Schore, *Affect Dysregulation*.
[445] Joseph LeDoux, *Synaptic Self*.

stimulus it is processing (the echoes from the auditory cortex are a close enough match), but after the cortex processes the different stimuli, it will send the amygdala different signals. The auditory cortex and the amygdala receive the danger signal at the same time. The auditory cortex interprets the signal for any emotional content, then signals the amygdala accordingly.

Although the thalamic system cannot make fine distinctions, it has the important advantage of time over the cortical input pathway to the amygdala. It takes about twelve milliseconds for an acoustic signal to reach the amygdala through the thalamic pathway and twice as long through the cortical pathway. The thalamic pathway can't tell the amygdala what is there, but can provide a fast signal that warns that something dangerous may be there; it is fast and dirty.[446]

Imagine walking through the forest. A crackling sound occurs; it goes straight to the amygdala through the thalamic pathway. The sound also goes from the thalamus to the auditory cortex, which recognizes the sound to be either a dry twig that snapped under the weight of your boot or a rattlesnake shaking its tail. By the time the prefrontal cortex processes the difference, the amygdala already started a fear response to the potential rattlesnake. The information from the thalamus is unfiltered and biased to provoking a reaction. The prefrontal cortex's job is to prevent the inappropriate response rather than to produce the appropriate one.

Alternatively, suppose there is a slender, curved shape on the path; the curvature and slenderness signals from the eye are matched to echoes (of curvature and slenderness of snake) by the thalamus and automatically relayed to the amygdala. If it is a snake, the amygdala is already ahead of the game. The fight-flight response is automatically activated. If it weren't a snake, the prefrontal cortex would then send a signal to the amygdala to stop the response, in essence confirming a false alarm. The cost of treating a stick as a snake is less, in the long run, than the cost of treating a snake as a stick.

It has now been established that the amygdala and the prefrontal cortex are reciprocally related: in order for the amygdala to respond to fear reactions, the prefrontal region has to be shut down. Pathological fear may occur when the amygdala is unchecked by the prefrontal cortex. Clearly, decision making in emotional situations is impaired when there is damage to the medial and ventral prefrontal cortex[447]

The medial prefrontal cortex may serve as an interface between cognitive and emotional systems, allowing cognitive information to regulate emotional responses. In return, emotional processing in the amygdala influences decision-making (the types of echoes and handshakes sent out are different, depending on the emotion) and other cognitive functions (how the signals are interpreted and what memories are activated) of the prefrontal cortex.

The amygdala, by way of its connections with the hippocampus and other regions of the explicit memory system, strengthens the relation between emotions and the event. Later, an emotion, because of the particular chemistry of neurotransmitters, neuropeptides and hormones, will more easily activate the related memories. On the other hand, the connections from the hippocampus help recreate the emotion that is related to a memory.

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[446] Joseph LeDoux, *The Emotional Brain*.
[447] Ibid.

The hippocampus will put the emotion into a particular context if possible. When a particular context is determined, the related, activated memories are even more specific. For example, fear is activated when falling from a certain height. But within the context of falling, only very specific behaviors, like rolling as soon as you make contact with the ground are activated. This specific injury-avoiding response is automatic and quickly activated. All other responses or memories are blocked so as not to intrude on the very specific act of avoiding injury and focus very narrowly on the correct response. Conversely, when fear is activated outside a specific context or outside a previously experienced context, as when you start spinning for the first time while driving a car, a sensation of my-whole-life-flashed-by-instantaneously, as the brain in an extremely fast way rifles through many memories in a search for specific responses that can aid in regaining control of the vehicle.

When threatening stimuli induce stress, the amygdala is activated and cortisol is released.[448] The hormone travels to the brain and binds to receptors in the hippocampus, which has the effect of disrupting hippocampal activity and weakening the temporal lobe memory system to form explicit memories.

Repeated exposure to the same ECS makes the thalamus more sensitive. As a result, the echo signals that match the ECS are more easily matched or are greater in number so that fear will be triggered at a much lower threshold. If for some reason the cortex's signals that instruct the amygdala to turn off the fear response are unable to do so or are blocked, the fear response escalates because the amygdala interprets falsely that the danger is still present. The echoes in the cortex relating to this false signal will, over time, make the thalamus relays ever more sensitive to the false ECS. Eventually a very small (in proportion to what is a real danger) stimulus can activate the full range of the fight-flight response,[449] eventually culminating in a panic attack.

Interestingly, the thalamo-amygdala and cortico-amygdala pathways converge in the lateral nucleus of the amygdala. Once the signal is received there, it can be relayed through the internal amygdala pathways to the central nucleus, which in turn releases the full repertoire of defensive reactions. The amygdala sends impulses to the hypothalamus to release a hormone called corticotrophin releasing factor, or CRF, which signals the pituitary and adrenal glands to flood the bloodstream with epinephrine (adrenaline), norepinephrine and cortisol. These stress hormones shut down nonemergency systems, such as digestion and immunity, and direct the body's resources to fighting or fleeing. Perspiration increases to regulate body temperature, breathing quickens to take in more oxygen, the heart beats faster, the liver releases sugar into the blood for added energy, blood pressure rises. All the benefits produced by this response to a passing threat can, over a longer term, wear the body down. Constant stress can lead to impaired memory, a weakened immune system, high blood pressure and stomach ulcers.[450]

Under normal conditions, fear is a short-term response to an immediate threat signaled by the amygdala involving the release of stress hormones by the paraventricular hypothalamus. Compared to fear, anxiety is a long-term response, an emotion triggered by unpredictable threats from stimuli that indicate something is not right. In this case, the bed nucleus of the stria terminalis signals the paraventricular thalamus to release the

[448] Robert M. Zapolsky, *Why Zebras Don't Get Ulcers*.
[449] Joseph LeDoux, *The Emotional Brain*.
[450] Robert M. Zapolsky, *Why Zebras Don't Get Ulcers*.

stress hormones. In the case of anxiety the response is to heighten attention to locate a potential threat.

The fear circuit is lateralized to the right. It involves among other structures the right amygdala, the right insula, which generates an image of the interoceptive condition of the body, and the vagus nerve that delivers viscero-sensations from the stomach, bowels, heart, lungs, pancreas and liver to the awareness level.[451]

The right ventromedial prefrontal cortex is where the [echoes] emotional trace of a conditioned fear is formed and stored.[452]

We can think of a fear circuit in a simplistic way: danger stimulus goes from the senses to the thalamus. If a match is made between a dangerous stimulus and a dangerous echo, a signal is sent to the amygdala. The signal is mirrored (relayed) simultaneously to the sensory cortex. The amygdala triggers the fear response. The sensory cortex processes the stimulus, determines what it is, handshakes go out to the prefrontal cortex, which in turn, determine how much of a threat the stimuli is or isn't. If the prefrontal cortex determines it is not a threat, it will signal the amygdala to dampen and stop the fear response. If it determines it is a threat, it will quantify how much of a threat and signal the amygdala to amplify or dampen the fear accordingly.

The hippocampus will also be alerted when a danger stimulus is detected (ECS matched with an echo) and will quickly assess the context of the stimulus. In the right context, the hippocampus (through projections to the basolateral nucleus through the hippocampal formation) reinforces the danger signal to the amygdala. If the stimulus is in a wrong context, the hippocampus will signal the amygdala to dampen the fear response. The hippocampus signals can override the signals from the sensory cortex as they enter the amygdala farther down the fear circuit. In the absence of a signal from the prefrontal cortex and the hippocampus, the amygdala locks into a positive feedback loop and the fear response automatically escalates until, in less than ten minutes, it becomes a panic attack.

Phobias and Panic Attacks

People suffering from panic attacks and phobias have lost the ability to turn the fear response off. Panic attacks can happen within the context of any Anxiety Disorder as well as any Mood Disorder.[453] The knowledge that something is wrong and beyond control, might be enough of an emotional competent stimulus to trigger an attack. . Possible therapies might involve methods to increase activity in the prefrontal areas so that the amygdala is less free to activate fear.

The essential feature of a Panic Attack is a discrete period of intense fear in the absence of real danger that is accompanied by at least 4 of 13 somatic or cognitive symptoms: palpitations, sweating, trembling or shaking, sensations of shortness of breath or smothering, a choking feeling, chest pain or discomfort, nausea or abdominal distress, dizziness or lightheadedness, derealization or depersonalization, fear of losing control or

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[451] Allan Schore, *Affect Regulation.*
[452] Fischer, H., Anderson, J.L.R., Furmark, T., Wik, G., & Fredrikson, M., *Right-sided human prefrontal brain activation during activation of conditioned fear.*
[453] *Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR.*

going crazy, fear of dying, paresthesias, and chills or hot flashes.[454] All of these are physical normal reactions when fear is engaged, except for fear of going crazy.

The attack has a sudden onset and builds to a peak rapidly. It is often accompanied by a sense of imminent danger or impending doom and a strong urge to escape. The anxiety that accompanies a Panic Attack can be differentiated from generalized anxiety by its discrete nature and its typically greater severity.[455]

In the right context, a panic attack can be life saving. For example, screaming and flailing arms when drowning might be enough to attract help or keep you afloat long enough to get assistance. Conversely, when faced by a predator, shortness of breath, chest pain, nausea, abdominal distress and so on convey the message that you are not healthy or are poisoned, and therefore not a good meal. Ultimately, when escape from a predator is no longer possible, shouting and flailing arms might convey an exaggerated aggressive stance, which might produce enough doubt or even fear in the predator to the point that it disengages. Moreover, shouting and flailing purposelessly could also be interpreted as a sign of going crazy (as a result of poisoning), and deter a predator from attacking for food.

When the thalamus confuses an incoming signal with a wrong echo (one that is not reflecting an ECS), it incorrectly detects a danger signal and triggers the fear mechanism. The signal is then mirrored to the cortex where the echo originated. Since the echo originated in an area not connected to the amygdala, no dampening fear signal is sent. A real threat, in normal conditions, would be mirrored to the right area of the cortex (one that can evaluate stimulus to determine if it is dangerous); the cortex would then signal the amygdala and reinforce the original thalamic fear signal. Likewise, if the processing of the signal were determined to be no threat, the cortex would signal the amygdala and quickly dampen the fear.

In a panic attack, after the thalamus initiates the fear response, the signal is mirrored to a cortical area that does not detect threats (because of the confusion between signal and echo) and consequently this area cannot signal (there are no projections) the amygdala either way. For the same reason the cortex doesn't alert the hippocampus either, and it also doesn't detect a threat. In the presence of real danger, the hippocampus's role is to determine if the context is inappropriate, and if so, to dampen the fear. In the absence of a danger signal, the hippocampus, independent of the context, does not emit a damping fear signal to the amygdala. Therefore, the amygdala locks into the fear response and it quickly escalates. In this case, neither the interpretation of the stimulus or its context can regulate the fear. When the Panic Attack is triggered for no reason and is completely unexpected, it is called uncued.

When the thalamus detects a signal and matches it to a danger echo, it initiates the fear response and mirrors the signal to the cortex; but when the cortex evaluates the danger and does not signal the amygdala that it was a false alarm (it's a stick not a snake), the amygdala continues escalating the fear signal. This is what is known as a situationally bound (cued) Panic Attack.[456] The presence of the stick is enough to trigger the attack.

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[454] Ibid.
[455] Ibid.
[456] Ibid.

And last, but not least, there can be a situation in which the thalamus matches a stimulus to a dangerous echo, initiates the fear response, mirrors the signal to the appropriate area in the cortex, the appropriate signal is sent to the hippocampus to evaluate the context, but the hippocampus fails to evaluate that the signal is in the wrong context, and sends a danger signal instead of a false alarm signal to the amygdala. This signal (the stick bites, watch out) overrides the sensory signal (it's a stick not a snake; sorry, false alarm). Particular objects in any context can trigger the fear. This is known as situationally predisposed Panic Attack. The attack is similar to situationally bound Panic Attacks but is not invariably associated with the cue. Sometimes they happen, sometimes they don't; or the Panic Attack occurs sometime later as the hippocampus belatedly sends a danger signal.

It is clear that there are small differences in each of these different types of Panic Attacks, and each one will require a different therapeutic approach. With recurrent unexpected Panic Attacks, over time, the attacks typically become situationally bound or predisposed,[457] although unexpected attacks may persist.

The essential feature of Panic Disorder is the presence of recurring, unexpected Panic Attacks followed by at least one month of concern over having another Panic Attack or worry about the possible implications or consequences. There can also be a significant behavioral change related to the attacks.

A Panic Attack can be present with other disorders, in which case it would be diagnosed as Depression or Schizophrenia With Panic Attack, for example, and not diagnosed as Panic Disorder With Depression.

In contrast, Panic Attacks that are situationally bound or situationally predisposed occur generally within the context of other Anxiety Disorders.

The essential feature of Specific Phobia is a marked and persistent fear of clearly discernible, circumscribed object or situations. People suffering from phobias have an exaggerated fear or anxiety response to a stimulus, even when the stimulus is rationally known (processed by the cortex) to be no threat. The presence of the stimulus (e.g., a specific object or animal, potentially injurious, or the sight of blood, specific situations or places, or fear of choking) triggers the fear response in a continuous fashion. Any action, including extreme reactions to remove the stimulus (e.g., running or shouting to engage others to help remove the stimulus, or even to carry the person away from the stimulus) is a predictable reaction. People suffering from phobias will go to extremes to avoid the trigger stimulus in the first place.

When the response is fear (as opposed to anxiety) it will present itself as a situationally bound or situationally predisposed Panic Attack. There are several subtypes of Phobias: related to the situationally bound circuit are Animal Type (animals or insects) and Blood-Injection-Injury Type; related to the situationally predisposed circuit are Natural Environment Type (storms, heights, water) and Situational Type (public transportation, bridges, tunnels, elevators, flying, or tight places); and last, Other Type (fear of choking, vomiting, falling if away from walls, etc.), which might fit into either group.[458]

Fear and anger are clarifying emotions. Anxiety, since it is an error-detecting scheme, often is confusing. The resolution of anxiety is achieved by figuring out what is

[457] Ibid.
[458] Ibid.

wrong and correcting it or simply by realizing that there is nothing wrong: it's a false alarm, and the anxiety is automatically dampened.

There exist rich connections between the frontal lobes (areas 9 and 10) with the neighboring voluntary eye motor control center (area 8).[459] Anxiety automatically triggers eye movement as the brain tries to identify the potential threat. This is why rapid eye movements in EMDR (Eye Movement Desensitization and Reprocessing) therapy can reduce anxiety. Emotions trigger automatic physical responses, and a physical response can also elicit an emotion. Try smiling and see if you don't feel better.

In a sense, contextual conditioning is incidental learning. During conditioning, the subject is paying attention to the most obvious stimulus (the fear tone or ECS) but the other stimuli present get learned simultaneously. From an evolutionary point of view, this is very useful because everything that might relate to the danger, the smell, the sounds, the place, the hour of day, etc., will expand the impact of the conditioning. This allows the organism to use remotely related cues to avoid or escape from danger.[460] Each different stimulus will have a corresponding echo capable of triggering the fear reaction. The relations between all the stimuli are the context. In the most primitive sense, the context is the spatial relations where the event took place, the place and its associated objects. All the stimuli will generate an echo with the appropriate tag for contextual purposes in our memory systems. For future reference there will be more echoes to match, related to context, thus triggering more easily the appropriate emotion.

A context gives us not a particular stimulus but a collection of many. The hippocampus, unlike the amygdala, receives pooled information from the different senses: the smells, sounds and sights.[461] The hippocampus surveys (through the echoing signals with tags) all the different regions that might have information about the collection of stimuli, activates them (when it matches echoes) by use of the switching-relays with the hippocampus' electrically fused neurons, thus activating various regions simultaneously. These regions in turn activate handshakes, which are related to the event, and create a context.

In short the amygdala receives low level (rough) sensory signals from the thalamus, higher level information from sensory-specific cortex, and still higher level (sensory independent) information about the general situation from the hippocampus. Through such connections, the amygdala is able to process the emotional significance of individual stimuli as well as complex situations. The amygdala is involved in the appraisal of emotional meaning. It is where trigger stimuli do their triggering!

It is easy to see how a malfunction of any of these pathways might lead to emotional disorders. In some individuals, thalamic pathways can become dominant or become uncoupled from cortical pathways, and might form emotional memories on the basis of stimulus events that do not coincide with their ongoing conscious perceptions. Because thalamic pathways to the amygdala exit the sensory system before conscious perceptions are created at the cortical level, which only represent features and fragments of stimuli, the echoes, the signals to the amygdala will not necessarily coincide with the perceptions occurring in the cortex. Such people would have very poor insight into their emotions. Similarly, if the hippocampal system were uncoupled (stopped receiving

[459] Jean Talairach, Pierre Tournoux, Co-Planar Stereotaxic Atlas of the Human Brain.
[460] Joseph LeDoux, The Emotional Brain.
[461] Ibid.

echoes) from the thalamic and cortical projections to the amygdala, you might have people who express inappropriate emotions to the immediate context, including the social context.[462]

Clinical evidence links the neuropeptide cholecystokinin to the production of panic attacks—most robustly in patients with panic disorder, but also in patients with other anxiety disorders.[463]

Thanks to neuroimaging research, social phobic patients who's symptoms improved after psychotherapy, showed a significant reduced blood flow in amygdala-limbic circuits, particularly in the right hemisphere, reflecting an "alteration of the emotional experience.[464]

These concepts could point the way to some possible therapies. By adding or inhibiting echoes, and strengthening or limiting handshakes, and investigating which pathways are weak or nonexistent, researchers could develop therapies to strengthen or create new emotional landscapes.

The Phobothymic Switch

On the other hand, literally on the other side of the brain, we encounter anger attacks. Anger produces more activity in the left frontal lobes compared to fear responses.[465] As part of the fight-flight response, anger is to fighting as fear is to fleeing. Under normal conditions, when a threat is present, at some point the organism determines that fleeing is impossible or useless or that direct action can remove the threat. When this happens, the fleeing mechanism automatically is switched to fight mode. This automatic response is what I have termed the phobothymic switch (from the Greek phobos=fear and thymos=anger or wrath). When the frontal lobes determine that removing the threat is a better alternative to fleeing, or the only alternative, they signal the hippocampus and thalamus to activate the phobothymic switch transferring activity from the right frontal lobe to the left frontal lobe and the right and left amygdala receive different signals accordingly. The right hippocampus checks non-verbal, spatial contexts, and through the hippocampal commissure compares with the left hippocampus' verbal, deductive reasoning contexts and helps determine when to activate the phobothymic switch.

It is also well established that stimulation of the amygdala in awake mammals elicits freezing, escape, and defensive attack responses, in addition to autonomic changes.[466] The communication between the central nucleus and the midbrain, pons, medulla and hypothalamus control some of these well known reactions and indicate they are integral components of the phobothymic switch.

The hypothalamus sets the threshold for the phobothymic switch and is the chemical regulator of anger. The hypothalamus links the central nuclei of the amygdala with the lateral hypothalamus for autonomic nervous control and with parvocellular

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[462] Ibid.
[463] Bradwejn, J., & Koszcyki, D., *The cholecystokinin hypothesis of panic and anxiety.* Annals of the New York Academy of Sciences, 713, 273-282., 1994.
[464] Allan Schore, *Affect Regulation and the Repair of the Self.*
[465] Jack Wacker, Marcus Heldman, and Gerhard Stemmler, *Separating Emotion and Motivational Direction in Fear and Anger: Effects on Frontal Asymetry.*
[466] Joseph LeDoux, *The Emotional Brain.*

neurons for neuroendocrine control. The central nuclei of the amygdala influence corticotropin hormone release by parvocellular neurosecretory neurons of the paraventricular nucleus. This control is exerted by disinhibition. GABAergic neurons of the central nuclei synapse on GABAergic neurons in the hypothalamus that control the neurosecretory neurons.[467]

Philip Bard demonstrated that the hypothalamus is part of the anger response, because in its absence, only fragments of emotional reactions, rather than fully integrated reactions could be mustered, and only in response to very intense, painful stimuli. The animals might crouch, snarl, hiss, unsheathe their claws, retract their ears, bite and/or exhibit some autonomic reactivity, but these did not occur together in coordinated fashion.[468]

Anger is a state that hopefully leads to the avoidance of fighting by activating the fear response in the menacing organism. Anger serves as a warning signal. Anger is a preparative state to a fight response as opposed to fear as preparative to flight. The physical changes like those involved as preparation for fleeing, serve the organism equally well for fighting.

Similarly to panic attacks, which trigger fear inappropriately, anger attacks trigger anger for no apparent reason. Anger attacks are sudden intense spells of anger, but, in contrast to panic attacks, lack the predominant emotion of fear and anxiety. Patients have described anger attacks as uncharacteristic behavior inappropriate for the situation, followed by remorse. Physical features of autonomic activation included sweating, trembling, tachycardia, feeling out of control, desire to attack others and hot flashes accompanied the outbursts of anger. In an anger attack, typically anger and rage are directed inappropriately at others. This is manifested as physical or verbal attacks directed at others (63%), and less common, throwing objects or destruction of property (30%). After the attack, guilt or regret is almost universal (93%).

The prevalence of anger attacks in patients with panic disorder is approximately 33%. Similar rates have been found with patients with other anxiety disorders. Depressed patients were twice as likely to report anger attacks as patients with anxiety disorder. Moreover, anxiety patients with anger attacks were significantly more depressed than anxiety disorder patients without anger attacks. Anger attacks have also been reported in women with eating disorders: anorexia nervosa and/or bulimia nervosa (31%), compared with normal female volunteers (10%).[469]

Posttraumatic Stress Disorder

When an individual is exposed to an extreme traumatic stressor, generally involving actual or threatened death or serious injury, or even witnessing an event that involves death, injury or threat to the physical integrity of another, or learning about unexpected or violent death, serious harm, or threat or injury experienced by a loved one, certain symptoms can appear. The characteristics of these symptoms include persistent

[467] John H. Martin, *Neuroanatomy.*
[468] Joseph LeDoux, *The Emotional Brain?*
[469] Jarrold F. Rosenbaum, *Anger Attacks in patients with Depression,* J Clin Psychiatry 1999;60[suppl 15]:21-24

reexperiencing of the traumatic event and increased arousal. When these symptoms are present for more than a month, it is diagnosed as Posttraumatic Stress Disorder.

Generally, the individual's response to such traumatic events involves intense fear or helplessness. The traumatic events experienced directly that can lead to Posttraumatic Stress Disorder include (but are not restricted to) military combat, violent personal assault, being kidnapped or tortured, natural and man made disasters, or being diagnosed with a life-threatening illness. Witnessed events include observing serious injury or unnatural death of another person due to violent assault, accident, war, or disaster; learning about violent personal assault, serious injury, or the sudden, unexpected death of a family member; or learning that one's child has a life-threatening disease can also lead to Posttraumatic Stress Disorder.[470]

About one month after my son Mitchell took his life, and for the next four months I tottered on the brink of Posttraumatic Stress Disorder. I continuously experienced a feeling of anxiety. The anxiety woke me up at night and I had a hard time falling back asleep. When I woke up in the morning, I immediately became anxious. I had a recurrent vision, wide-awake, where I see Mitchell starting the act. I can still see him; he is in the landing of the stairwell in our apartment in New York. He is unafraid, even smirking, with an expression of concentration, such as he would show when preparing to do a complicated skateboard trick. He leaps, is in mid-air…

Then, the vision changes. The light is different; perhaps a few hours later. The sun has set. It is dark. Mitchell is there, hanging immobile in the dark, at the bottom of the stairwell. The vision kept repeating itself as if it had been a real past event; I kept seeing him as he does it, as if I had been there watching, as if I had actually witnessed his death.

Later, I was in our apartment in New York, still suffering from these visions. I had the opportunity to check the facts with a friend who discovered my son's body. Eerily, except for a small element in his clothing, every detail was like I saw it. However, after inspecting the stairwell, what is strange was that my angle of vision was such that I would have to have been inside a wall of the stairwell to have the proper perspective. This confirmed my imagination had created the event, yet the associated emotions were so strong that the illusion was perceived as if it had been a real past, witnessed event. The vision, now a memory, still has this feeling, even though I rationally know that it was created by my heightened emotional grieving state.

The emotions generated when a highly traumatic event occurs are proportionately intense. All associated stimuli to the event become related to the emotion, even when they are just incidental and not an intrinsic part of the event. The sounds, sights or smells surrounding the individual when the traumatic event occurs, due to the intensity of the emotional state, become deeply embedded to that moment, and can, alone, when encountered subsequently, trigger the emotional state. In this way, incidental stimuli like the vegetation, the place, the weather, the time of day, the presence of certain objects or people or sounds or smells, which are totally unrelated otherwise to the traumatic event, can trigger the intense emotion. The intense emotion in turn will activate the memory forcefully. The amygdala will signal de nucleus accumbens in proportion to the intensity of the emotion, very intensely in these traumatic cases. The memory accompanied by the real intense quality of the emotion is perceived by the brain as actually being real; as if the remembered even is actually happening in the present. Imagined events, because of

[470] *Diagnostic and Statistical Manual of Mental Disorders*, DSM-IV-TR.

the intense emotion, can feel like reality; the remembered event is perceived as actually occurring in the present, or the imagined event takes on the quality of a real past experience, even with the knowledge that this can't be possible. The construction of the present involving automatic triggered emotions and incoming sensory signals, is similar to recalled events accompanied by extremely intense (by comparison) emotions, and as such, can easily be confused one with the other. In the same fashion as memories fade with time, the intensity of the emotion of the traumatic event fades with time, and the memory stops seeming real.

Similarly, when reality lacks an emotional component, the brain resolves the paradox resorting to disbelief. We mentioned the case of a man who suffered damage to the amygdala and as a result could not generate the associated emotion that the presence of his parents automatically, under normal conditions, triggered. His brain resolved this paradox by believing that they must be impostors.[471]

The re-experienced, intrusive, intense memories are set as echoes that represent an emotionally competent stimulus. When the thalamus matches one of these echoes to incoming sensory signals, it shifts attention to the activated, associated memory and automatically triggers the corresponding emotion. The intensity of the emotions reinforces the feeling that the memory is an actual event and is experienced presently.

PTSD is an intense defense mechanism to aid the organism in avoiding anything related to life-threatening experiences. If the environment was constant, i.e., it continues to be life-threatening, PTSD would be a great survival aid. Because of the multiple stimuli that became associated with the traumatic event, any one of them can trigger the emotion and it is re-experienced as recurrent and intrusive recollections with varying degrees of belief it is really happening. Because of this, stimuli associated with the trauma are persistently avoided. Deliberate efforts are made to avoid thoughts or feelings or people who activate memories associated with the event. In some cases the intrusive re-experiencing of the event, because of the intense emotions generated, leads the isorropic circuit to narrow the spectrum of possible emotions, producing a diminished participation in previously enjoyed activities, and a noticeable reduced ability to emote, which in turn generates feelings of detachment or estrangement from other people. Under these conditions, the signals emanating from the isorropic circuit trigger a persistent anxiety and/or increased arousal. This condition leads to difficulty sleeping, hypervigilance, exaggerated startle response, irritability or outbursts of anger and difficulty concentrating.

Only through a process similar to grieving, revisiting and recalibrating each emotion that triggers the reexperience of the event, can the event become separated from the associated emotions. The knowledge that, in the present, one can exert some control over the various components of the traumatic event, slowly leads to a distancing from the emotion.

There is evidence to show that maltreated children diagnosed with PTSD manifest right-lateralized metabolic limbic abnormalities (De Bellis, Keshaven, Spencer, & Hall, 2000; De Bellis et al., 2002), and that right brain impairments associated with severe anxiety disorders are expressed in childhood. Neurological studies of adults confirm that

[471] V.S. Ramachandran, *Phantoms in the Brain.*

dysfunction of the right frontal lob is involved in PTSD symptomatology (Freeman & Kimbrell, 2001) and dissociative flashbacks.[472]

14
Those Other Feelings, Hope They Are Good.

Emotions have powerful influences over cognitive processing. Attention, perception, memory, decision making, thinking – all can be changed by an emotion. An emotion, when the brain detects it, is expressed as a feeling. The feeling intrudes on the attentional systems. Conversely, as we have seen, the anterior cingulate and orbital areas are connected with one another and to the amygdala as well as to the lateral prefrontal cortex, and all receive information from the sensory processing areas (and their memory systems), so they can impact emotions. Moreover, shifts of attention produce slight changes in the activity of the brain facilitating the activation of an emotion.

Emotions intrude on attention. When attention is focused on a stimulus, and a second stimulus is emotionally significant (another echo is matched by the thalamus), the amygdala can override the attentional systems by sending a signal back to the thalamus. The thalamus then shifts attention to this new stimulus. In other words, the amygdala makes it possible to shift attention to a previously unattended event.

The caudate is responsible for activating particular modes of thinking or specific memories related to emotions as surely as certain memories can elicit the related emotions. This two-way avenue produces strong motivation to act in ways that produce advantageous outcomes.

Emotions, through external manifestations, serve to communicate the internal emotional state to others. While the left hemisphere mediates most linguistic communications, the right hemisphere is important for broader aspects of emotional communication. What can be communicated verbally might be quite independent of what can be emotionally communicated through gestures, expressions and body posture.

Social Emotions

From reptiles upward on the evolutionary ladder, the most obvious interaction requiring two individuals is sexual reproduction. Most other behaviors can be accomplished individually. The male reptiles possess a copulatory organ, either a single penis (turtles, tortoises and crocodilians) or a pair of hemipenes (lizards and snakes) and two testicles housed inside the body. Independent of whether the reptile is oviparous or viviparous, sex is an interaction between two individuals, guided by species-specific markings, secondary sexual characteristics and interpersonal exchanges of behavior.

Reptiles exhibit sexual species-specific conduct but do not exhibit parenting behaviors as do birds and mammals. The complex behaviors of parenting, as well as social interactions are part learned, part genetically wired, and evolutionarily speaking, perhaps in their external expressions, related to sexual reproductive behaviors.

[472] Allan Schore, *Affect Regulation and the Repair of the Self.*

As mentioned, neurobiological research indicates that complex fine-tuning emotional circuits are located in the frontal, especially in orbital prefrontal cortex. The orbital prefrontal cortex is located behind the eye in the ventral and medial surfaces of the prefrontal lobe. These circuits develop postnatally within a social environment. This area is interconnected with the limbic association area in the forebrain,[473] and contains the highest levels of opioids and dopamine in the cortex, as well as very high numbers of serotonin receptors. The prefrontal lobes project to the limbic areas in the temporal pole and the amygdala, to subcortical centers in the hypothalamus, and to dopamine neurons in the ventral tegmental area. The orbitofrontal cortex is expanded in the right side, and, more so than the left has, extensive interconnections with limbic and subcortical regions.

The orbitofrontal areas are capable of carrying out an adaptive role in socioemotional functioning. This frontolimbic system projects to the limbic forebrain-midbrain circuits and is involved in the excitatory and inhibitory aspects of the limbic system. It is also a central-nervous-system control center of the sympathetic and parasympathetic branches of the autonomous nervous system. Orbital stimulation leads to autonomic effects (e.g., changes in heart rate, skin temperature, blood pressure) involved in emotional behavior. These two autonomic components determine the individual's unique excitation-inhibition autonomic responses. This capacity to shift states between ergotropic and trophotropic arousal allows for the re-establishment of autonomic balance after emotional stress.[474]

There are extensive orbitofrontal-hypothalamic connections influencing the production of hypothalamic releasing factors that directly regulate the secretion of pituitary, thyroid, adrenal, and gonadal hormones that are responsible for the somatic and visceral components of emotions.[475]

Social emotions comprise a wide range and assist in guiding behavior in very complex social interactions. The expressions and behaviors of social emotions are partly learned and have a cultural component as well. Social emotions include, among others, shame, arrogance, rage, envy, jealousy, guilt, empathy. In humans, mutual gaze interactions represent the most intense form of interpersonal nonverbal communication. This moment-by-moment exchange of facially expressed emotions increases the degree of engagement. Disengagement is accomplished by subtle shifts in gaze.

J.M. Gottman has coded various emotions that married couples might express during interactions. It is known as the Specific Affect Coding System. The system draws on facial expressions based on Ekman & Friesen's (1978) system of facial action coding, vocal tone, and speech content to characterize the emotions displayed.[476] On the positive side he has: interest, validation, affection, joy and humor. On the negative side, from more to less, disgust, belligerence, contempt, defensiveness, whining, fear/tension, domineering/stonewalling, sadness and anger. Using sensors and electrodes to measure various bodily reactions and matching them in time with the various coded emotions observed while a couple interacts for as little as fifteen minutes, feeding this into a complex equation, Gottman can predict with 90% accuracy whether the couple will still

[473]John Martin, *Neuroanatomy.*
[474] Allan Schore, *Affect Dysregulation.*
[475]Ibid..
[476] Sybil Carrere, John Mordecai Gottman, *Predicting Divorce among Newlyweds from the First Three Minutes of a Marital Discussion.* 1999.

be married fifteen years later. Sybil Carrere discovered that with only three minutes of a couple talking, they could still predict with fairly impressive accuracy who will get divorced. Gottman has found that for a marriage to survive, the ratio of positive to negative emotion in a given encounter has to be at least five to one.[477]

Gottman is carefully recording the automatic emotional responses triggered by the echoes of each spouse, which in turn generate an emotional response. This indicates that echoes that trigger emotional responses to a spouse or loved one are fairly stable over long periods of time and are strengthened by experience in such a way that the emotional responses, over time, become more intense; in some cases intense enough to lead eventually to divorce.

Gottman tracks the ups and downs of a couple's level of positive and negative emotion, and it doesn't take very long to figure out which way the line on the graph is going. "Some go up, some go down," he says. "But once they start going down, toward negative emotion, ninety four per cent will continue going down. They start on a bad course and can't correct it. It's an indication of how they view their whole relationship."[478]

Learned, as well as genetically wired responses to various emotionally competent stimuli (ECS) will be represented as echoes in various part of the cortex specializing in interpreting the various types of sensory stimuli. The various echoes representing different stimuli are set up according to new experience and will help set up models for future interactions. These echoes contain an emotional as well as a cognitive component, and together, both assist in creating a context. Any one of these three components aid in activating (constructing) specific memories and serve as future quick-reference guide. The memories, in the form of echoes and handshakes, represent experiences, loved people, lessons learned, books read, movies watched, skills learned, and together form an opinion by producing subtle emotional responses to various stimuli.

Visually, the right cortex is involved in the recognition and interpretation of emotional expression of faces; whether they are happy, or unpleasant, sad or angry faces. The right hemisphere can appraise facially expressed emotional cues in less than 30 milliseconds (Johnsen & Hugdal, 1991). Auditorily, this is also true for the processing of prosody. Through experience, echoes are set up in the respective areas to automatically trigger the appropriate emotional response, which now becomes a component of the stimuli. In this way the internal visceral responses accompanying the changes in emotional state reflect the visual and prosodic information of a face. The orbitofrontal cortex, not only because of facial expressions, but depending on whether his or her face represents friend or foe, will fine-tune or change the emotion adapting to the changing faces in the social environment. Not surprisingly, the right hemisphere is instrumental to the capacity of emphatic cognition and the perception of emotional states of other humans.[479]

The orbital prefrontal cortex is especially expanded in the right cortex and it comes to act in the capacity of an "executive control system" for the entire right cortex and the visual system that is centrally involved in selective attention to facial expressions

[477] Malcolm Gladwell, *Blink.*
[478] Ibid.
[479] Allan Schore, *Affect Regulation and the Repair of the Self.*

and appraisal. Endorphins are partially responsible for the pleasurable qualities of social interactions.

The right hemisphere, because of these lateralized specializations used to evaluate various social emotional stimuli, contains extensive reciprocal connections with limbic and subcortical regions, more so than the left. The right cortex is dominant in globally directing attention and processing novel stimuli. The early maturing and "primitive" right cortical hemisphere (more than the left) is dominant for the processing, expression, and regulation of emotional information (Joseph, 1988). It also mediates biologically primitive emotions that serve motivational and social communication functions.[480]

The activity of the nondominat right hemisphere, and not the later maturing dominant verbal-linguistic left, is instrumental in the perception of the emotional states of others. Through the expression of these emotional states as subtle facial expressions, body postures and speech prosody, the right hemisphere can evaluate the overt behavior of others as well as try to understand one's self (our feelings) in the course of social interactions.

The non-verbal expressions that bind the infant to its parent continue throughout life as a primary medium of intuitively felt (triggered by echoes) affective and relational communication with others. This non-verbal activity (matching of echoes and automatic triggering of corresponding emotions) of the right hemisphere, and not the verbal-linguistic left, permits emphatic cognition and the perception of emotional states in others.

Allan Schore continuously stresses the importance of the orbitofrontal circuits in his groundbreaking books, *Affect Dysregulation and Disorders of the Self* and *Affect Regulation and the Repair of the Self.* The orbitofrontal circuits play a role in the organization of behavior and in adjustments of emotional responses, efficiently monitoring and regulating the duration, frequency and intensity of both positive and negative affect states (mood regulation). Successful emotional adaptation requires the capacity to tolerate positive and negative emotions of relative intensity. In other words, the isorropic circuit's attractor should be able to return rapidly to the true neutral calmness state, but tolerating a drift wide enough and for sufficient time (one or two minutes to produce the required response), allowing for maximum adaptability.

The emotional interactions between infant and mother (care-giver) are entirely nonverbal. This very efficient system of emotional exchanges with others will continue throughout life.

It has been observed that the pupil of the eye acts as a nonverbal communication system and that large pupils in the infant release caregiver behavior (Hess, 1975).[481]

Experience will dictate not only the specific types of emotion that can be experienced, but also its levels of intensity. Accordingly, the orbitofrontal cortex, using the sympathetic, excitatory circuits of the ventral tegmental dopaminergic or the noradrenergic circuit in the locus ceruleus, or the parasympathetic, inhibitory noradrenergic circuit of the lateral tegmental will influence the final excitation-inhibition of emotional balance.

The excitatory ventral tegmental limbic forebrain-midbrain circuit is associated with positively valenced states. The inhibitory circuit, the lateral tegmental limbic

[480] Ibid.
[481] Ibid.

forebrain-midbrain circuit is associated with negatively valenced states.[482] In this elegant manner, the orbitofrontal circuits alter the brain's basic rates of signaling: the positive states speeding up the rate of signaling and the negative states reducing the rates.

Dopamine acts as an excitatory influence (D1) in the prefrontal areas. Noradrenaline, through the reciprocal connections of the orbitofrontal regions to the medulla oblongata solitary nucleus and the vagal complex in the brain stem reticular formation, and on to subcortical parasympathetic autonomic area, acts in an inhibitory capacity.[483] Dopamine is associated with positive states, noradrenaline with negative emotions.

This autonomic balance-regulating system can be biased to predominance of excitatory dopaminergic ventral tegmental activity or towards an inhibitory noradrenergic lateral tegmental circuit. In part, and depending on some of these biases, stress hormones diminish the capacity to return to a neutral state in different degrees. Thus early experience will dictate later patterns of behavioral response. A dysfunction of psychobiological regulatory systems is most obvious under stressful and challenging conditions that call for behavioral flexibility and emotional regulation.

In a constant environment, one with no changes, the simple, learned social responses of early childhood would be sufficient to deal with most situations, as there is no need to adapt. Stressful conditions would be non-existent, as all possibilities would have been experienced and appropriate responses learned. In general, the parent's environment will reflect the child's. However, when parents interact with a reduced range of emotional responses that do not reflect the external conditions, children grow up with a limited repertoire of responses, and more importantly, will respond with seemingly inappropriate behavior, particularly in a social context. The inability to adapt to stress, defined as the continued activation or inhibition of an emotion that is inappropriate to the environmental situation, essentially sets the coping limits. This would also hold true in an extremely rapidly changing environment; the responses learned in one environment would not apply in another, very changed world.

Allan Schore proposes that the early social environment, mediated by the primary caregiver, the close interactions between mother and child, guide the ontogeny and neurobiology of emotional development, especially during the first two years of life. These interactions directly influence the final wiring of the circuits of the infant's brain that are responsible for the future socioemotional development of the individual. He postulates that this process is guided by a mother-right-brain to child-right-brain process and has a critical effect on the early organization of the limbic system. He suggests that in psychobiologically attuned face-to-face transactions the infant's right hemisphere, which is dominant for recognition of the maternal face, and the perception of facial expressions and prosody, appraises the output of the mother's right hemisphere, which is dominant for non-verbal communication and the processing and expression of emotional information.

This "emotional vision" can induce mood modification by mimicking emotional states through our own facial expressions, gestures and body language, as emotional transference.

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[482] Ibid.
[483] Ibid.

Alterations in gene-regulating hormones, such as opioids, corticosteroids, and other neuropeptides, are induced and regulated by interactions with the external environment [learned, primarily from the parents, nurture], and these changes trigger the activation of genetic programs and thereby the microarchitecture of brain regions in the "internal environment" [genetically determined, nature].

The orbitofrontal cortex circuits not only appraise positive and negative visual-facial and auditory stimuli, but also processes responses to pleasant touch, taste, smell and music. It acts to assign emotional-motivational significance to cognitive impressions through the association of emotion with memories and thought.

The proximity of this area to the ventral and medial hemispheric surfaces serves to act as a convergence zone between cortex and subcortical structures. It is thus situated at the top of a hierarchical circuit of interconnected limbic areas, such as the insular cortex, anterior cingulate, and amygdala. The orbitofrontal circuits is also connected into the autonomic nervous system, and due to the tact that it is the only cortical structure with such direct connections it can regulate autonomic responses to social stimuli,[484] and modulate emotional behavior.

Each emotion produces a slightly different chemical alteration. For example, shame elicits a painful distress state, manifest in a sudden decrement of pleasure, a rapid inhibition of excitement, and cardiac deceleration by means of vagal impulses in the medulla oblongata. This shift reflects the reduced activation of the excitatory dopaminergic ventral tegmental limbic forebrain-midbrain circuit and increased activation of the inhibitory noradrenergic lateral tegmental limbic forebrain-midbrain circuit. Shame produces low levels of endorphins and corticotropin releasing factor and elevated levels of corticosteroids.[485]

Bonding

Each emotion has its own circuits and loops, activated by a specific chemical brain milieu in response to external and internal stimuli. In studies of bonding in prairie (monogamous) and montane voles (don't form sexual preferences after mating), researchers determined that the hormones, vasopressin and oxitocyn, found only in mammals and related to ancestral hormones that play key roles in behaviors like nest building in nonmammalian species, are important in reproductive behavior. Oxytocin evolved in fish about 100million years ago to aid mating.[486] In the brain they function as neurotransmitters and/or modulators. If oxytocin is not present (blocked), the female prairie vole mates but does not bond with their mate. This suggests that the release of oxytocin during sex produces a bonding behavior. In contrast, males, in the absence (by blocking) of vasopressin, mate but don't bond; moreover, they don't engage in mate-guarding aggression. The female sex hormone estrogen is a key to oxytocin's action; vasopressin in males needs testosterone for its normal function. The details of the circuit haven't been fully worked out, but areas in the amygdala have been implicated (medial

[484] Ibid.
[485] Ibid.
[486] Robert Lee Hotz, *Researchers Find Trust to be a Hormonal Affair*, Los Angeles Times, June 2, 2005.

and posterior nucleus), as well as the so-called extended amygdala, the striatum (especially the nucleus accumbens) and the hypothalamus.[487]

Given that both prairie and montane voles have neurons with receptors for oxytocin and vasopressin, it is tempting to think that they form circuits responsible for sexual behavior and pair bonding. Areas of the amygdala are included in both the fear and sex circuits; however, the circuits are distinct. Otherwise, as Joseph LeDoux suggested, we might engage in sex with a predator with predictably disastrous results.

Oxytocin is released when people hug their loved ones, a spouse or their children, as well as when mother's nurse their babies.[488]

The medial and posterior nuclei are implicated in the sex circuit; the fear circuit involves the lateral and central nuclei. This emphasizes the importance of mapping the circuits for different emotions. However, this doesn't mean that different emotions can't interact, like the fear and sex circuits. The medial nucleus sends projections to the central nucleus, where oxytocin receptors are present. Oxytocin, controlled vagally, is released by sensory stimuli that convey warmth and familiarity, such as tone of voice and familiar faces. This might help explain why oxytocin and positive social interactions can reduce fear and stress.[489] Some physical reactions might be common to fear and sexual behavior, e.g., increased blood pressure and heart rate, and sweating, for example. Likewise, many are not, i.e., fear of dying, urge to flee, etc.

Sandler and Sandler, in their discussion of states of "primary identification" – of moments when the boundary between self and object is lost – argued that this is the essential basis of the process of projective identification, and that it occurs in a "reciprocal love relationship".[490] Love does not happen in a vacuum; it is a process of emotional emphatic interchanges. For it to flourish, a dyad is necessary. Current developmental models emphasize that projective identification is not unidirectional but is a bi-directional process in which both members of an emotionally communicating dyad act in a context of mutual reciprocal influence. These emotional communications have unique operational properties, occur in specified contexts and are mediated by nonverbal signs.[491] I would go as far as saying that this holds true across cultures and even species.

Arthur Aaron, from Stony Brook University in New York, recruited a group of men and women and placed opposite sex pairs to perform a series of talks, including telling each other personal details about themselves. He then asked them to stare into each other's eyes for two minutes. Most couples, previously complete strangers, reported feelings of mutual attraction.[492]

Hormones produce longer lasting changes in the brain chemistry and can promote prolonged motivations for specific behaviors. Helen Fisher of Rutgers University and a multi-disciplinary team of experts recruited 40 young people madly in love - half with love returned, the other half with love rejected - and put them into an MRI with a photo of their sweetheart and one of an acquaintance. When viewing the picture of the loved one, the right ventral tegmental area was active. This is the part of the brain where

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[487] Robert M. Zapolsky, *Why Zebras Don't Have Ulcers.*
[488] Lauren Slater, *Love, National Geographic.* February 2006.
[489] Robert M. Zapolsky, *Why Zebras Don't Have Ulcers.*
[490] Sandler, L & Sandler, A.M., *Psychiatric footnotes on Love.*
[491] Allan Schore, *Affect Regulation.*
[492] Lauren Slater, *Love, National Geographic.* February 2006.

dopamine cells project into other areas of the brain, including the posterior dorsal caudate and its tail, both which are central to the brain's system for reward and motivation. In addition, several parts of the prefrontal cortex that are highly wired in the dopamine pathways were mobilized, while the amygdala, associated with fear, was temporarily quieted.[493]

Rita Valentino of the University of Pennsylvania has shown that the nucleus of Barrington in the hindbrain, formerly believed to control maturation (bladder-emptying), send axons containing the neuropeptides CRF through the vagus nerve to the most distant part of the large intestine, near the anus. Rita proved that sensations of colonic distention (i.e., feeling like pooping) as well as those of genital arousal are carried back to the nucleus of Barrington. From there, a short projection hooks up to the locus ceruleus, the norepinephrine-containing source of the "pleasure pathway," high in opiate receptors. It should be no surprise that occasionally there are sexual practices related to bathroom behaviors. The nucleus of Barrington contains many neuropeptides receptors, and feelings related to sexual arousal or excretory functions can be switched or modified. Emotions and bodily sensations are thus intricately intertwined, in a bi-directional network in which each can modify the other.

Dr. Fisher reports that sex involves three separate brain systems: the craving for sexual gratification, driven by androgens and estrogens; attraction (or passionate love), characterized by euphoria when things go well and mood swing when not, focused attention, obsessive thinking and craving for the partner, driven by high levels of dopamine and norepinephrine and low levels of serotonin; and attachment, (a sense of peace, calm and stability) driven by hormones oxytocin and vasopressin. Levels of oxytocin rise during orgasm, which might contribute to the bonding of the couple. Contemporary pharmacologists, neurobiologists, and physiologists like Sue carter, Tom Insel and Jaak Panksepp have shown that oxytocin produces the uterine contractions of sexual orgasm in women.

Blood endorphin levels in hamsters increased about 200 percent from beginning to the end of the sex act. There are some preliminary results that have not been published that suggest that this is so in humans; endorphins from the testes cause the orgasmic spasms of the vas deferens.

Sex hormones are a good example of how hormones can affect more than overall behavior. John Money, psychiatrist at John Hopkins showed that female fetuses exposed to testosterone-like steroid hormones (aberrantly produced by their pregnant mothers' adrenal glands) were more likely to become tomboys and avoid dolls.[494]

In an experiment whose results were published in the journal *Nature*, researchers at the University of Zurich in Switzerland and Claremont Graduate University determined that people who inhaled half a dozen puff of oxytocin nasal spray were measurable more likely to risk all their money with a stranger without knowing why. Although the researchers set up the experiment to test the effects of oxytocin on financial decisions, they believe the hormone is a keystone of a normal social life. Oxytocin plays a role in human childbirth by enhancing uterine contractions, and for nursing mothers it

[493] Allan Schore, *Affect Regulation.*
[494] Candace B. Pert, *Molecules of Emotion,* 1997.

eases milk production. Paul J. Zak the author of the research paper said, "If I increase your levels of oxytocin there is a decrease of anxiety in trusting a stranger.[495]

Trust is a major component of love, friendship and leadership. The latter behaviors are of primal importance in social animals and could not exist without trust.

High levels of oxytocin and vasopressin may interfere with dopamine and norepinephrine pathways, Dr Fisher explained in the same talk, which may explain why attachment grows as mad passionate love fades. Meanwhile, elevated testosterone can suppress oxytocin and vasopressin. There is good evidence, Dr Fisher said, that men with higher testosterone levels tend to marry less often, be more abusive in their marriage, and divorce more regularly. The reverse can also be true. If a man holds a baby, levels of testosterone go down, perhaps in part because of oxytocin and vasopressin levels go up up. Although the brain images of the men and women in Dr Fisher's study were basically the same, she and her colleagues did find activity in men in a region of the parietal of the temporal lobe associated with the integration of visual stimuli. In women, there was more activity in regions associated with memory recall.[496] This might suggest that men are more prone to choose sexual partners on the basis of physical appearance, whereas women have a greater tendency to consider other attributes.

Laughing

From the point of view of an ethologist, any stereotyped vocalization, like laughter, almost always implies that the organism is trying to communicate something to others in the social group. The main purpose of laughter could be to alert others in the social group (usually kin) that a detected anomaly is trivial, nothing to worry about. The laughing person in effect announces her discovery that there has been a false alarm; that the rest of the group need not waste precious energy and resources responding to a spurious threat. This would also explain why laughter is contagious, for the value of the signal would be amplified as it spread through the social group.[497]

The brain has some subsystems that respond to unexpected or novel events, particularly the hippocampus. The false alarm theory of humor may explain slapstick. You see a respectable person walking down the street, he slips on a banana peel, and you laugh as soon as you determine that he is not injured. Occasionally in evolution, once a mechanism is in place, it can be exploited for other purposes. The ability to reinterpret events in the light of new information may have been refined through generations to help people playfully juxtapose larger ideas or concepts – that is, to be creative. Laughter and humor might be a rehearsal for creativity.

Different studies of the brain suggest the existence of a laughter circuit. Patients laugh spontaneously when a region in the supplementary motor cortex, close to a region in the frontal lobes that receives input from the brain's emotional centers, is stimulated. In cases where a person literally died of laughter (she could not stop laughing, until,

[495] Robert Lee Hotz, *Researchers Find Trust to Be a Hormonal Affair*, Los Angeles Times, June 2, 2005.
[496] The Brain in Love and Lust, McMan's Depression and Bipolar Web http://www.mcmanweb.com/love_lust.htm
[497] V.S. Ramachandran, *Phantoms of the Brain*.

exhausted, she died), subsequent autopsies revealed damage to portions of the limbic system: the hypothalamus, mammilary bodies and the cingulate girus, all of which are involved in emotions. Given the well-known role of the limbic system in the fear circuit, it is not surprising that it is also involved in the aborting of a reaction in response to a false alarm – laughter. The feeling of merriment that accompanies laughter is a further indication that the limbic system is activated.[498]

Laughing at humorous remarks is only an aspect of the use of laughter. Robert Provine, author of *Laughter: A Scientific Investigation* reports that speakers laugh 46 percent more than listeners. A person is thirty times more likely to laugh in the presence of other people than when alone.

Normal laughter is triggered by a specific, usually mirthful stimulus accompanied by mood elevation. It is a coordinated motor-function involving facial and respiratory muscles.

Laughing as a communication strategy might promote social bonding. Roger Fouts, who has taught sign language to a number of chimpanzees reports that tickling is so popular among chimps that they engage in tickle-fests. In both human and chimpanzee societies, tickling usually appears in parent-child interactions and has an essential role in strengthening initial bonds.[499] Laughter, thus, might be carried on to the adult phase to continue strengthening social bonds.

A patient with a peculiar form of simple partial sensory seizure is reported. She had episodes of tickling sensations in a localized region of the body. In most of the episodes there was only a sensory ticklish feeling but in some, there was associated emotional response in the form of laughter. EEG, CT and MRI scans localized lesion to the corresponding sensory cortex.[500]

Tickling exploits the sensorimotor system's awareness of the difference between self and other.[501] This is the reason why people can't tickle themselves; there is an element of surprise for tickling to produce laughter.

Laughter is possibly produced by a medullary effector center (the laughter center) and is subject to tonic inhibition from the cerebral cortex and limbic system via an integrator located in or around the hypothalamus. It has also been suggested that volitional (cortex) and emotional (limbic) influences interact with the laughter center in the lower brainstem through distinct pathways. It is possible that the anterior cingulate region is involved in the motor act of laughter, while the basal temporal cortex is involved in processing the emotional content.

There is a curious neurological disorder called pain asymbolia. Patients with this condition do not register pain when they are deliberately jabbed in the finger with a sharp needle. They report that they can feel the pain, but that it doesn't hurt. Many start giggling, as if they were being tickled and not stabbed.

This syndrome is often seen when there is damage to the insular cortex – buried in the fold between the parietal and temporal lobes (and closely linked to the hypothalamus, mammilary bodies and the cingulate gyrus). This structure receives sensory input,

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[498] Ibid.
[499] Steven Johnson, *Mind Wide Open.*
[500] Pradhan S, Kalita J, *Tickling Seizures.* 1999
[501] Steven Johnson, *Mind Wide Open.*

including pain from the skin and internal organs, and sends its output to the cingulate gyrus so that you begin to experience the strong averse reaction – the agony – of pain.

Let's assume, as Ramachandran does, that we can disconnect the insular cortex from the cingulate gyrus. If that were to happen, Ramachandran theorizes, one part of the brain would signal, "there is something painful", while another part would signal a moment later, "Don't worry this is no threat at all." Thus the two ingredients – threat followed by deflation – would be present, and the patient would resolve the paradox by laughing.[502]

Sufferers of amyotrophic lateral sclerosis – Lou Gehrig's disease – which targets the brain stem, often experience spontaneous burst of uncontrollable laughter without feeling happiness or mirth. They also undergo a similar experience with bouts of crying.[503]

The laughter circuit might be explored for further therapeutic uses in phobias and panic attacks as a mechanism to disengage these loops when they are locked. Laughter could be used as a natural process to switch from a perceived threat to a false alarm, thus turning off the fear reaction.

Norman Cousin, in his *Anatomy of an Illness,* recounts that he had been diagnosed with a life-threatening illness, which led him to question the whole foundation of Western medicine. He rejected what little help was offered by his doctors, he checked out of the hospital and checked into a hotel, where he holed up with an assortment of Charlie Chaplin videos and literally laughed himself to health. He had felt, intuitively, that what the body needed was a life-affirming, joyous experience of laughter. He postulated that laughter had triggered a release of endorphins, which, by elevating his mood, had somehow brought about a total remission.[504]

Blushing

The face and neck have more veins near the surface and can carry more blood than veins of similar size in other areas of the body. When certain conditions are met, some blood vessels dilate, whereas others contract; for example, the hands turn white and clammy while the face turns red with blushing. What is this phenomenon of blushing? An emotion? The expression of an emotion?

Darwin argued that it is not shame, but the prospect of exposure, of humiliation that causes blushing. Then again, we blush when we are praised, and only blush when there is direct eye contact. More disturbing is the fact that it can cause secondary effects: self-embarrassment, intense self-consciousness, confusion, and a loss of focus. But the secondary effects can also cause blushing.

Some people theorize that we blush to show embarrassment, just like smiling shows happiness. This would explain why only the visible regions of the body react and redden. Everyone blushes despite skin color and in spite of the fact that blushing is nearly invisible in some people. Embarrassment is generally detected before blushing. It takes about fifteen seconds for blushing to reach its peak, but most people recognize that someone is embarrassed in less than five seconds from other signs, like an immediate

[502] Ibid.
[503] Steven Johnson, *Mind Wide Open.*
[504] Candace Pert, *Molecules of Emotion.*

shift in gaze or a sheepish, self-conscious grin that follows about a half second later. The effect of intensifying embarrassment may be what blushing is for. Embarrassment provides a notice to others that one has crossed certain boundaries and also serves to signal an apology of some sort.[505]

If blushing serves to heighten sensitivity in others, this may be to one's ultimate advantage. It keeps us in good standing. If embarrassment causes blushing, and blushing causes embarrassment, what makes the cycle stop? A number of people experience severe, frequent and uncontrollable blushing. It is often called severe or pathological blushing. Most people blush less with age, but chronic blushers report an increase as they age.

Some doctors have prescribed anxyolitics, like Valium, on the assumption that the real problem is anxiety. Others have tried to prescribe beta-blockers, which blunt the body's stress response; others Prozac or some other antidepressant. The one therapy that has been shown to have modest success is a behavioral technique known as paradoxical intention in which patients actively try to blush instead of trying not to.

A surgical procedure called an endoscopic thoracic sympathectomy involves severing fibers of a person's sympathetic nervous system, part of the autonomic nervous system, which controls breathing, heart rate, digestion, sweating, and, among other things, blushing. The operation is performed primarily to control hyperhidrosis (uncontrolled hand and facial sweating) patients. It was noticed, however, that it also stopped blushing.

There are some side effects in about 15 % of patients ranging from Horner's syndrome, in which unintended damage to nerves feeding the eye results in a constricted pupil, a drooping eyelid, and a sunken eye ball, to less serious conditions where patients no longer sweat from the nipples upward but most, experience a substantial increase in lower-body sweating as compensation.

A few patients report gustatory sweating, sweating caused by certain tastes or smells. Most patients suffer a ten percent reduction of their heart rate as some sympathetic branches that go to the heart are removed. Because of all these reasons, surgery should be a last resort.

Patients that have undergone a thoracic sympathectomy report a phantom feeling occasionally, almost randomly, of blushing even when they aren't. The knowledge that they can't blush helps them deal more effectively with situations that previously triggered blushing, instead of worrying whether they are going to blush. They also can look at people longer, and sometimes report that they have to train themselves not to stare. They partially lose the ability to disengage automatically and self-regulate their affective state.

It is almost as if people suffering from pathological blushing were wearing a red mask, and the endoscopic thoracic sympathectomy removed the mask. This red mask prevents people from being who they really mean to be. Once the mask was removed, they seem bolder, more confident. The original personality, however, is still there and some patients that have undergone this surgical procedure now become embarrassed that they don't get embarrassed! They feel, strangely, that they are fakes.

Slowly, over time, they adapt to their new condition and reach a happy medium: free from the intense self-consciousness that blushing provoked, and the acceptance that

[505] Atil Gawande, *Complications*.

the feeling of blushing never entirely disappears.[506] In time, they learn new methods of self-regulation.

It is very important to emphasize that even though we are speaking of circuits for particular emotions, the sum of the activity of the brain is always greater than the sum of the activity of all circuits. The individual should only be seen as a totality, and cannot be broken into parts, or considered one emotion at a time.

Happiness

Martin Seligman's research focused on optimism has shown this trait to be associated with good physical health, less depression and mental illness, longer life and happiness. Happiness, of course, is a changing state. Some factors that seem to be associated with happiness are spirituality and/or religious faith. It is hard to separate the God part from the community aspect of religion, but friends are a resounding part of happiness.

Edward Diener and Seligman in a 2002 study conducted at the University of Illinois found that the most salient characteristics shared by the 10% of students with the highest levels of happiness and the fewest signs of depression were their strong ties to friends and family and commitment to spending time with them.

Happiness is not a static state. The cheeriest 10% felt blue at times, and even the most depressed have some moments of joy. David Lykken of the University of Minnesota studied the role of genes in determining one's sense of satisfaction in life. He gathered information on twins born between 1935 and 1995. After comparing happiness data on identical vs. fraternal twins, he came to the conclusion that about 50% of one's satisfaction with life comes from genetic programming. Lykken found that circumstantial factors like income, marital status, religion and education contribute only about 8% to one's overall sense of well-being.[507]

This seems to indicate that there is a genetic influence on whether the isorropic attractor is set at neutral calm, or drifts more into the positive or negative emotional side of individuals. Some people's isorropic attractor, in chaos theory terminology, seems to drift more time into the positive emotional side instead of wandering around neutral calm. This would naturally activate more positive, or optimistic ideas. In the case of the reverse, more gloomy, or pessimistic ideas would be activated. There could be a genetic tendency to pessimism, optimism, happiness and depression.

This doesn't mean that our levels of happiness are set. According to Seligman, working on three components of happiness – getting more pleasure out of life, becoming more engaged in what you do and finding ways of making life more meaningful – will increase its levels. Seligman adds, "This is not to say that you can turn a curmudgeon into a giggly person."

At the University of California at Riverside, psychologist Sonja Lyubomirsky is studying different happiness boosters. One is a gratitude diary. She found that doing five kind acts a week, especially in a single day, gives a measurable boost of happiness. At the University of California at Davis, psychologist Robert Emons found that gratitude

[506] Ibid.
[507] Claudia Wallis, *The New Science of Happiness*, Time, January 17, 2005.

exercises could do more than lift one's mood; they improve physical health and raise energy levels. Other happiness boosters are performing acts of altruism or kindness.

Seligman has tested other factors at Penn. The most effective booster, he found is to make a gratitude visit – writing a testimonial thanking anyone to whom you owe a debt of gratitude, and then visiting them to read the letter of appreciation. The effects of this can be measured up to a month later but it's gone by three months. Less powerful but more lasting is an exercise he calls three blessings –taking time each day to write down a trio of things that went well and why. Seligman hates to admit that, "the cerebral virtues – curiosity, love of learning—are less strongly tied to happiness than interpersonal virtues like kindness, gratitude and a capacity for love."

Happiness seems to be a social grace. "Almost every person feels happier when they're with other people," observes Mihaly Csikzentmihalyi (pronounced cheeks sent me high).[508]

15
Other Feelings, Not So Good

Anxiety

Anxiety is a generalized feeling indicative that something is not right and that perhaps a threat is imminent. Fear is a response to a specific threat, while anxiety is a response to potential threats.

The hippocampus is intimately involved in learning and memory and spatial tasks. From an evolutionary point of view, the hippocampus can be viewed as a brain structure specialized in remembering advantageous places. For this purpose it creates a spatial context, using cues from the various sensory memory systems, such as vision, olfaction, tactile and proprioreceptive senses. Once a particular context is established, the hippocampus sends a signal to the nucleus accumbens, which is perceived as a need to seek a space. The urgency to find or get to this place depends on the intensity of the signal. The type of place needed depends on the context and the emotion(s) present. If fear is present, a threat is imminent, and the place sought is one that offers protection. The presence of a sexual mate will trigger a different urge and the place needed will be conducive to sex. When hunger or thirst is detected, the hippocampus' signals will activate a need to find spots conducive to finding food and water. The context will determine the urge to seek a particular type of place

Needless to say, in Homo sapiens, the contexts and range of emotions becomes much greater, and thus the needs or urges that can be generated are much more varied.

The nucleus accumbens is composed mostly (95%) of medium spiny GABAergic projection neurons and the rest cholinergic interneurons. The nucleus accumbens receives projections from the hippocampus, the basolateral nucleus of the amygdala and dopaminergic projections from the ventral tegmental areas. Membrane potential transitions in nucleus accumbens neurons are correlated with electrical activity in the ventral hippocampus, suggesting that hippocampal neural activity can determine ensembles of active accumbens neurons. The electrical activity of nucleus accumbens'

[508] Ibid.

neurons and dorsal striatal medium spiny neurons is characterized by periodical shifts from a very negative resting membrane potential (DOWN state) to a more depolarized (UP) state, which depends on excitatory synaptic inputs. Because activation of inputs from the prefrontal cortex (PFC) can evoke action potentials in nucleus accumbens medium spiny neurons only during the UP membrane potential state, it has been hypothesized that hippocampal afferents gate PFC-nucleus accumbens information flow by setting accumbens neurons into this depolarized state. Such a gating mechanism may define the ensemble of neurons appropriate to be active in a given context.[509] The output of the nucleus accumbens is mostly GABAergic to the globus pallidus external and globus pallidus internal, with enkephalin and substance P, respectively. The output of both the globus pallidus internal and external is also GABAergic. It follows that two serial GABAergic outputs produce an excitatory effect, ultimately reaching the thalamus.[510] The echoes streaming from the cortex into the thalamus will aid in determining where in the cortex the thalamus will mirror these excitatory signals (glutamate and aspartate). The areas in the cortex where these signals were relayed will determine how this need is perceived, and consequently will define the type of need. Different areas will interpret specific needs.

Dense distribution of GABA receptors has been found in the frontal cortex, hippocampus and the amygdala. Benzodiazepines are commonly used anxiolytic medications, which functionally are coupled to the GABA receptors. Binding of the benzodiazepines to its receptors increases the GABA receptors affinity for available GABA, therefore the net effect of benzodiazepines administration is overall inhibitory neurotransmission, with concomitant reduction in anxiety.[511]

Pre-clinical evidence demonstrates that GABA is one of the important neurochemical systems involved in anxiety.[512]

However, the reduction of anxiety must be achieved in the double-serial GABAergic output from the striatum to the globus pallidus external and the GABAergic afferent to the subthalamic nucleus. This double GABAergic relay has a net excitatory effect and the output of the subthalamic nucleus (glutamate) increases to the substantia nigra pars reticulata and the globus pallidus internal, thus increasing the GABAergic output of these last two structures to the thalamus. The net result, because of increased GABAergic activity, is the thalamus decreases its output to the cortex. An increase of GABAergic activity also affects other circuits. Looking at the isorropic circuit and its GABAergic connections, when activity in the brain picks up, the GABAergic interneurons of the this circuit slow it down; when activity in the brain slows down, the activity of GABAergic interneurons slows down, and brain activity increases.

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[509] Yukioro Goto and Patricio O'Donnell, S*ynchronous Activity in the Hippocampus and the Nucleus Accumbens In Vivo.* The Journal of Neuroscience, 2001, 21:RC131:1-5

[510] John H. Martin, *Neuroanatomy.*

[511] Heimberg, R.G., Turk, C.L. and Menin, D.S., Editors, *Generalized Anxiety Disorder, Advances in Research and Practice.* 2004.

[512] Goodard, A.W. & Charney, D.S., *Toward an integrated neurobiology of panic disorder*. Journal of Clinical Psychiatry, 58(Suppl.), 4-11. 1997.

However, the increase or decrease of brain activity modulated by the habenula is not a linear function because GABAergic interneurons also slow down or speed up cholinergic activity inversely. Simultaneously, the cholinergic activity increases or decreases the inhibitory action of GABAergic projection neurons, but because the cholinergic excitation is through slow muscarinic receptors, a time lag exists.

We also need to keep in mind the dopamine containing neurons of the substantia nigra pars compacta and ventral tegmental area, and their connections to the to the nucleus accumbens, the striatum and frontal cortex. This is an activation-excitatory circuit. An increase of GABAergic activity slows down the dopaminergic excitation.

Noradrenaline, the primary neurotransmitter in the sympathetic nervous system becomes more active during periods of stress and anxiety. The locus ceruleus has the most widespread noradrenergic projections to the thalamus, the cortex, the amygdala and the hippocampal formation.[513] Several studies have shown that noradrenaline is abnormally increased in anxiety disorders, particularly panic disorder. Unfortunately, studies of noradrenaline function have been inconclusive.

Serotonin (5HT) is currently recognized as important in the pathology of diverse anxiety states. This has been due to the efficacy of several serotonergic agents (i.e., buspirone, paroxetine) across the entire disorder spectrum. Serotonergic pathways arise from the raphe nuclei and project to diverse areas of the brain that are involved in the regulation of anxiety, including the amygdala and the septo-hippocampal areas. Lesions along this substrate or agonists such as buspirone result in anxiolytic effects. Though low levels of 5-HT have been linked to anxiety, aggression and impulsivity, studies linking this to generalized anxiety disorder have had mixed results.

The neuropeptide cholecystokinin (CCK) has been implicated in the etiology of both normal and pathological anxiety. Two CCK receptors have been identified, a CCK-a and a CCK-b; CCK-b receptors are densest in brain regions that mediate anxiety.[514]

Decreased GABAergic stimulation of the thalamus as a result of anxiety decreases the threshold for attentional shifting. This lowered threshold allows attention to shift to new stimuli easier. Under this condition, I speculate, the hippocampus--controlling context--must be biasing the attentional systems to favor the processing of threat related stimuli. Memories with fear as a related emotion would be favored. These biases are most evident on tasks that asses selective encoding and interpretation, and have also been observed in implicit memory tasks.[515]

The amygdala has important afferent and efferent connections to specific brain areas that help regulate the physiological manifestations of anxiety.

Generalized Anxiety Disorder

[513] John Martin, *Neuroanatomy.*
[514] Heimberg, R.G., Turk, C.L. and Menin, D.S., Editors, *Generalized Anxiety Disorder, Advances in Research and Practice.* 2004.
[515] Ibid. Page 131.

Generalized Anxiety Disorder (GAD) is characterized by excessive anxiety or worry for a prolonged period of time or the worry is uncontrollable. In addition, the anxiety or worry needs to present at least three more symptoms from a list that includes restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension and disturbed sleep. Associated with muscle tension, there may be trembling, twitching, feeling shaky and muscle soreness. It is also common to experience somatic symptoms such as sweating, nausea or diarrhea and an exaggerated startle response.[516]

Patients with GAD demonstrate higher levels of restlessness, insomnia, irritability, nausea and headaches than patients with Panic Disorder.[517] Some authors conclude (Noyes, 1992) that GAD is characterized by central nervous system hyperarousal, whereas panic disorder is characterized by autonomic arousal.

It has been argued that worry should be viewed as the cognitive component of anxiety. But whether worry is a cognitive component or not is only important if one is trying to elucidate its functional relationship with other variables, because worry and anxiety share the same behavioral concomitants. In this presentation, when referring to an emotion, I shall use anxiety and worry will be used as a description for a verbal thought. Worry, is part of other conditions; particularly as rumination it is related to the onset of depression and severity of depression.[518]

It has been observed that fear, as a response to a stressor is a sufficient, but not a necessary, condition for worry or anxiety. Conversely, anxiety can be present in the complete absence of fear. It is noteworthy that the DSM-IV-TR (as opposed to de DSM-III) does not use the word worry in relation to GAD. Also, some call into question the mood disorder criterion in which one may not diagnose GAD. Since a mood disorder is obviously an indication that something is very wrong, and anxiety is a normal response to potential threats, anxiety must be a healthy response to a mood disorder. If anxiety is not part of the diagnosis of a mood disorder, this should be interpreted as a worse case.

There is a genetic contribution to the variance in anxiety symptomatology and disorders. Kendler and colleagues showed that GAD and major depression were largely influenced by the same genetic factor. The study also showed that a shared genetic risk for panic disorder, phobia and bulimia nervosa. This seems to indicate there may be two separate genetic pathways to these disorders: one for GAD and depression, and another for panic and phobia.[519]

The overall evidence seems to point to a predisposition more than hereditability. Evidence from family studies of anxiety suggests that the environment, more than genetics, is primarily responsible for the development of anxiety disorders, even though there is an increased risk for GAD in individuals that have first degree relatives with

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[516] *Diagnostic and Statistical Manual of Mental Disorders. DSM-IV-TR.*

[517] Nisita, C., Petracca, A., Akiskal, H.S., Galli, L., Gepponi, I. & Cassano, G.B., *Delimitation of generalized anxiety disorder: Clinical comparisons with panic and major depressive disorders.* Comprehensive Psychiatry, 31, 409-415. 1990.

[518] Nolen-Hoeksema, S., *Responses to depression and their effects on the duration of depressive episodes.* Journal of Abnormal Psychology, 100, 569-582. 1991.

[519]Kendler, K.S., Walters, E.E., Neade, M.C., Kessler, R.C., Heath, A.C., & Eaves, L.J. *The structure of genetic and environmental risk factors for six major psychiatric disorders in women: Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism.* Archives of General Psychiatry, 52, 374-383. 1995.

GAD. Results from twin studies indicate a stronger relation to environmental factors compared to factors shared by siblings.[520]

OCD

Most of the points regarding Obsessive Compulsive Disorder (OCD) in the next paragraphs are from Dr. Jeffrey Schwartz's excellent book *The Mind and the Brain.* This is a good example of how a circuit locks into a certain behavior and how therapy can change this condition.

Dr. Schwartz refers to neuroplasticity as the ability of neurons to forge new connections, to blaze new paths through the cortex, and even to assume new roles. This is an area that should be pursued vigorously to find new therapies to treat various mental disorders and damage to certain regions of the cortex.

One of the most striking aspects of OCD urges is that, except in the most severe cases, they are ego-dystonic: they seem apart from, and at odds with, one's intrinsic sense of self. They seem to arise from a part of the mind that is not you, as if an impostor were inside your mind.

OCD can manifest itself as obsessions about order or symmetry. It can be expressed in an irresistible need to line up the silverware or hoarding. Paradoxically, giving in to the urge to wash or check or count or sort, which is done in the vain hope of making the dreadful feeling recede, backfires. An OCD compulsion does not dissipate like a scratched itch. Instead, giving in to the urge exacerbates the sense that something is wrong.

OCD patients dread the arrival of the obsessive thought and are ashamed and embarrassed by the compulsive behavior. They carry out behaviors they are desperate to escape, either because they hope that doing so will prevent some imagined horror or because resisting the impulse leaves the mind unbearably ridden with anxiety and tortured by insistent, intrusive urges. Since the obsessions can't be silenced, the compulsions can't be resisted. The sufferer feels like a marionette at the end of a string, manipulated and jerked around by cruel puppeteers – their own brains.

From PET scans it has been determined that OCD sufferers show hypermetabolic activity in the orbital frontal cortex, which is tucked into the underside of the front of the brain above and behind the eyes.

Rhesus monkeys were trained to get a little sip of black currant juice by licking a tube every time they saw blue. E.T. Rolls at Oxford University in the 1970's and 1980's, implanted electrodes in the brains of these very alert animals. As soon as blue was shown to them their orbital front cortex became active. However, when Rolls switched signals (green for juice and blue for salt water) and the monkeys got brine instead of juice when they saw blue and licked the tube, cells in their orbital frontal cortex fired more intensely and in longer bursts. Yet these cells did not respond when the monkeys sipped salt water outside the test situation. This group of cells fired only when the color previously associated with juice became associated with something non-rewarding. Apparently the

[520] Heimberg, R.G., Turk, C.L. and Menin, D.S., Editors, *Generalized Anxiety Disorder, Advances in Research and Practice.* 2004.

orbital cortex functions as an error detector, alerting you when something is amiss. Expectations and emotions join together here to produce a neurological spell-check. Once the monkeys learned to associate green with juice, the orbital frontal cells quieted down, firing like they did before when blue was associated with juice.

Intense and persistent firing in the orbital frontal cortex causes an intense visceral sensation that something is wrong. Action of some kind – such as counting or checking if appliances are on – is needed to make things right. The reason for the visceral sense of dread that OCD patients suffer is that the orbital frontal cortex and the anterior cingulate gyrus are wired directly into the gut control centers of the brain.[521]

After signals from the sensory areas have been processed and are considered by the orbital frontal cortex, through certain handshakes, to be warnings about potential threats, signals will be sent to the thalamus and hypothalamus to initiate the sequence to release stress hormones, which are felt as anxiety. Among the differences between anxiety and fear, one is that fear is triggered before the signal is processed by the sensory areas in the cortex; the thalamus matches a danger signal with an echo and automatically triggers the flight-fight response. In contrast, anxiety is triggered after the signals are processed in the sensory cortex. The cortex sends out handshakes to the frontal lobes and alerts other areas that something is amiss. Anxiety deals with potential threats; fear with immediate danger.

As we have mentioned, the presence of dopamine on the nucleus accumbens from the ventral tegmental area reinforce urges by sending dopaminic signals to the prefrontal cortex (via de thalamic MD). The hippocampus' projections to the nucleus accumbens reinforces urges or needs, whereas the amygdala's projections (because of their emotional component) create or reinforce beliefs that guide responses. Within the context of particular situations, the hippocampus' signals are perceived as an overwhelming urge to control certain aspects of the environment. Along with the anxious feelings, the amygdala's signals to the nucleus accumbens will be interpreted as a belief, which reinforces the urge.

An experiment was set arranging decks of cards where the winnings and losses are big with big net losses in one case, and small winnings and losses but with net big winnings in another case. The two decks of cards were placed before volunteer subjects and by measuring skin conductance responses (like a lie detector machine), normal volunteers begin to generate anticipatory responses when they are about to select from the "losing" deck. Even when volunteers couldn't verbalize why they avoided the losing deck, they consistently did so. Patients with damage to the inferior prefrontal cortex didn't generate skin conductance responses and they were attracted to the high-risk deck. These actions suggest intuition or gut feeling is a more dependable guide and more potent than reason! Half the subjects with damage to the inferior prefrontal cortex (which includes the orbital frontal cortex) eventually found out why, in the long run, the first deck led to losses and the second to net winnings. Even so they would continue choosing to play the bad deck.

Patients with damage to the inferior (underside) prefrontal cortex are unable to access intuition. This is particularly important because it mirrors the situation in OCD patients, who have the opposite malfunction of the very same brain area. OCD patients, who have an overactive inferior prefrontal cortex, get an excessive, intrusive feeling that

[521] Jeffrey Schwartz, *The Mind and the Brain*.

something is wrong, even when they know nothing is. The patients in the gambling study showed the damaged area was underactive; therefore, they failed to sense that something was not right even when they knew, rationally, that something was wrong.

Another overactive region in OCD patients is the striatum. The striatum is composed of two major information receiving structures: the caudate nucleus and the putamen, which nestle beside each other deep in the core of the brain just in front of the ears. The putamen acts as a major relay and switching station for motor activity; the caudate nucleus, for linking thought and emotion.

Striosomes are small clusters of neurons where information from an emotion processing part of the brain, the amygdala (primary emotions) and the prefrontal cortex and anterior cingulate cortex (secondary emotions), reaches the caudate. Matrisomes are clumps of axon terminals where information from the thinking, reasoning, prefrontal cortex regions associated with planning and executing complex behaviors reaches the caudate. The matrisomes are typically found near striosomes.

Tonically active neurons (TANs) tend to be found between striosomes and matrisomes in the caudate. By virtue of their position, TANs can integrate emotion and thought. TANs are the neurons responsible for activating related thoughts to specific emotions and vice versa. Different gating patterns or switching patterns in the striatum thus play a critical role in establishing patterns of motor as well as cognitive and emotional responses to the environment. It seems that distinct environmental cues, associated with different emotional meanings, elicit different behavioral and cognitive responses as TANs shift the output flow in the striatum.[522]

When a particular emotion is detected, the TANs fire in specific patterns activating matching echoes; when found, they close the connection and activate the relevant thoughts by sending out handshakes. Conversely, when certain thoughts or memories are active, they intrude by sending stronger echoes to the striatum and in turn make the TAN neurons lock and send the appropriate signals to initiate an emotional response. According to echoes from the cortex and feedback signals from the dopaminergic neurons of the substantia nigra pars compacta and the ventral tegmental areas, TANs fire in a characteristic pattern when they detect something with a positive or negative emotional meaning. The echoes themselves have certain characteristics whether those past experiences were felt to be positive or negative, and whether the outcome of a certain response was deemed beneficial or not.

The striatum has two output pathways: one direct and one indirect. The indirect pathway runs from the striatum to globus pallidus external, to the subthalamic nucleus, back to the globus pallidus internal, and finally to the thalamus, and then to the cortex. The indirect pathway is inhibitory of movement. The direct pathway runs from the striatum through the globus pallidus internal, then to the thalamus and back to the cortex. The crucial difference is that the direct pathway provides excitatory inputs to the thalamus, and the indirect pathway provides inhibitory input. The excitatory pathway is cholinergic; the inhibitory pathway is dopaminergic (D2).

The striatum receives input from the entire cortex, with the caudate receiving specifically strong input from the prefrontal areas. Prefrontal inputs include those from the orbital frontal cortex and anterior cingulate error-detection circuitry, now often called the “OCD loop”. When this loop is working properly, the result is a finely tuned

[522] Ibid.

mechanism that can precisely modulate the orbital frontal cortex and anterior cingulate by adjusting the degree to which the thalamus drives these areas. When the modulation is faulty, the error detector circuit can be over-activated and thus locked into a pattern of repetitive firing. This triggers an overpowering feeling that something is wrong (anxiety), accompanied by compulsive attempts to somehow make it right.

As a result the direct pathway seems to be stuck in the "on" position. This is what Jeffrey Schwartz calls Brain Lock: the brain can't move to the next thought and its related behavior. The thalamus continuously receives a "something is wrong" signal and, as a consequence, triggers anxiety.

Located behind and above the orbital cortex, the anterior cingulate gyrus also has connections to the vital brain centers that control the gut and heart. The anterior cingulate gyrus seems to amplify the gut-level feeling of anxiety.

With this, a picture of the brain abnormalities underlying OCD emerges. The malfunctions center on the circuitry within the orbital frontal cortex (the "error alarm" circuit) and the basal ganglia, which acts as a switching station. In OCD this error circuit is inappropriately and chronically activated, probably because a malfunction in the gating function of the TANs in the caudate nucleus allows the prefrontal cortex to be stimulated continuously. The result is a persistent feeling (which engenders thoughts) that something is wrong or excessively risky.

TANs could be crucial in the acquisition of new behavioral skills in cognitive-behavioral therapy (or any therapy). This is a crucial point. Such therapies teach people purposefully to alter the response contingencies of their own TANs. In the case of OCD, therapy teaches patients to reinterpret their environment and apply their will to alter what had been an automatic behavioral response to disturbing feelings.[523]

Any successful therapy for OCD would need to enhance the gating function of the caudate so that the worry circuit can quiet down and allow a patient to resist OCD urges. The first step is to become aware that the urge is a manifestation of a mental disorder by directing attention to the urge and becoming convinced that how one responds to the urge can change the brain's circuitry. This process is called Relabeling. When done regularly, Relabeling stops the unpleasant feelings of OCD from being unpleasant; understanding their true nature gives a feeling of control. By Relabeling their thoughts as manifestations of a medical disorder, patients willfully make a cognitive shift away from self-identification with the experience into the stream of consciousness.

The second step is to make the patients conscious that there is a neuroanatomical basis of their symptoms, an overactive region in their brains that is causing the OCD. This is called Reattributing. Having Relabeled an intrusive thought or insistent urge as a symptom of OCD, the patient then attributes it to aberrant messages generated by a brain disease and thus fortifies the awareness that it is not his true self.

Relabeling clarifies what is happening and Reattributing affirms why it's happening. The accentuation of Relabeling and Reattributing tends to amplify attention and allows the patient to separate himself from the intrusive experience determined entirely by pathological forces. The essence of attention during a bout of OCD is to recognize obsessive thoughts as soon as they arise and Refocus attention onto some adaptive behavior. Directed focusing of attention becomes the key action during treatment. The goal of this step is not to obliterate or banish the thought, but rather to

[523] Ibid.

initiate an adaptive behavior unrelated to the disturbing feeling even when the feeling is very much present.

Refocusing requires significant willpower. Even when the patient has Relabeled and Reattributed the obsession and compulsions, the anxiety and dread can still feel frighteningly real. Refocusing, therefore, has to center on a pleasant, familiar "good habit" kind of behavior. In essence the patient must substitute a "good" circuit for a "bad" one. In other words, he must change the firing pattern of the TANs and slowly change a negative situation for a positive one. Through repetition other competing positive echoes will dampen the effect of the locked negative echoes. The diversion can be anything, but a physical activity is especially effective, like dribbling and shooting baskets or gardening. The most difficult part of treatment, Refocusing attention away from the intrusive thought rather than waiting passively for the feeling to go away, requires will and courage.

Setting a finite length of time, say fifteen minutes, to resist giving in to an urge helps patients. The fifteen minutes should not be a passive waiting period; it must be an adaptive activity intended to activate a new brain loop. Refocusing alleviates the overwhelming sense of being "stuck in gear". This is where Relabeling and Reattributing come in handy: they both help the patient keep a clear mind about who he or she is and what the disease process is. This mental clarity has tremendous therapeutic value, for it keeps the Refocusing process moving forward. It also reinforces the insight that active will is separable from passive brain processes. Attention is extremely important to help encode the newer, positive experiences and slowly overwhelm the negative ones.

In OCD sufferers, the orbital frontal cortex, the caudate nucleus, and the thalamus operate in lockstep. By actively changing behaviors, Refocusing changes which brain circuits are activated and thus also changes the gating in the striatum. As noted earlier, the striatum has two output pathways: direct and indirect. The direct pathway tends to activate the thalamus, increasing cortical activity. The indirect pathway inhibits cortical activity. Refocusing changes the balance of gating in the striatum so that the indirect, inhibitory pathway becomes more used, and the direct, excitatory pathway used less. The result is to damp down the activity in this OCD loop.

The connections of the basal ganglia are remarkably specific. Anatomical loops have been identified from separate cortical regions, through different parts of the basal ganglia and thalamic nuclei, to distinct areas of the frontal lobe. Each loop is thought to mediate a different set of functions. Primarily, four loops have been identified: the skeletomotor, oculomotor, prefrontal cortex and limbic loops. Three important points relate to the general organization of these neural circuits: 1) each of the loops originates from multiple cortical regions that have similar general functions; 2) each loop passes through different basal ganglia and thalamic nuclei or separate portions of the same nucleus; 3) the cortical targets of the loops are separate portions of the frontal lobe.[524]

The next step in therapy is to exploit the brain's tendency to pick up on repetitive behaviors and make them automatic – to form new habits. Ideally, patients would change their focus from "I have to wash again" to "I'm going to the garden". If done regularly, the urge to wash will produce a habitual association: the impulse to go work in the garden.

[524] John H. Martin, *Neuroanatomy.*

The last step is Revaluing. Revaluing is a deep form of Relabeling. Relabeling is a superficial encoding which leads to no diminution or improved ability to cope. Revaluing means quickly recognizing the disturbing thoughts as senseless, as false, as errant brain signals, a pathological manifestation not worth acting on.

Done regularly, Refocusing strengthens a new automatic loop and weakens the old, pathological one – training the brain, in effect, to replace old bad habits programmed into the caudate nucleus and basal ganglia with healthy new ones. When the focus of attention shifts, so do patterns of brain activity. Neurologically, the new activity excites the dorsal prefrontal cortex that connects to adaptive basal ganglia circuits instead of the orbital frontal cortex circuit that connects to the caudate and the anterior cingulate. With regular use of the frontal cortex, changes occur in the gating function of the caudate, and mental function improves. Relabeling and Refocusing attention begin to be automatic. In this way frontal cortex thought processes begin to be wired directly to the caudate.

PET scans on OCD patients during and after a ten-week treatment period showed significantly diminished metabolic activity in both the right and left caudate, with the right-side decrease particularly striking. There was also a significant decrease in the abnormally high and pathological correlations among activities in the caudate, the orbital frontal cortex and the thalamus in the right hemisphere. This was the first study ever to show that cognitive-behavior therapy – or, indeed, any psychiatric treatment that did not rely on drugs – has the power to change brain chemistry in a well-identified brain circuit.[525]

Dr. Schwartz's studies suggest that we can develop successful therapies for other mental disorders. The lesson is clear: we can change our brains; we can change how we think. More importantly, we can change how we feel!

Smoking

Nicotine addiction is very similar to OCD in that, as soon as an emotion is felt, whether positive or negative, anxiety accompanies it, and the desire to smoke becomes overwhelming. Smoking, then, eliminates the anxious feeling.

After smoking for forty years, I quit smoking in May 2002. The method that I used is extremely similar to the therapy just described for OCD. The program consisted of four consecutive sessions lasting between two and three hours each day.

At the first session, the doctor quickly went over the dangers of smoking. "You're lucky if you get cancer, so I'm not going to discuss that. I say lucky, because you die quickly. And then, there is always a chance that you won't get cancer." He continued with other possible effects of smoking.

"When tobacco is stored to dry, rats can run over the leaves and piss on them. Rats are carriers of Ebola virus, so contracting Ebola virus is a possibility. Then again, perhaps you will never get Ebola from smoking." And so it went until he said, "What I want to make sure you know is not *if* but *when* you will get emphysema. We might not be able to ascertain when, but you will get it for sure if you continue smoking." He then explained in detail the slow and gruesome death that ensues from emphysema: the

[525]Jeffrey Schwartz, *The Mind and the Brain.*

coughing, choking, inevitable intravenous feeding. And lastly, since visiting someone in such a state is so unpleasant, it is almost a certainty you will die alone.

That was the bad news.

The good news -- by quitting now, our lungs would not deteriorate further.

He then explained that there is no physiological dependence on nicotine. "No one has ever reported a person dying from quitting smoking," he interjected for dramatic effect. "There is a psychological-emotional dependence. Smoking is always associated with an emotion. We smoke more when we feel good. We smoke more when we feel bad. We smoke more at a party when we are with friends and family and we smoke more when we are nervous or under pressure. We feel that our negative feelings are less negative, and our positive feelings are more positive. The reality is that when we smoke, we create a bad habit. What this program is going to do is help you substitute other habits for the bad habit of smoking, habits that are not dangerous to your health. Habits that you will eventually be able to abandon completely, because you will realize how stupid and irrational these habits really are. For reasons that are unknown, creating new habits or abandoning old habits is a process that takes twenty days.

“We are going to change all your usual habits for twenty days. For example, if you drink coffee in the morning, we are going to substitute it with tea. If you like to have a drink in the afternoon, you will change this drink for a drink you don't like. For example, if you like to have rum and coke and you hate gin, then you will order a gin and tonic.

“If you follow my program religiously, you will have all the tools at your disposal to lick the bad habit of smoking.

“You will now proceed to give me your cigarettes and lighter. I will give you in exchange a small kit. This kit contains the following: a pack of Delicados without filter. Why Delicados? Because it is one of the few cigarettes that is made with rice paper. This paper tastes different. Also the tobacco has fewer chemicals."

He pulled a box of matches from the bag. "If you light up, you will use matches, no lighter. Also in the bag we have a pipe. I want you to put a little bit of cotton in it, and then apply a few drops of this liquid." He held up a small plastic container that looked like eye drops.

He continued, "These drops have a little bit of a taste and aroma, different than cigarettes, but a taste and a smell. We want you to continue to enjoy the sensation of a taste and a smell. There is nothing wrong with that.”

I had already given up my cigarettes to a trashcan, so I gave up my lighter.

“When you leave here, I want you to buy some cinnamon sticks and some all spice,” the doctor continued. "If you are a guy, you will carry your cigarettes and matches in your sock. If you are a woman, you will carry them in your bra. We don't want to change your habit of looking for your cigarettes; after all, once you have them with you, you feel secure. We don't want to alter that good feeling. Also, whenever you become aware of your cigarettes, I want you to remind yourself why you are quitting smoking, and that’s why you're carrying your cigarettes in a different place.

“In the morning, when you wake up and it is time for your coffee, you will have your tea. Then, if you feel like smoking, you will refrain from smoking until fifteen minutes have passed. We don't know why, but fifteen minutes is the least amount of time that we need to enforce to change our behavior.”

This is an adaptive willful behavior, similar to OCD therapy.

“If after fifteen minutes you still feel like smoking, go ahead and light up. The most important thing is to follow the next steps.

“After each meal, you will immediately get up and go brush your teeth. You will not linger at the table. Then you will gargle with a mouthwash for a couple of minutes. Look at yourself in the mirror and inhale deeply and exhale slowly fifteen times. We don't know why fifteen times, but we find that fifteen is again a minimum to change behavior.”

We recognize the bad habit ‘smoking’ and Relabel it.

“The reason we do this is because when you finish eating, your mouth is full of bacteria. If you smoke after the meal, the hot smoke helps the bacteria with its decaying process, which in turn helps break down the small pieces of food in your mouth. This is a pleasurable feeling. We don't want to change a true pleasurable feeling, so we'll sidestep it by brushing our teeth and gargling. We will quickly rid our mouths of the small bits of food.

“When you inhale deeply when you smoke, it pushes your diaphragm down." He showed us by taking a deep breath and expanding his chest. "This is a nice sensation; again we don't want you to forgo this positive sensation you are used to. That is why we inhale and exhale.”

This is equivalent to Reattributing the aberrant behavior ‘smoking’.

He continued, “After all this, then you can go back to the table. This is terribly important: No matter what, for the next fifteen minutes you will not smoke.”

Adaptive behavior, Relabeling and lastly, Reatributting.

“If at the end of these fifteen minutes, you feel like smoking, you will breathe in and out deeply fifteen times, just like after gargling. When you have the urge to smoke again, you will pull out your pipe. You will pull air through it, chew on it, play with it with your hands, suck it, and do anything you want with the pipe for as long as you find it bearable; the longer the better. My experience shows me that the craving subsides in just a few minutes.”

This is the same as Refocusing while replacing the bad habit with a new good one.

“Then, if later you feel an urge to smoke again, you will start chewing on one of your cinnamon sticks. The reason we do this is that you have become habituated to punish your mouth with hot smoke. In this case we will give your mouth a tickle with the cinnamon. Chew on the cinnamon as long as you can. Then when you feel like smoking again, you will chew on your all spice. This is the only thing we are using that will cause a physical, calming effect. It is spicy, but it will give you a nice sensation of cleanliness in your mouth, a freshness of breath. Chew on it as long as you can.”

These last two steps are the equivalent of Revaluing.

“Now, if you still feel like smoking, pull one of your cigarettes out and smoke it. The only thing I am going to ask of you when you follow all this, is that you don't rush through it – don’t rush your breathing, then chew on your pipe for two seconds, then the cinnamon stick for ten seconds, then the all spice for five seconds, and then light up. That is not the idea. After smoking, start all over with the procedure. Deep breathing, followed by the pipe, then the cinnamon and lastly the all spice. If you can't finish all the steps between meals and it is again time to eat, when you finish your meal start with brushing

your teeth, gargling, breathing, your fifteen minutes, then the pipe, then the cinnamon, then the all spice, and then smoke if you still feel like it."

He then answered questions. Many sat there in disbelief that you could smoke while you were trying to quit smoking. He explained, "The first day you will wait for fifteen minutes after your breathing after each meal, but every successive day we will add to that another fifteen minutes. So, the second day you will have to wait 30 minutes; the third day, 45 minutes and the fourth day, one hour. On the fifth day you will not smoke. I guarantee you that. You then complete this for another fifteen days and you will be cured of the bad habit of smoking."

He answered more questions. "After the nineteen days, you might find some of these new habits pleasurable; if so continue one or any of them. I'm referring to the breathing, or the pipe, the cinnamon or the allspice. These new habits are not bad for your health; keep them up for as long as you want. I have had a few people come back and report to me that they started smoking after completing the nineteen days. I only have one response for that: "I have no cure for stupidity. If you smoke when you have no desire, it is only because you are stupid."

The doctor then proceeded to hypnotize us to the accompaniment of music. The hypnosis was to increase and re-enforce our desire to be well. The music provided a calming or soothing effect. He encouraged us to listen to this music if we felt like smoking. He then wished us good luck and sent us off with, "We'll see you tomorrow at the same time."

I proceeded to do all that he had asked. I found I was too busy with all the routines to remember smoking between meals. Many times I found that I didn't even have the time to complete a whole routine (brushing teeth, gargling, breathing, pipe, cinnamon and all spice combination) between meals! It seemed so stupid to be doing all this, and by extension so stupid to smoke. From that first day on I never smoked again.

16
I Can’t Stop and Pay Attention.

The basal ganglia system integrates the extrapersonal space with the intrapersonal map of the body to coordinate movement through the environment. Simultaneously an emotional evaluation of the incoming stimuli is performed. The essential feature of Attention-Deficit/Hyperactivity Disorder is a persistent pattern of inattention and/or hyperactivity-impulsivity that is more frequently displayed and is more severe than is typically observed in individuals at a comparable level of development.[526]

The attention deficit and the hyperactivity tend to point to a malfunction of the circuits that integrate the extrapersonal and internal spaces. Several loops are used to accomplish this with different neurotransmitters. Reviewing these neurological loops, (see page 89) we have: the skeletomotor loop, related to the body; the oculomotor loop,

[526] *Diagnostic and Statistical Manual of Mental Disorders*, DSM-IV-TR.

related to vision; the prefrontal loop, related to evaluating a stimulus; and the limbic loop, which performs an emotional evaluation of a stimulus.

Attention-Deficit/Hyperactivity Disorder

The essential feature of Attention-Deficit/Hyperactivity Disorder is inattention and/or a hyperactivity-impulsivity that is more frequent than "normal".

When the activity of certain loops (the hypokinetic and hyperkinetic loops) is slightly disrupted, the attentional systems are affected. Reviewing a couple of known pathological conditions will enable us to understand better how this is so.

In Parkinson's disease, focusing on the hypokinetic loop, with diminished or lost dopamine from the substantia nigra pars reticulata to the striatum, there is a major impairment in initiating movements (akinesia) and a reduction in the extent and speed of movements (bradykinesia). These are called hypokinetic signs because movements are impoverished. The lack of dopamine disrupts the direct path. The GABAergic output of the striatum to the globus pallidus external increases, thus, because of the inhibitory action, decreases the GABAergic input to the subthalamic nucleus. Consequently, the subthalamic nucleus in turn increases its glutamatergic signaling to the output nuclei, thus increasing inhibitory signals to the thalamus, which in turn reduces its output to the cortex. In common English, this translates to less movement.

In contrast to Parkinson's, Huntington disease is a hyperkinetic disorder. One hyperkinetic sign is chorea, characterized by involuntary rapid and random movements of limbs and trunk. Pathological changes occur earliest in striatal neurons that contain enkephalin, which are part of the indirect path, the hyperkinetic loop. In this case, the inhibitory signals from the striatum to the globus pallidus external are greatly reduced and the reverse action of the hypokinetic loop ensues. The thalamus ends up sending an outburst of excitatory signals to the cortex.[527]

The signaling from the globus pallidus internal and the substantia nigra pars reticulata to the thalamus in the former loop is greatly increased and in the hyperkinetic loop greatly diminished, with the thalamus signaling the cortex in an inverse proportion.

Because of the lack of enkephalins the indirect path from the striatum to the globus pallidus external produces increased GABAergic (inhibitory) activity to the subthalamic nucleus, which in turn reduces glutamate (excitatory) signaling to the output nuclei. This coupled with extra dopaminergic activity from the substantia nigra pars compacta produces increased GABA and substance P signaling to the output nuclei. The diminution of excitatory activity from the subthalamic nucleus, together with increased inhibitory signals from the striatum to the output nuclei, reduces substantially the GABA (inhibitory) signaling to the thalamus. This produces a huge outpouring of excitatory signals to the cortex.

The targets of this increase in excitatory thalamocortical projections from the ventral anterior, ventral lateral and the medial dorsal nuclei can be summarized as follows: motor areas (6, 8 and 4), frontal lobe executive functions (areas 9, 10, 11, 44, 45, 46, and 47), the attentional systems (areas 7 and 40), auditory integration (area 42) and

[527] John H. Martin, *Neuroanatomy.*

the associative somatosensory (area 5). Some of these areas receive input from two of the thalamic nuclei (areas 4, 6, 8, 44 and possibly area 40).[528]

Attention deficit disorder can be accompanied by hyperactivity or not. This leads to expect two slightly different, though very similar, conditions.

The excess signaling from thalamus to cortex produces two notorious behaviors. First, increased purposeless activity as a combination of excess excitation to the motor areas (4, 6 and 8) and the executive and planning frontal lobe areas (9, 10, 11, 46). Second, a greatly increased shifting of attention, which is produced by a combination of factors: a diminution of the threshold for shifting attention by the increased signaling to the auditory integration areas (42) and the associative somatosensory area (5); and more importantly, the increased activity of the attentional systems (areas 7 and 40), which also reduces the threshold for shifting attention, coupled with a disturbance of the frontal lobes' capacity to evaluate what is important, disrupting the capacity to focus attention. In an endless cycle, as the neural activity in the attentional areas of the cortex increases beyond a certain point, the thalamus responds with an automatic shift of attention attempting to bring the neural activity to a more normal level, and again, automatically, as the activity increases in the thalamus, the attentional areas follow, and the thalamus shifts attention.

Normally, the skeletomotor and the oculomotor loop attempt to integrate internal and external space. When a change or an unexpected object intrudes in the environment, attention is focused on the object, thus allowing the limited brain resources to focus and integrate the unexpected into the internal-external space. When the glutamate signaling from the subthalamic nucleus to the substantia nigra pars reticulata and the globus pallidus internal decreases because of increased GABA signaling from the globus pallidus external to the subthalamic nucleus (which is a result of decreased GABA signaling from the striatum to the globus pallidus external), the GABAergic output of the substantia nigra pars reticulata and the globus pallidus internal to the thalamus decreases. Focusing on the skeletomotor loop, the decrease of GABA to the ventral anterior and ventral lateral nuclei of the thalamus produces excitatory signaling to the primary motor, lateral premotor and the supplementary motor areas. This excitatory signaling is reflected as hyperactivity. Focusing on the oculomotor loop, the decreased GABAergic signaling to the ventral anterior and the medial dorsal nuclei of the thalamus, produce excitatory activity to the frontal eye field and the supplementary eye field. This excitatory activity is reflected as eye movements unrelated to new stimuli, and therefore the lack of attention.

The fact that there exist four GABAergic projections in these loops (from the striatum to the globus pallidus external, from the globus pallidus external to the subthalamic nucleus, from the striatum to the globus pallidus internal and the substantia nigra pars reticulata, and from the globus pallidus internal and the substantia nigra pars reticulata to the thalamus) indicates how difficult it is to affect this activity pharmacologically. However, there are other projections from the striatum to the globus pallidus internal and the substantia nigra pars reticulata and to the globus pallidus external that use Substance P and Enkephalin respectively, which might be more amenable to a pharmacological solution.

Normally, as the internal and external spaces are integrated into one, the expected is compared to the incoming signals. As soon as there is a deviation from the expected,

[528] Ibid.

the attentional systems are activated to correct for this departure. In this way the unexpected is integrated into our internal-external space. In ADHD this beautiful system stops integrating the unexpected and even the expected into our internal/external space.

In a study of children with attention-deficit/hyperactivity disorder using MRI it was found that performance in response inhibition deficits correlated only with specific frontostriatal circuits observed to be abnormal in children with ADHD (e.g., the prefrontal cortex, caudate and globus pallidus, but not the putamen). There was a significant correlation between task performance and measures of activity of the prefrontal cortex and caudate nucleus predominantly in the right hemisphere, supporting a role of right frontostriatal circuitry, which suggests involvement of the right prefrontal cortex in suppressing responses to salient, but otherwise irrelevant events while the basal ganglia appear to be involved in executing behavioral responses.[529]

In essence, the attentional systems are not activated when the basal ganglia fail to detect unexpected or new stimuli, or conversely the attentional systems are focused on irrelevant or "old" stimuli, because the loops of the basal ganglia signal the thalamus incorrectly.

When we encounter attention deficit disorder without hyperactivity, the problem is mostly in the thalamus' ability to detect matches between expected echoes with expected stimuli. The thalamus erroneously detects a mismatch when there is none (shifts attention unnecessarily), or does not detect a mismatch when it exists (does not shift attention when needed). Under normal conditions, when entering familiar spaces, we know what to expect. Our memory systems anticipate (remember) what is going to happen. For example, the characteristics of the door to our house: it's color, where the knob is, how heavy it is when we open it. If anything was changed, our attentional systems would normally be activated, otherwise, all goes unnoticed.

The attentional systems can all be affected (i.e., visual, gustatory, hearing or proprioceptive), or disrupted individually. Because of this, inattention can be manifested across a wide spectrum of activities or sometimes only in certain categories of activities. Work is performed carelessly, and completion of tasks becomes almost impossible. More often there is a shift from one uncompleted activity to another. Occasionally, tasks that require sustained concentration are experienced as unpleasant and aversive. Irrelevant stimuli frequently interrupt ongoing tasks to attend to trivial noises or events.

Hyperactivity can be manifested as simple fidgetiness or squirming or, in more extreme cases, as running or climbing where it is inappropriate, or talking excessively. Impulsivity is less of a problem and can be manifested as impatience, like blurting out answers, inability to wait for one's turn, and frequently interrupting or intruding on others. The combination of hyperactivity and impulsivity can lead to accidents, like grabbing hot pans, running into people and to potentially dangerous activities without consideration of the consequences, like riding a skateboard over extremely rough terrain repeatedly.[530]

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[529] Casey BJ, Castellanos FX, Giedd JN, Marsh WL, Hamburger SD, Schubert AB, Vauss YC, Vaituzis AC, Dickstein DP, Sarfatti SE, Rapoport JL, *Implication of right frontostriatal circuitry in response inhibition and attention-deficit/hyperactivity disorder.* J Am Acad Child Adolesc Psychiatry. 1997 Mar;36(3):374-83

[530] *Diagnostic and Statistical Manual of Mental Disorders*, DSM-IV-TR

Two different mechanisms lead to improper shifting or activation of the attentional systems. First, attention deficit without hyperactivity or impulsivity, is mostly a thalamic inability to detect matches or mismatches correctly of expected echoes with expected stimuli. And, second, attention-deficit with hyperactivity or impulsivity as a result of the excess thalamocortical signaling produced by the reduced GABAergic output of the substantia nigra pars reticulata and the globus pallidus internal to the thalamus.

16
Oh, No! Delirium, Dementia and Amnestic Disorders.

A glimpse into some of the basic glitches that can go wrong in the brain helps to understand delirium, dementia and amnestic disorders. A review of these disorders is helpful to understand better the principles of brain functioning as well as to understand how different disturbances can, when the brain goes haywire, produce responses detrimental to the organism and even death.

The cortex is an extension of the primitive reptilian brain. It essentially allows the mammalian brain to do slightly more complicated things, like emoting and learning. It has been determined that in birds the equivalent of the cortex has evolved inward, inside the primitive reptilian brain, instead of outward as in mammals.

The predominant disturbance in the case of Delirium, Dementia, and Amnestic and Other Cognitive Disorders is a deficit in cognition.[531]

Delirium

The essential feature of Delirium is a reduced clarity of the awareness of the environment. This is manifested in changes in cognition (that might include memory impairment, disorientation, or language disturbance) or development of a perceptual disturbance.[532] This happens when the thalamus' ability to focus, shift and sustain attentions is impaired. This suggests problems to engage one or all attentional subsystems (the visual, hearing and somatosensory). The thalamus's shifting rhythms become too slow and uncoordinated; as a result the attentional systems are impaired or grossly unsynchronized. The thalamus's ability to refer in time the sequence of stimuli is also affected. There is considerable evidence that hippocampal circuits are engaged in consolidating explicit memories and spatial memories. Memory impairment is noticeable mostly in recent memory.[533] Disorientation and memory impairment clearly implicate the hippocampus. The ability to form new memories is greatly diminished when the hippocampus or the hearing and visual attentional subsystems are not functioning properly. The anterior thalamic nuclei project to the limbic cortex (areas 23 and 24 and perhaps areas 29 and 32)[534] and the major inputs to the hippocampal formation are from the limbic association cortex.[535] When the thalamic signaling to the limbic cortex with its efferents to the hippocampus is disrupted, the person is easily distracted (attention

[531] Ibid.
[532] Ibid
[533] John Martin, *Neuroanatomy.*
[534] Jean Talairach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[535] John Martin, *Neuroanatomy.*

shifting at the wrong time) by any irrelevant stimulus. Disorientation is generally manifested in time or place (not knowing if it is day or night or where one is), which is indicative of a loss of the referral quality (in time) of attention. In mild delirium, disorientation to time might be the first symptom to appear.[536]

When the hearing attentional subsystem is affected, speech or language disturbances may be evident as dysarthria (impairment to articulate), dysnomia (inability to name objects), dysgraphia (impairment to write), or even aphasia. As the hearing attentional system is shifted improperly, speech can be rambling and irrelevant, or pressured and incoherent, with unpredictable switching from subject to subject. Perceptual impairment might be present as misinterpretations, when, for example, a knock on the door is confused with a gunshot. Misperceptions range from simple and uniform to highly complex, and can include other sensory modalities such as gustatory, olfactory, visual and tactile.[537] When the thalamus shifts attention incorrectly, instead of activating the handshakes of the relevant memories, it tends to activate the wrong sensory memories, which results in misperceptions. These in turn send the wrong echoes to the basal ganglia, which are trying to integrate the external space with the body. When improper shifting impairs the visual attentional subsystem, perceptual disturbances may include illusions (confusing the folds in the bedclothes as animate objects) and hallucinations (seeing something that isn't there). Illusions arise as a result of the visual attention shifting rapidly in an improper sequence and confusing some shapes or borders with wrong categories, in other words activating the wrong visual memories. These false or wrong memories are fed into the basal ganglia circuits, which mistake this for real visual sensory signals. Normally, imagination is not accompanied by visual sensory signals, and the basal ganglia easily discern the difference. Delirium could be defined when the basal ganglia can't discern this difference. Hallucinations are produced when the visual or hearing attentional systems cannot differentiate between reality and imagination.

The handshakes and tags that are normally used by attention to jump-start relative memories quickly are disrupted and wrong groups of handshakes activate irrelevant memories. As a result, the individual might have delusional convictions of the reality of his hallucinations, but exhibit emotional and behavioral responses consistent with their content, which implies that the caudate nucleus is unaffected.

The incorrect shifting of the attentional subsystems tends to fluctuate during the course of the day and the level of disturbance varies accordingly. The person can present a normal picture in the morning and change later in the day or night.[538]

When the sensorimotor attentional system is disrupted, disturbed psychomotor behavior ensues; this might include groping or picking at bedclothes, attempting to get out of bed when it is unsafe, and sudden body movements. On the other hand, the person might have decreased psychomotor activity manifested as sluggishness, lethargy and even stupor. Psychomotor activity often shifts from one extreme to the other. In general, when one attentional system is perturbed by quicker or slower shifting, all attentional systems are perturbed in the same way. While hyperactive, the individual is more likely

[536] *Diagnostic and Statistical Manual of Mental Disorders*, DSM-IV-TR.
[537] Ibid.
[538] Ibid.

to have hallucinations, delusions and agitation. Whereas the individual in the hypoactive state is less likely to show these symptoms.

All of these disturbances can bring on emotional disturbances also. Some are natural, like anxiety, fear, anger and depression. Other emotions are just the result of the caudate nucleus matching thoughts to feelings, a rapid shifting of moods: apathy, irritability and euphoria.

If fear is marked, the person might attack those that are perceived to be threatening or sustain heavy injuries trying to escape from a falsely perceived danger. These emotions might bring on accompanying physical responses like calling out, screaming, muttering or moaning.[539]

Dementia

The essential feature of dementia is multiple cognitive deficits (including memory impairment), and at least one of the following: aphasia (deterioration of language function), apraxia (impairment of motor activities), agnosia (failure to recognize objects), or a diminution of executive functions. Executive functions include the ability to think abstractly and to plan, initiate, sequence, monitor, and stop complex behavior. [540]

In dementia, in contrast to delirium, one or several of the attentional systems might be affected by local trauma in the cortex or echoes from the cortex are being improperly sent to the thalamus. The improper echoes generate improper handshakes. As a result there is a disruption in the accessibility of certain types of memories.

If the hearing attentional system is affected (area 40 with projections to areas 22 and 42), difficulty in accessing certain language-related memories would be manifested as difficulty in producing the names of individuals or objects. The speech might become vague with long circumlocutory phrases. Comprehension of spoken or written language might be compromised. In extreme cases, when the attentional system locks into a fixed stimulus, the individual might be mute or have a speech pattern characterized by echolalia (echoing what is heard) or palilalia (repeating sounds or words over and over).

If the somatosensory attentional system is affected on the right (area 7), this will be manifested as reduced ability to execute motor activities despite intact motor abilities, correct sensory function and comprehension of the task required. If it is affected on the left side, the affected individual might be impaired in his/her ability to pantomime the use of objects (like combing hair) or to execute a known motor act (like waving good-by). Specific deficits can be expressed in specific particular actions like cooking, dressing or drawing. Also, even though dementia patients might exhibit normal tactile sensations, they are unable to identify objects placed in their hands by touch alone.

In turn if the visual attentional system is impaired (area 40 and projections to areas 18 and 19), individuals will exhibit agnosia; in spite of having normal vision they lose the ability to recognize categories of objects like a chairs or pencils. In extreme cases they can’t recognize members of their families or even their own reflection in the mirror. They might also be spatially disoriented and have difficulty with spatial tasks.

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[539] Ibid.
[540] Ibid.

Executive functions can also be impaired as one or more of the attentional subsystems can't focus. Since the attentional systems are required to access various kinds of information, many planning functions are disrupted. The individual having difficulty with novel tasks may manifest impairment of abstract thinking. Poor judgment and poor insight are also common. The affected individuals may make unrealistic assessments of their abilities; they may underestimate the risks involved in their activities. Occasionally, they may become violent; suicidal behavior may occur, particularly in the early stages as a result of distortion or loss of sense of self.

And last, Delirium might be superimposed on Dementia: the thalamus switches attentional subsystems incorrectly and simultaneously in an uncoordinated manner; and the attentional subsystems are also impaired by a disruption of handshakes and echoes from the cortex.

Amnestic Disorders

The main feature of Amnestic Disorders is the inability to learn new things[541] or make new memories or recall previous events. The Amnestic Disorders are characterized by a disturbance in memory caused by a direct physical trauma, the physiological effects of a general medical condition or the persisting effects of a substance (i.e., a drug abuse, a medication, or toxin exposure). The ability to learn and recall new information is always affected, whereas remembering previously learned information occurs more variably. When the amnestic disorder is severe, the patient might lack insight into his or her memory deficits. Most cognitive functions remain unimpaired. Occasionally, with profound amnesia, there is disorientation to time and space, but rarely to self.[542]

In manifestations of memory loss, exactly what kind of past events or types of information can't be remembered? What kind of new information can't be encoded or learned? There are many different memory subsystems. When one or several of these are affected, different kinds or types of memory are inaccessible even if the relevant attentional subsystem is functioning properly. The specific memory deficits will be manifested depending on which area of the cortex has been damaged or where the flow of the loop has been interrupted. Essentially, the correct handshakes that are associated with other memories are disrupted, and this causes the memory to be inaccessible. Sometimes, accidentally, a different association handshake might be triggered and the memory will suddenly be available for recall.

Memory is inextricably connected to emotions and learning. Memory problems are generally manifested when anything goes wrong in the limbic system controlling some of these functions. Any interruption in the circuits between the cortex to the amygdala and the hippocampus and vice versa can equally disrupt memory.

Researchers have identified different types of memory, each associated with different cortex areas, some, with multiple areas. The disruption of each one of these memory systems produces different amnesia symptoms.[543]

Short-term memory: involved in remembering what happened just a few seconds or minutes before.

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[541] Ibid.
[542] Ibid.
[543] Daniel L. Schacter, *Searching for Memory*.

Working memory: involved in tackling a problem of longer duration, and that draws from other memories information relevant to the problem.

Intermediate and long-term memory: for relatively recent events and long ago events, respectively.

Explicit memory: when we engage in trying to remember something specific, like who sat next to us last Thanksgiving. Explicit memory involves a systematic search. Hippocampal circuits are engaged in consolidating explicit memories and forming spatial memories. The hippocampal formation works closely with the adjoining entorhinal cortex, which in turn receives sensory and cognitive information from the limbic association cortex.

Implicit memory: opposed to explicit memory, one where we aren't aware of how we remembered something; it just "pops" into mind.

Flashbulb memory: like remembering where you were when Kennedy was shot.

Source memory: remembering where or how we learned something, e.g., did we hear it in a conversation or on the television, or read it in a book or newspaper?

Episodic memory: related to sequencing events in time and context.

Semantic memory: divided into rules, algorithms, facts, concepts, and functions. Damage to the entorhinal cortex or the hippocampus can produce impairment of semantic and episodic memory.

Procedural memory: consists of habits like eating, showering, dressing, etc.; and skills like speaking, writing, language, motions, recognizing names or objects or living organisms, recognizing patterns or faces, etc.

Autobiographical memory, subdivided into three categories: a lifetime memory (i.e., I lived in Carmel), a general event memory (I vacationed in Carmel), and an event specific memory (I visited 17 Mile Drive).

There are different strategies to encode and retrieve memories. Each different memory may use some or all of these strategies. To encode, we have deep, shallow and associative strategies.[544] Perhaps there are more. By a repeat/rehearse mechanism we can strengthen these memories. By a leading/distortion mechanism we can change these memories. Retrieval uses various mechanisms: associative, strategic, implicit and explicit, priming, and cues. The types of handshakes established in each case will activate the memory depending on the retrieval mechanism used. Some retrieval strategies can even be state dependent, that is, one can access a memory when one is in the same state as when the event happened, i.e., under the influence of a drug or alcohol.[545]

Encoding and retrieval are not necessarily mirror images of each other and could be using different mechanisms. It also seems that cues and priming are related to the senses: taste, sight, tactile, hearing and smelling. Cues are also related to emotions. Sight in turn is related to movement, form and spatial orientation. Movement is related to action.

Studies of damage to certain areas of the brain lead us to suspect that the hippocampus is involved in explicit memories. These memories will assist in interpreting sound. The frontal lobes have been identified with activity in strategic retrieval, the purposeful search for memories. The temporal lobes have to do with memories for specific skills, like speaking, reading and writing, recognizing faces and remembering

[544] Ibid.
[545] Ibid.

names. Also certain regions of the temporal lobes have to do with memories of categories of objects, like furniture, living or inanimate, tools (which in turn seems to be connected to the motor cortex, which is used to manipulate the tools.), etc.[546]

Impairment of any one or several of these memory systems can produce a wide range of conditions ranging from hardly noticeable to completely incapacitating behavior. Worse, inability to remember certain things or events might bring on, over time, a different psychiatric disorder.

Amnestic Disorders can be Transient (hours or days, up to a month) or Chronic (more than a month), as defined by the DSM-IV-TR.

How can these conditions be cured or improved? Therapies based on a better understanding of the attentional subsystems seem like a rich area for research. Treatment will also depend on whether there is injury to the pertinent areas in the cortex or to specific structures of the limbic system that participate in a memory loop. Therapies might be discovered by learning to activate alternative loops that could be used to trigger lost memories or learning to use alternate methods of recall (implicit or cued, instead of explicit for example).

There are many documented cases where a patient, one day, all of a sudden, for unknown reasons, recovers much if not all of his or her lost memories. This seems to imply, in some cases, that the memories are not lost, but simply inaccessible temporarily.

18
Up and Down, Mania and Depression.

We have, for the most part, looked at circuits that were working correctly. In some of the situations we reviewed, problems arose when loops locked and couldn't disengage, or disconnected inappropriately.

To try to grasp the essence of Major Depressive Disorder and Manic Depression and its related cousins, Dysthymic Disorder, Cyclothymic Disorder, Bipolar I, Bipolar II, Mixed Episode and Hypomanic Episode, we need to look at neurotransmitters.

Glutamate is not only an essential metabolite but also a major excitatory neurotransmitter. Glucose and pyruvate are precursors to synthesize the protein alfa-ketoglutarate. Glutamate is synthesized from this protein or from glutamine with the proper presence of the enzyme glutaminase. To weave the tapestry tighter, glutamate is also used to produce GABA (gama-aminobutyric acid). The delicate balance between the right amounts of glutamate and GABA depends on a complicated web of other chemicals: principally glutamic acid decarboxylase and pyridoxal phosphate; the latter derived from vitamin B6 (necessary for the production of GABA from glutamate); and the GABA transporters (GATs) that control the reuptake of GABA. Dietary deficiencies of B6 affect the production of pyridoxal phosphate.[547]

GABA reuptake is accomplished by removal of GABA from the synapse by GABA transporters (GATs). Four GATs are known: GAT-1, GAT-2, GAT-3 and BGT-1. These are primarily located in glial cells and interneurons. GATs are often found in

[546] Ibid.
[547] *GABA and Glycine*, Neuroscience

GABAergic neurons thus allowing for collected GABA to once again be concentrated into synaptic vesicles for release. The GATs require Na+ and Cl- as co-transporters. Their operation is powered by the Na+ gradient.

GABA is degraded into succinate by the mitochondrial enzymes, GABA aminotransferase and succinic semialdehyde dehydrogenase. Neuropeptides and neurotransmitters, such as peptide somatostatin and GABA, influence each other. Any problem with any one of these chemicals or a combination of them can lead to a very small imbalance that could produce extra excitation, either by more glutamate activity or less GABA inhibitory action.

Another example of the complex balance between glutamate and GABA is found in the hippocampus. Synaptic glutamate release might decrease inhibition in GABAergic interneurons via an effect at presynaptic kainite receptors in addition to its conventional excitatory effects mediated by postsynaptic AMPA (alfa-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid), kainite and NMDA receptors. On the other hand, kainite receptors attenuate evoked inhibitory postsynaptic potentials or currents (PSCs). There is some disagreement as to whether they reduce the frequency of miniature inhibitory PSCs, raising a question over their purported presynaptic site of action. Also, kainite receptor agonists have been shown to depolarize interneurons, greatly enhancing their spontaneous firing rate. And, the synaptic excitation of interneurons is partly mediated by kainite receptors. This leads to the possibility that the net role of kainite receptors may be pro- rather than disinhibitory.[548]

Ming-Yuan Min et al notes that none of the above studies addresses the effect of glutamate release from excitatory synapses (as opposed to exogenous agonist application) on monosynaptic inhibition. Any inference about the physiological role of kainite receptors on interneurons is therefore based indirectly on predicting the consequences of the different processes listed above.

However, for brief periods, activity in excitatory fibers depresses GABAergic inhibition in a kainite receptor-dependent manner.[549]

It is also becoming evident that, in response to neuronally released glutamate, glial cells, astrocytes in particular, can themselves release glutamate.[550]

Research into these chemicals might produce some promising pharmacological therapies.

Individuals suffering manic-depression show a decrease in glial cells in the frontal lobes. Glial cells supply neurons with oxygen, glucose and other nutrients.

The endocrine system, to complicate matters more, might also be involved. Many aspects of the endocrine system are regulated by the hypothalamus: regulation of sleep, appetite and sexual drive. In addition, the secretion of hormones by the hypothalamus depends on levels of hormones secreted by the pituitary, thyroid, adrenal and sex glands (testes and ovaries).[551] This complex feedback system could be affected at any one of several levels.

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[548] Ming-Yuan Min, Zare Melyan, and Dimitri M. Kullmann, *Synaptically released glutamate reduces gamma-aminobutyric acid (GABA)ergic inhibition in the hippocampus via kainite receptors.* Proc. Natl. Acad. Sci. USA, Vol 96, pp 9932-9937, August 1999, Neurobiology.

[549] Ibid.

[550] Gallo V., & Chittajallu, R. (2001). *Unwrapping glial cells from the synapse: What lies inside? Science, 292, 872-873.*

[551] Robert M. Zapolsky, Why Zebras Don't Get Ulcers.

Also, it is hard to determine cause and effect. Are mania and depression caused by abnormalities of the hypothalamus and/or various components of the endocrine system? Or are the endocrine abnormalities merely incidental manifestations of the underlying brain dysfunction? I tend to believe the latter. However, in manic-depressive patients and even more so in unipolar depressive cases, abnormalities from all three parts of the endocrine system have been observed. In patients with rapid cycling, low thyroid functioning has been detected.

Mania and depression don't necessarily occur in a vacuum, they can be triggered by outside stimuli. Just like the brain produces a continuous map of extra and intrapersonal space, the brain is continuously trying to create a seamless interface where the internal emotional landscape matches the external, environmentally rich set of impulses conveyed by the senses. When there is a genetic tendency to be predisposed to one or another disorder, outside influences have to be seriously considered as being an integral part of producing mania or depression. Ultimately, stress has been linked in many cases to the onset of unipolar depression and manic-depression.[552] The stress response also fits nicely with the hypothalamic-pituitary-adrenal axis.[553] This would also be compatible with a genetic predisposition. However, stress can be a natural response to prolonged depression.

Let us first look at mania and hyppomania.

If we consider a very slight boost in the excitation of neurons by a slight increase of glutamate, activity will speed up slightly in the cortex. The increase in excitatory activity will slightly increase the levels of most other neurotransmitters. Speeded-up thinking will trick the brain into triggering (feeling) some positive emotions. There is a genetic predisposition for this slight imbalance, as relatives of manic-depressives tend to be more likely to also be manic-depressive, unipolar depressive or schizophrenic.

It is suspected that drugs reducing glutamatergic activity or glutamate receptor-related signal transduction may have antimanic effects. There is also evidence that antidepressant drugs directly or indirectly reduce NMDA glutamate receptor function.[554] In studies of antiepileptic drugs, two global categories have been identified. One group has sedating effects in association with fatigue, cognitive slowing and weight gain, as well as anxyolitic and antimanic effects. These actions may be related to the potentiation of GABA inhibitory neurotransmission. The other group is associated with predominant attenuation of glutamate excitatory neurotransmission and has activating effects in relation to weight loss and possibly anxiogenic and antidepressant effects.[555]

The most important role of lithium is probably in reducing glutamatergic activity and keeping it down to more normal levels. By doing so, the excess glutamate excitatory activity is reduced and the probability of eventually depleting other neurotransmitters is lessened. Lithium may exert certain antagonistic or sensitivity-modifying actions at synapses mediated by catecholamines. These actions include inhibition of the release of epinephrine and dopamine as well as weak actions on the uptake (increases) and retention (decreases) of chatecolamine neurotransmitters in presynaptic nerve terminals, but

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[552] Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR
[553] Robert M. Zapolsky, Why Zebras Don't Get Ulcers.
[554]Ibid.
[555] Ketter TA, Post RM, Theodore WH, *GABA Med, vs. Lowering Glutamate*, Neurology 1995;53(5 Suppl 2):S53-67.

possible facilitation of release of serotonin in some forebrain regions. Lithium interferes with the ability of some hormones to produce cyclic-AMP by stimulating adenyl cyclase, which is believed to be an important component of the receptor mechanism of several hormones, including catecholamines and antidiurectic hormone (ADH).[556]

A study of a patient who experienced bipolar 48-hour ultrarapid cycling for several years showed blood cortisol and growth hormone levels elevated on depressive days, and urinary metanephrine (dopamine metabolite) and norepinephrine levels elevated on manic days. It was also determined that blood flow in the left thalamus was lower than the right thalamus on the manic days.[557] This increase in metanephrine and norepinephrine might be caused by the increase in glutamatergic excitation.

There is some pre-clinical and clinical evidence that antidepressant drugs directly or indirectly reduce NMDA glutamate receptor function. Drugs that reduce glutamatergic activity or glutamate receptor-related signal transduction might also have antimanic effects. Recent studies employing magnetic resonance spectroscopy suggest that unipolar, but not bipolar, depression is associated with reductions in cortical GABA levels.[558]

When neurons signal each other faster, thoughts and speech become accelerated, accompanied by increased physical activity, decreased need for sleep, increased sexual activity and a possible enhancement of the senses. Prior to the availability of medication, the increased activity could lead to exhaustion and even death. Studies show normal individuals change their thoughts every five to six seconds, compared to less than two seconds for manic patients. The number of syllables spoken in a minute by a manic patient is between 180 and 200; a normal person's, 120 to 155.[559] This acceleration of brain activity will interfere with attention as the individual becomes more easily distracted and have greater difficulty concentrating.

In my opinion Mania and Depression are each a Thought Disorder and not a Mood Disorder; the thought modes trigger the respective emotions. The speeded-up thinking in mania or the slowed-down thinking of depression is the cause of the mood shifts and not the other way around. Manic-depressive patients may have subtle deficits in short- and long-term memory, attention, and executive functions. In studies of identical twins, the ill twins were more impaired in visual processing. This is consistent with the notion that the non-dominant hemisphere (the right hemisphere, which is more concerned with visual spatial skills) is more impaired in those with manic-depressive illness.[560]

In chaos theory terms, another way of thinking about this is that the isorropic attractor of the isorropic circuit tends to the positive side in mania and to the negative side during depression.

The increased speed and patterns of thought excite the associated emotions by signaling the thalamus and caudate nucleus, and tricking them to trigger positive feelings, like joy or even euphoria, sometimes with inappropriate spontaneous laughter. As the

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[556] Armand M. Nicholi, Jr. Editor, *The Harvard Guide to Psychiatry.*
[557] Juckel G, Hegerl U, Mavrogiorgou P, Gallinat J, Mager T, Tigges P, Dresel S, Schroter A, Stotz G, Meller I, Greil W, Moller HJ, *Clinical and biological findings in a case with 48-hour bipolar ultrarapid cycling before and during valproate treatment.* J Clin Psychiatry 2000 Aug; 61(8):585-93.
[558] Krystal JH, Sanacora G, Blumberg H, Anand A, Charney DS, Marek G, Epperson CN, Goddard A, Mason GF, *Glutamate and Gaba systems as targets for novel antidepressant and mood-stabilizing treatments.* Mol Psychiatry 2002;7 Suppl 1:S71-80.
[559] E. Fuller Torrey & Michael B. Knable, Surviving Manic Depression.
[560] Ibid.

isorropic attractor wanders farther into the positive emotional side, self-esteem grows disproportionately with decreased inhibitions and a greater sense of importance. As a result of the increased self-esteem, risky and bizarre behavior is common. Grandiose delusions or paranoid delusions are also quite possible. Increases in use of alcohol and drugs are frequent.[561] The increased speed of thoughts activates associated positive emotions and activates the pleasure centers. It is also known that some agents that increase dopamine (e.g., L-dopa, bromocriptine and cocaine) may induce mania or mania-like behaviors and feelings; the good feelings induce a faster mode of thinking. Also, some agents that block dopamine (e.g., haloperidol) may decrease mania.[562]

As a result of the increased self-esteem, all these changes in activities seem perfectly logical to the person in a manic phase. Sensuality is pervasive and the desire to seduce and be seduced irresistible. The manic-depressive's erratic behavior may seed social violence or sometimes self-destructive behavior. In a few cases, as a result of their actions, they may provoke others to try to kill them or even, in a few cases, they may try to kill themselves.

The symptoms of mania (or depression) mix with each individual's personality and thoughts to create a unique medley that differs from person to person and even from day to day. Since each person has a unique stream of thoughts, these thoughts will bring on their unique, associated emotions. In the manic phase, irritable and quickly shifting moods are common. Just as emotions activate associated memories and ways of thinking, speeded-up thinking and certain memories will elicit a sense of elevated mood. The euphoric states in turn will feedback and activate positive thoughts and make bad memories inaccessible. The result: an inflated sense of self, grandiose plans and extremely dangerous behavior to self and others

When manic symptoms are somewhat lesser, the condition is called hypomania. The symptoms last less than four days; delusions and hallucinations are not present; and, in contrast to mania, hypomania is not severe enough to cause marked impairment in functioning. In some individuals the change in functioning may even take the form of a marked increase in efficiency, accomplishments or creativity.

Varying from person to person, the excess glutamatergic excitation will eventually produce a slight deficit of other neurotransmitters as their normal replacement rate can't keep up with the increased consumption rate. This period of excitation can last for as little as one day or as long as several weeks. Levels of serotonin, norepinephrine, dopamine and acetylcholine eventually drop slightly below normal. When this happens, the speed of thinking changes. Now the cortex's signaling slows to rates that are less than normal. As the neurons slow down their firing, glutamate is made available for GABA synthesis. This will increase the GABAergic activity (inhibitory) and push GABA levels back to their normal levels, but also contribute to slowing down the signaling rates.

The slower neuronal firing rate will activate negative emotions. Some of the emotions are sadness, emptiness, fear, anxiety, diminished pleasure, feelings of worthlessness and excessive or inappropriate guilt. Persistent anger and increased irritability might also be present, even an exaggerated sense of frustration as moods shift quickly.

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[561] Diagnostic and Statistical Manual of mental Disorders, DSM-IV-TR.
[562] Harold I. Kaplan, Benjamin J. Sadock, Synposis of Psychiatry.

This slowed down brain produces physical symptoms as well: facial expressions and demeanor associated with sadness; decrease or increase in appetite, psychomotor agitation (inability to sit still, pacing, hand-wringing, rubbing or pulling of the skin, clothing or other objects) or retardation (slowed speech and body movements; increased pauses before answering; speech that is decreased in volume, inflection, amount or variety of content and even muteness), insomnia or hypersomnia and fatigue or loss of energy. A significant reduction in sexual desire is present occasionally.[563] The slower brain also exhibits diminished ability to think, to remember (mostly the positive) and to concentrate. Under stress, or the more severe the glucocorticoid excess (as happens during depression), the more severe the memory problems and hippocampal atrophy. There is also a reduced storage of glucose in hippocampal neurons by about 25 %, making them more susceptible to other neurological damages.[564] Schacter reports that volume of the left hippocampus in sexually and physically abused women when they were young is significantly reduced compared to a control group.[565]

Compounding the fact that intense negative emotions decrease the ability of the isorropic circuit to re-establish a neutral calmness, the stress produced by depression elevates levels of glucocorticoids. The glucocorticoid damage to the hippocampus reduces the cholinergic signals to the lateral septum. The right hemisphere, more than the left, is more concerned with the regulation of emotions due to a higher number of projections to the limbic areas. This combination explains why glucocorticoids affect the right hippocampus more than the left. The feedback projections from the medial septum back to the hippocampus are GABAergic and as cholinergic activity slows down, inhibitory feedback signals also slow down. This slight asymmetry of cholinergic signaling affects the isorropic circuit's activity in such a way, that as it tries to regain balance, the right hemisphere is activated more than the left, and the imbalance exacerbates the effect of pushing the isorropic attractor more to the negative side. The overall reduction of activity in the brain, added to the imbalance of greater activity in the right cingulate cortex compared to the left, tricks the brain to continue triggering negative emotions. The farther the isorropic attractor wanders from neutral calmness, the more severe the depression is expressed.

Depressed people's brains show decreased excitability after exercise compared to depressed people that had recovered within six months, who in turn demonstrated decreased excitability compared to healthy individuals. This suggests that reduced excitability in depressed brains is a reversible state, and perhaps can be used as a therapy.[566]

However, the ventromedial frontal cortex (areas 9 and 10) shows marked hyperactivity during depression. This area of the brain is responsible for planning and detecting possible future threats as well as participating in other higher planning functions. This area is involved in executive functions and voluntary actions as well as computing the affective significance of environmental stimuli and modulating emotions accordingly. In depression, this hyperactivity of the ventromedial frontal cortex results when negative emotions are felt as the ventromedial frontal cortex sends out handshakes

[563] Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR.
[564] Robert Sapolsky, *Why Zebras Don't Get Ulcers.*
[565] Daniel Schacter, *Searching For Memory.*
[566] Klaus Ebmeier, *American Academy of Neurology Scientific Journal,* August 11, 1999.

to try to determine what is wrong, and, unable to find an answer, locks into this state. This neatly explains the general feeling of anxiety that is commonly reported.

There is also a marked area of hypoactivation in the ventro/dorsolateral prefrontal cortex (area 47). This area is connected with the orbital portion of the frontal convolutions by its thalamohypothalamic connections and has vegetative functions.[567] This probably has to do with the disruption of orbitofrontal-hypothalamic connections changing the production of hypothalamic releasing factors that regulate the secretion of pituitary, thyroid, adrenal, and gonadal hormones that are responsible for the somatic and visceral responses of emotions, which are responsible for changes in the chemical milieu, and consequently, the brain's mode of operation.

The symptoms of unipolar depression and those of the depressed phase of manic-depression are virtually indistinguishable. However, there are some small differences.[568] There is small evidence that there are reductions in cortical GABA levels in unipolar depression but not in bipolar depression. Individuals with unipolar depression are more likely to have decreased sleep, psychomotor agitation and weight loss. On the other hand, those with depressive episodes in bipolar disorder are more prone to have increased sleep, psychomotor slowing and weight gain. These differences, however, are not impressive.

Also, unipolar depression is about five times more common and is more likely to affect women.[569] While unipolar depression is associated with an excess of births in March through May, manic-depressive illness is associated with an excess of births in December through March. Relatives of individuals with manic-depressive illness are more likely to have this illness than are relatives of individuals with unipolar depression. Manic-depressive illness is characterized by an earlier average age of onset and shorter intervals between episodes. On average, unipolar depression has a more benign long-term course. Postmortem neurochemical and neuropathological measures indicate more dissimilarities than similarities.

While lithium is more effective for treating manic-depressive illness, antidepressants are more effective for treating unipolar depression. Antidepressants, in many cases, can induce mania in some manic-depressive patients.[570] The tricyclic antidepressants will increase the action of dopamine and this indirectly increases the release of norepinephrine. The activity of the pleasurable centers is likewise increased, and with more glutamate released, excitation increases and speeds up thought. Selective serotonin reuptake inhibitor antidepressants (SSRIs) will increase the action of serotonin, and this increased firing could push the glutamate signaling up. These two mechanisms could account for why, in some cases, when antidepressants are administered to manic-depressive patients, they can bring on mania.[571] It also is suggestive of why the medications work sometimes, sometimes only partially, and other times, not at all.

In contrast to the depressive phase of bipolar disorder, the onset of unipolar depression is produced independently of a manic episode. The difference is that the balance between GABA and glutamate has gone in the opposite direction. There is a slight decrease in glutamatergic activity with a consequent slowing-down of brain

[567] Jean Talairach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[568] E. Fuller Torrey, Michael B. Knable, *Surviving Manic Depression.*
[569] Ibid.
[570] Ibid.
[571] E. Fuller Torrey, Michael B. Knable, Surviving Manic Depression

activity. This decrease will eventually lower the levels of GABA, norepinephrine, serotonin and dopamine, but probably not acetylcholine. This might explain the difference in psychomotor agitation (unipolar) and psychomotor retardation (bipolar).

In the case of unipolar depression, the slight decrease in glutamatergic activity relating to increased psychomotor activity is probably due to the glutamatergic output of the subthalamic nucleus to the globus pallidus internal and substantia nigra pars reticulata, which decreases the GABAergic output to the thalamus, with similar results to the hyperkinetic loop.

In the case of bipolar depression, glutamate is present at almost normal levels, so the psychomotor retardation is probably due to the lowered dopamine levels at the substantia nigra pars compacta, acting in a similar fashion to the hypokinetic loop.

These different routes to depression also explain why antidepressants might produce mania in bipolar patients, since a slight increase in activity by any of the neurotransmitters (serotonin, norepinephrine and dopamine) might increase the activity of glutamate, which is present in almost normal amounts. When administering antidepressants to patients with unipolar depression, glutamate might be at lower than normal level; a slight indirect increase of any other neurotransmitter will help restore its normal level.

The difference between the depressive phase of manic depression and unipolar depression is a small but subtle one. In the bipolar case, depression is brought by a slight lowering of the normal levels of various neurotransmitters (serotonin, norepinephrine and dopamine) through the excessive action of glutamate. In other words, the brain crashed. In the unipolar case, depression is brought by a lowering of levels of the same neurotransmitters because of a slight decrease in glutamate excitatory action. A small, but an important difference. As a consequence, not surprisingly, the pharmacology of these two illnesses is different.

In some individuals the neurochemical levels and similarities between depression in manic-depression and in unipolar depression might be almost indistinguishable at a given time, but for the most part there are important differences between these two. Given the fact that there are many receptors for each neurotransmitter, it should not be surprising that, even from person to person, the pharmacology would also vary accordingly. Much more needs to be done in this important area.

There can be other chemical alterations due to lowered levels of neurotransmitters during depression. There is a brain growth factor called brain-derived neurotrophic factor (BDNF). It has been known that depressed people have abnormally low levels of BDNF in their blood; depressed people receiving antidepressants have higher levels of BDNF in their blood. In rat studies, conducted by Amelia Eisch and coworkers at the University of Texas Southwestern Medical Center, when the animals were given antidepressants, BDNF levels increased in the hippocampus.[572] BDNF might have a role in neurogenesis, which is a major aspect of encoding memory and learning in the hippocampus. The low levels of BDNF might be a result of the prolonged action of stress hormones on the hippocampus. This suggests that low BDNF levels in the hippocampus are part of the problem in depression. Part of the isorropic circuit, the diagonal band of Broca and the medial septal nucleus contain GABAergic interneurons, GABAergic projection neurons

[572] Joan Arehart-Treichel, *Researchers Try to Explain Link Between Depression, Brain Chemical.* Psychiatric News, Dec 19, 2003.

whose axons innervate the hippocampal formation as well as cholinergic neurons.[573] These GABAergic neurons inhibit hippocampus activity and could be related to lower levels of BDNF.

The ventral tegmental area is known to send BDNF to the nucleus accumbens. However, when Eisch and her coworkers injected BDNF into the ventral tegmental area, expecting this to have an antidepressive effect, it produced the opposite, depression. When they injected a protein that blocks BDNF's action into the nucleus accumbens of rats, the injected rats were happier than the controls. This suggests that BDNF made in the ventral tegmental area and then sent to the nucleus accumbens has a depressive effect.[574] There can also be a relation between BDNF and dopamine. The nucleus accumbens receives dopamine inputs from the tegmentum; in a depressed state, the dopamine levels fall.

When people suffer a depressed mood for most of the day more days than not, it is called Dysthymic Disorder.[575] Dysthymic Disorder is to Unipolar Depressive Disorder like hypomania is to mania -- a less severe form. If mania or hypomania occurs, then the diagnosis would be for Manic Episode or Hypomanic Episode, not Dysthymic Disorder. The diagnosis for Cyclothymic Disorder is used if the manic and depressed moods alternate more than four times in one year.[576]

Dysthymic disorder is probably brought on by the lowering of just one or two of the neurotransmitters (serotonin, norepinephrine or dopamine) associated with depression.

Patients with strokes that have damaged the left frontal lobe or the left thalamus quickly become depressed.[577] Moreover, depressed patients show reduced activity in the left frontal lobe. The reduced activity is probably related to the negative emotions that are orchestrating a particular type of functioning of the brain in which thoughts related to positive emotions are inaccessible. Major depressive disorders were found in patients with left hemisphere lesions involving the basal ganglia, whereas none of the patients with right hemisphere stroke exhibited major depression.[578] The isorropic circuit receives two primary inputs, from the thalamus to the habenula and from the hippocampus to the lateral septal nucleus. If the left orbitofrontal or left thalamus is damaged with a stroke, the isorropic circuit will detect this greatly slowed down excitatory activity. However, because of this damage, the right to left habenular excitatory signals, which under normal conditions would slowly restore equilibrium by exciting the reticular formation, and through feed back connections increase activity of the cortex, and specifically the left anterior cingulate, now are unable to do so. This type of damage perpetuates the (-)(-) (decreased excitation from the thalamus and cortex) signaling to the left habenula, which normally is typical of negative emotions.

In contrast, when right stroke damage is present, the isorropic circuit's ability to restore balance is much less impaired. The left habenula's functions are intact --

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[573] Edward C. Cooper, Emily Harrington, Yuh Nung Jan, & Lily Y. Jan, *M Channel KCNQ2 Subunits Are Localized to Key Sites for Control of Neuronal Network Oscillations and Synchronization in Mouse Brain.*
[574] Ibid.
[575] Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR.
[576] Ibid.
[577] Paul Beger, *Gene Linked to Stress, Severe Depression,* Associated Press.
[578] Manfred Herrmann, Claudius Bartels, Martin Schumacher, Claus-W. Wallesch, *Poststroke Depression,* Stroke. 1995;26:850-856.

excitatory (+)(+) of positive emotions or (-)(-) excitatory of negative emotions – and because normally the right habenula is receiving (+)(-) (increased excitatory from the right thalamus and decreased from the whole cortex with negative emotions) or (-)(+) (decreased from the right thalamus and increased excitatory from the cortex with positive emotions), a stroke on the right side probably affects less the normal signaling on the right side. It could be possible that the right habenula, due to a stroke on the right side, would receive (-)(-) excitation, in which case the left habenula, if in (+)(+), would quickly restore one or another circuit to (+) tricking the brain to perceive a restored balance. If the left habenula were in (-)(-) of a negative emotion, then nothing happens, as the isorropic circuit is fooled into believing that a balance already exists, and the unpleasantness of the negative emotions is not perceived.

The lessened activity in the left frontal lobe, relative to the right, is manifested as an unpleasant feeling by the isorropic circuit. The habenula-septal system will promote a balanced activity of both hemispheres. In the case of depression, where the activity of left frontal lobe has decreased, the isorropic circuit will engage circuits that might increase left activity; among them, the anger circuit. The prevalence of anger attacks in depressed populations has been determined to be between 30 and 40 percent, 28 percent in patients with dysthymia, and 0 percent in patients with no previous mood disorder histories.[579]

In the case of depression, especially if accompanied by fear and/or anxiety, the activity of the isorropic circuit will decrease the threshold of the phobothymic switch. Irritability will also be manifested as part of the attempt to restore balance.

The brain undergoes a prominent developmental transformation during adolescence after a relatively long period of slow growth during childhood. An fMRI study showed that adolescents exhibit greater activation in the amygdala than in the frontal lobe during identification of an emotional state from a facial expression, in contrast to adults who show greater frontal over amygdala activation (Yergelun-Todd, 1998).[580] These two facts, brain growth coupled with greater amygdala activation, might be part of the reason why the onset of depression and schizophrenia is common during late adolescence.

Anger and irritability may be part of a depressive symptomatology. Irritable mood is a core symptom of Major Depressive Disorder in children and adolescents but is emphasized less as a symptom of depression in adults. However, Snaith and Taylor report 37 percent of depressed patients had moderate-to-severe outward directed irritability.[581] They also report that findings from the Epidemiologic Catchment Area surveys indicate that depression in adults is related to violent behavior. Moreover, a substantial number of patients seek medical treatment because of irritability and/or anger that causes distress and conflict in their lives.

It has been reported that patients with Major Depression with Anger Attacks may have a greater serotonergic dysregulation than depressed patients without such attacks. It is necessary to add that anger attacks are not unique to depressed patients.[582]

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[579] Jarrold F. Rosenbaum, *Anger Attacks in patients with Depression,* J Clin Psychiatry 1999;60[suppl 15]:21-24.
[580] Allan Schore, *Affect Dysregulation.*
[581] Snaith R.P., Taylor C.M., *Irritability: definition, assessment and associated factors.*, Br J Psychiatry, 1985;147:127-136.
[582] Jarrold, F. Rosenbaum, *Anger Attacks in patients with Depression,* J Clin Psychiatry 1999;60[suppl 15]:21-24.

Statistically comparing a series of variables in major depressive episode (MDE) with and without anger, with major depressive disorder (MDD) with and without anger and with bipolar II disorder showed that MDE with anger was significantly associated with bipolar II variables. MDD with anger compared to MDD without anger had a significantly lower age of onset, more marked depressive mixed states and a bipolar family history with more cases. MDD with anger, compared to bipolar II disorder, had a significantly higher age of onset, less atypical features, and a bipolar family history with fewer cases. MDD with anger might be halfway between MDD without anger and bipolar II disorder. However, MDD with anger responds equally or better to antidepressants than MDD without anger.[583]

In another study, Boulos-Paul Bejjani et al, reported one woman who had transient acute depression when high frequency stimulation was delivered to the left [but not the right] central substantia nigra, including part of the pars compacta (dopaminergic) and pars reticulata (GABAergic), 2 mm below the site where stimulation alleviated the signs of Parkinson's disease. A continuous current was delivered for seven minutes. Within five seconds after it was started, the patient's face expressed profound sadness. Although alert, she started to cry and verbally communicate feelings of sadness, guilt, uselessness, hopelessness [and fear and suicidal ideation], such as, "I'm falling down on my head, I no longer wish to live, to see anything, hear anything, feel anything…." When asked why she was crying and if she felt pain, she replied, "No, I'm fed up with life, I've had enough…I don't want to live anymore, I'm disgusted with my life…Everything is useless, always feeling worthless, I'm scared in this world." When asked why she was sad, she responded, "I'm tired, I want to hide in a corner…I'm crying over myself, of course…I'm hopeless, why am I bothering you…." She had no hallucinations, nor was there any changes in her motor or cognitive symptoms of Parkinson's disease. The depression disappeared less than ninety seconds after stimulation was stopped. For the next five minutes the patient was hypomanic, and she laughed and joked with the examiner.

In later sessions, the patient noted both acute sadness, although less severe than during previous sessions, and reported the sensation that her body was being sucked into a black hole. This illusion of bodily motion was not accompanied by hallucinations or confusion. A significant increase in blood flow was detected in the right parietal lobe (area 40), in the left orbitofrontal cortex (areas 10 and 11), in the left globus pallidus, and also in the left amygdala and the left anterior thalamus.[584]

Stimulation may have affected the activity of GABAergic neurons in the substantia nigra (pars reticulata) innervating the ventral nuclei of the thalamus, which project to the prefrontal and orbitofrontal cortexes. [The ventral anterior projects to area 6 (supplementary motor area), 8 (voluntary movement of eyes) and 44 (motor speech); the ventro-lateral projects to areas 4 and 6 (motor areas), and the ventral posterior projects to areas 3, 1 and 2 (somatosensory areas).] Dysfunction of these systems has been

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[583] Franco Benazzi, *Major Depressive Disorder with Anger: A Bipolar Spectrum Disorder?*, Psychother Psychosom 2003;72:300-306.

[584] Boulos-Paul Bejjani, Philippe Damier, Isabelle Arnulf, Lionel Thivard, Anne-Marie Bonnet, Didier Dormont, Philippe Cornu, Bernard Pidoux, Yves Samson, and Yves Agid, *Transient Acute Depression Induced by High-Frequency Deep-Brain Stimulation*, Centre d'Investigation Clinique, Federation de Neurologie and INSERM Unite 289.

implicated in mood disorders and in self-induced sadness in normal subjects.[585] The anterior nuclei project to the cingulate (areas 23, 24, 32 and 29).[586]

Positron-emission tomography revealed activation of the left orbitofrontal cortex, a finding consistent with involvement of the nigrothalamic pathway, which extends to the left amygdala and limbic structures and is implicated in the processing of unpleasant feelings. Activation of the left pallidum may result from retrograde stimulation of GABAergic projections from the external pallidum to the substantia nigra. The right parietal lobe was also activated (area 40).[587]

The substantia nigra pars reticulata projects GABAergic neurons to the pedunculopontine nucleus. The globus pallidus internal also projects to this nucleus. The pedunculopontine nucleus, in turn, through diffuse cholinergic projections to the thalamus and cortex, regulates arousal, and through reticular formation connections and direct reticulospinal projections regulates movement.[588] This channel reinforces the substantia nigra-thalamic activity.

The artificial stimulation of the left substantia nigra, through the thalamic connections to the primary cortex and somatosensory areas will reduce activity in these areas. The primary cortex and somatosensory cortex have dopaminergic (D1) projections to the putamen, which in turn has dopaminergic projections (D2) to the globus pallidus internal and external. Consequently, the inhibitory (GABAergic from the substantia nigra pars reticulata) signals to the thalamus reduce the excitatory (D1) signals to the putamen, which reduce the inhibitory (D2) signals to the globus pallidus, causing activity in the globus pallidus to increase. This activity is incidental, but it increases the inhibitory (D2) signals to the thalamus, thus reinforcing in a positive feedback manner the GABAergic signals from the substantia nigra, exacerbating the situation and decreasing frontal lobe activity even more.

Moreover, the nigrostriatal dopaminergic system originating in the substantia nigra pars reticulata has dopaminergic (D1, excitatory) projections to the caudate, the putamen and to a lesser degree, to the nucleus accumbens. The putamen has dopaminergic connections (D2, inhibitory) to the globus pallidus, which also has dopaminergic projections (D2) to the ventral thalamus. Excitation to the substantia nigra using the dopaminergic circuit will also have the same effect -- to decrease frontal activity.

The fornix is the main output of the hippocampal formation. It is an extremely large tract with over one million myelinated axons on each side. The fornix's major target is the ipsilateral mammillary body (part of the hypothalamus), whose output is also highly focused on the anterior thalamic nuclei. The anterior nucleus projects to the cingulate gyrus. The cingulate gyrus connects to the entorhinal cortex, which for practical purposes works almost as a unit with the hippocampus. The subiculum and the hippocampus also project back to the entorhinal cortex, which has diverse efferent corticocortical connections, sending handshakes to the prefrontal and orbitofrontal

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[585] Ibid.
[586] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[587] Boulos-Paul Bejjani, Philippe Damier, Isabelle Arnulf, Lionel Thivard, Anne-Marie Bonnet, Didier Dormont, Philippe Cornu, Bernard Pidoux, Yves Samson, and Yves Agid, *Transient Acute Depression Induced by High-Frequency Deep-Brain Stimulation,* Centre d'Investigation Clinique, Federation de Neurologie and INSERM Unite 289.
[588] John H. Martin, *Neuroanatomy.*

cortices as well as to the parahippocampal, cingulate and insular gyri. Collectively these areas also have widespread projections. Thus the hippocampal formation can influence virtually all association areas of the temporal, parietal and frontal lobes as well as some higher-order sensory areas with as few as three synapses.[589]

As part of the isorropic circuit, the lateral septal nucleus receives projections from the hippocampus as well. The medial septal gives rise to GABAergic and cholinergic projections back to the hippocampus. Consequently, when the hippocampal signals to the medial septal nucleus slow down, the GABAergic feedback signals slow down as well; the hippocampus' activity speeds up and, through the fornix, ultimately, the anterior nucleus becomes more active. The anterior nucleus in turn signals the cingulate gyrus. Under normal conditions, the cingulate gyrus speeds up and eventually the hippocampus speeds up, returning to normal. This is a damping system: when things slow down, it speeds them up and vice versa.

Connections from the emotional systems to the cognitive systems are stronger than the connections from the cognitive to the emotional. Emotions dictate cognition much more than memories and thought dictate emotions. The cingulate gyrus, with its rich cortical connections, under this artificial stimulation of the left substantia nigra, is tricked into assuming that depression (a whole array of negative emotions sending slowed down echoes and confusing signals) is present. As a result, the cingulate slows down its echoes to the reticular nucleus overlaying the anterior nucleus. When the reticular nucleus, inhibitory in nature, receives less excitatory signals, less inhibition produces more activity in the underlying interior of the thalamus. The decrease in inhibitory signaling to the anterior thalamic nucleus corresponds with increased activity (blood flow). This is a direct response to the artificial stimulation. Under normal conditions the activity of the anterior nucleus would dampen out.

The manipulation of the body is controlled to a greater degree from the right side (areas 7 and 5) with their rich connections contralaterally to the somatosensory areas (areas 1 and 2); the left side being in charge of manipulation of objects. If GABAergic (inhibitory) neurons in the left substantia nigra innervating the ventral nuclei of the thalamus are stimulated, the inhibitory signals mirrored to the left primary motor area (4), the left supplementary motor area (6) and primarily the left somatosensory area (areas 1, 2 and 3) will also be detected on the right side (because of the extensive contralateral connections), which controls body movement. The right side interprets these inhibitory signals on the left side to mean the absence of the body, a normally impossible situation, and resolves the paradox by feeling "the body being sucked into a black hole." It is a similar situation to the "blackness in the head" reported by depressed patients. The reduced activity in the cortex will immediately send different echoes to the thalamus. When the thalamus interprets these echoes, it automatically activates the corresponding emotions, in this case, a spectrum of negative emotions.

Moreover, when the lateral nucleus of the amygdala receives the appropriate signals (slower) from the sensory thalamus, and the basolateral nuclei receive slowed down echoes from the sensory cortical areas in the temporal and insular cortex and from the association cortex, depending on which particular combinations, particular negative emotions will be activated. The major afferent connections are directed back to the cortex, directly or indirectly. The cortical areas receiving a direct projection from the

[589] Ibid.

basolateral amygdala are the limbic association cortex – which includes the cingulate girus, temporal pole and the medial orbitofrontal cortex – and the prefrontal cortex. These projections mirror the thalamic projections of the thalamic ventral nuclei. In this way, the thalamus and amygdala are reinforcing a particular emotion through the echoes they receive from the cortex. The central nuclei regulate the autonomic nervous system as it receives viscerosensory information and will help mediate emotional responses.[590]

We have to keep in mind several other feedback loops. The primary somatosensory cortex sends afferent fibers to the red nucleus and, more specifically for area 2, to the substantia nigra, the pontine nuclei and the central gray nuclei. For areas 5 and 7, subcortical projections are to the lenticular nucleus and the tegmentum (ansa lenticularis and lenticular fasciculus). The primary motor area (4) has efferent fibers to the thalamus, lenticular nucleus, zona incerta and substantia nigra. The supplementary motor area (6) has afferents to the putamen, globus pallidus, the subthalamic nuclei and diencephalic nuclei, to the brainstem, in particular the pontine nuclei, relaying to the neocerebellar cortex. Also, it projects homolaterally to area 8 and contralaterally to areas 4 and 6, the gyrus cingularis and the parietal lobe.[591]

When the feedback loops reduce excitatory activity, particularly to the substantia nigra, this will tend to reduce the GABAergic (inhibitory) activity being conveyed to the thalamus, thus restoring a balance by increasing activity.

In this artificial case, where stimulation is being done electrically, the balance can't be restored. But as soon as the electrical stimulation stops, the reduced excitatory activity will produce a quick reduction of GABAergic signals to the thalamus. The lesser rate of inhibitory impulses will speed up the cortex and produce temporary hypomania until balance is restored.

The difference between stimulating the left or the right substantia nigra pars reticulata is the following: when you stimulate the left side, the activity of the brain slows down (especially in the left frontal lobe) *and*, coincidentally, the left hemisphere is less active than the right, tricking the emotional systems into triggering the whole array of negative emotions that is depression. The isorropic circuit will detect this and the brain will feel the unpleasantness of depression. In contrast, when stimulation is to the right side, the brain slows down (particularly the right frontal lobe) *but* the right hemisphere is less active than the left. This is interpreted as desirable by the emotional systems, so no emotional action is taken (no change, means more of the same). When the isorropic circuit detects this condition, the brain feels calm or neutral. This is a subtle, but a huge difference with respect to emotional responses and behavioral outputs of the brain.

Under stress, the adrenal glands release glucocorticoids into the blood stream. Glucocorticoids alter features of all three neurotransmitters (serotonin, norepinephrine and dopamine), the amounts synthesized, how fast each is broken down, how many receptors there are for each neurotransmitter, how well the receptors work, etc. Moreover, stress has been shown to produce similar changes as well. There is a link between stress hormones and depression. It has been shown that applying drugs that work on the adrenals to reduce glucocorticoid secretion lessens depression.[592]

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[590] John H. Martin, *Neuroanantomy.*
[591] Jean Talairach & Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*
[592] Robert M. Sapolzky, *Why Zebras Don't Get Ulcers.*

The hippocampus is especially loaded with receptors sensitive to glucocorticoids. Glucocorticoids have the ability to inhibit glucose storage in neurons, particularly in the hippocampus. It is not a huge effect, about 25 percent less than normal, but certainly enough to affect neuronal behavior. More important, excessive glucocorticoids, for prolonged periods, make synaptic connections shrivel and the complexity of neural networks decline. There is evidence that, in the extreme, prolonged exposure to stress or glucocorticoids can actually kill hippocampal neurons.[593]

The levels of glucocorticoids are much higher in depressed patients. The effects of these on the hippocampus are manifested as memory and learning problems.

The repeated assaults on the hippocampus due to stress hormones, cortisol and corticotropin make the hippocampal formation less responsive to any input, in particular the GABAergic input from the isorropic circuit, particularly from the medial septal and the diagonal band of Broca. As a result the hippocampus in turn, will send more signals to the lateral septal area.

Stress hormones probably affect the mesocorticolimbic dopaminergic system originating in the ventral tegmental region projecting to the nucleus accumbens and the amygdala as well as various parts of the cortex, particularly the frontal lobes. Thus, stress hormones increase the threshold at which the sensation of pleasurable will be perceived. Anhedonia will set in when stress levels are too high or prolonged.

The thoughts and memories of each person will be uniquely linked to individually varying negative emotions. As a consequence each person will express a depressed state differently or even express consecutive depressed states in varying ways. Depression seemingly manifests itself in many forms, but it really is a manifestation of each individual's thoughts, memories and his/her relationships with different negative emotions. In a depressed state, the strange calmness attractor of the isorropic circuit moves far into the negative emotional side with the result that the isorropic circuit now attempts to maintain a steady balance in this disturbed state. Our emotions lie at the center of the experience that most of us take for granted, the presence of a well defined, predictable and unique subjective entity we call the "self." When our emotions become disordered, our sense of self comes into doubt; because of this, the individual suffering depression can have great difficulty perceiving the difference between health and illness.

All the present negative emotions mixed up and coupled with the inability to remember and to think produce a feeling of indescribable blackness, of unfathomable emptiness, of interior doom, of unimaginable anguish, inexplicable fear, which adds to a greatly diminished sense of self. Because I believe it is so important to understand this state, I have given it its own special name, idiozimia (from the Greek, idios=self and zimia=loss). And, I have named a partial reduction or diminution of a sense of self, archidiozimia (from the Greek archi=beginning). Archidiozimia is similar to what psychologists and psychiatrists term dysphoria. Archidiozimia is likely to occur when the isorropic attractor is pushed far to the negative side by intense negative emotions. Under these conditions the isorropic circuit's balancing functions are locked into a negative emotional state. Archidiozimia is present in depression, and depending on the degree of depression this state will drift towards idiozimia, the total loss of self. Idiozimia or archidiozimia are possible in various intense emotional states, such as anger, mania, fear, and even hatred or jealousy.

[593]Ibid.

In depression most all negative feelings are experienced simultaneously, producing a body state that is impossible for the brain to interpret correctly. As a result, some of these negative feelings, of worthlessness and guilt trigger associated thoughts that may include negative evaluations of one's worth or guilty preoccupations over minor past failings. This feedback worsens archidiozimia, and leads in a downward spiral to idiozimia. In severe depression, idiozimia is a feeling worse than terrible grief.

The instability of the self can be seen in the unsuccessful regulation and uneven transition between emotional states. This disorderly activity negates access to LeDoux's "core of the emotional system," what I am calling the "self." The emotions, cognitions and memories formed during childhood that make up the "core of the self" are inaccessible, including the non-verbal affective memories.

In cases of intractable depression resistant to drugs, electro-convulsive treatment or other therapies, in an attempt to disconnect the negative memories and eliminate the negative emotions, in the extreme, cutting connections between the cortex and the rest of the brain, a procedure called a cingulotomy or a cingulum bundle cut, sometimes, can make the depressive symptoms abate. By the same token, cutting the projection pathways from the cortex to the rest of the brain prevents positive memories from activating positive emotions, which is why a cingulotomy is only used in very extreme cases.[594]

Depression is often a precursor to severe problems of the brain. It appears to predict, to some degree, senility and Alzheimer's.[595]

The brain is continuously attempting to maintain a perfect balance between the outside changing stimuli and the internal emotional make up. In this sense, there are endogenous changes produced as reactions to external events. Most people, given the right circumstances, can become depressed. The levels of vulnerability vary greatly, but in about two thirds of unipolar depression cases, severely threatening life events are responsible for triggering the depression.[596]

In general, but not always, the first episode of major depression is associated to a life event; the second somewhat less; and by the fifth episode, events have no relation to depression. Depending on the levels of vulnerability, the brain tries to adapt to repeat bouts of depression, to this impossible scenario of multiple negative emotions present simultaneously, and, in one in five, the depression becomes random, cyclical, internally generated and dissociated from life events.

The brain, while in a depressed state, cannot store or retrieve memories in a normal fashion relating to the multitude of negative feelings that are triggered concurrently. The confusion generated by all the various chemistries simultaneously present disrupts the retrieval (activation) of memories. But occasionally, the brain manages to store recent memories while in a depressed state. These memories will be activated in the future only when the same chemistry is encountered, that is, the chemistry of depression. Because of other retrieval mechanisms, such as implicit or associative memory, the memories created in a depressed state might be activated under certain conditions, and in turn trigger the depressed mood as if it was activating a single emotion. Under these conditions, the depression becomes cyclical, and represents a "new" emotion; an emotion (in this case mood) that has its own emotional competent

[594] Robert M. Sapolsky, *Why Zebras Don't Get Ulcers.*
[595] Andrew Solomon, *The Noonday Demon.*
[596] Ibid.

stimuli. When this happens, the pharmacotherapy and psychotherapy should change accordingly. When the brain creates a particular new emotion (state), one that doesn't produce appropriate responses, an avoidance strategy of the triggers of this state might be the only option.

Stress drives up the rates of depression. One of the biggest stresses is humiliation after loss -- the loss of a valued person, of a role or even of one's image of oneself. Depression rates are greatly exacerbated when they involve humiliation.

In most cases, depression appears suddenly and without warning. Then the brain restores balance slowly and depression disappears gradually.

When any organism is subjected to stress, cortisol and glucocorticoids are released into the blood. In studies of patients with Cushing's syndrome using very sensitive MRI brain scans in which, owing to any number of different tumors, people secrete great amounts of glucocorticoids, it was found that the hippocampus shrunk while the rest of the brain didn't; the more severe the hippocampal atrophy, the more severe the memory problems.[597] Because depressed people are under continuous stress, their cortisol and glucocorticoid levels are accordingly higher, resulting in damage to the hippocampus. When the memory problems become more severe, the likelihood that positive memories cannot be accessed is increased. When the hippocampus is functioning at lesser levels, the context of present emotional situations will be perceived wrongly. These two situations will exacerbate depression.

Under normal conditions emotional transference is routinely achieved. Positive affects facilitate the interactive generation of higher and more enduring levels of positive emotions. Particularly in a depressed state, negative affects generate higher and more enduring negative emotional levels. Emotional transference amplifies the external expressions of emotion, positively or negatively. In general, emotional transference in a depressed state triggers a disequilibrium in the receiver, which in turn forces the receiver to avoid the depressed person to re-establish equilibrium. This in turn leads most people to avoid being around depressed persons, in effect isolating them. This exacerbates the depression as the person participates less, or not at all, in positive emotional transferences.

Depression might be mild, moderate or severe. In cases of mild and moderate depression, the person might seem to be operating normally, but this appearance is only through great effort. The effort to diminish the negative emotional transfer, particularly with close, loved ones in order to avoid the generation of awful feelings in them, leads to isolation. The self-isolation leads to a worsening of depression. The illusion of protecting the loved ones from a depressed state is added to the illusion in others that avoiding the depressed person helps them feel better, to the detriment of the depressed person.

Great effort should be expended to lift the depression. Depressed people are able to receive positive emotional transferences, in spite of the negative emotional transferences they emanate. In fact, the oscillation of positive and negative states in an individual can help regulate the depressed person's state. This is certainly preferable to isolation, which inevitably leaves the depressed person with only internal mechanisms to attempt to reach equilibrium. The continued depression, inexorably, almost always, slowly leads to intolerable conditions.

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[597] Robert M. Sapolsky, *Why Zebras Don't Get Ulcers.*

The survival impulses of the organism are diminished in direct proportion to idiozimia. This greatly diminished or lost sense of self can produce recurrent thoughts of death, recurring suicidal ideation without a specific plan, or, worse, a suicide attempt or a specific plan for committing suicide. These thoughts might range from a belief that others are better off if the person were dead to actually carrying out a specific suicide plan. The frequency, intensity and lethality of these thoughts vary tremendously from person to person from day to day. Motivations for suicide may include a desire to give up in the face of perceived insurmountable obstacles or an intense wish to end an excruciatingly painful emotional state that is perceived as having no end.

19
Suicide, Where Am I When I Need Me?

Why do people commit suicide? For suicide to occur, several elements have to converge. Even though I enumerate them in a particular order, the first condition is the only one that is truly necessary, although not the only one, for suicide to become possible.

First, and foremost, a person must experience idiozimia (a loss of the sense of self). This condition is often, but not always, produced during depression, the depressed phase of manic-depression, and occasionally in schizophrenia, schizophreniform disorder and personality disorders. With slowed or disorganized thinking, negative emotions are triggered and brought to the surface. The isorropic attractor is pushed to the negative side in proportion to the intensity of the negative emotions. At the same time, because of the effect of the negative emotions on the brain, certain modes of thinking, with memories associated to the negative emotions become dominant, while all memories associated with positive emotions, become partially inaccessible. The fact that these latter memories are inaccessible produces a distortion of the sense of self, archidiozimia sets in, and ultimately idiozimia, when there is a complete loss of self. Under these conditions, the isorropic circuit is unable to restore balance.

Idiozimia is a condition that skilled writers that have suffered depression cannot begin to describe adequately. There are no words for it and the best one can hope for is a good image. As an example of these images I have found: I could not find love in myself; a skittering black darkness; reality becomes ghostly; a berth in a pounding hell; a veritable howling tempest;[598] downwards into hell's loneliest black depths; and darkness crashed through the dread. Putting together several authors descriptions probably brings us closer to describing the feeling of depression: The hidden, shadowy terror of devouring misery crashed down on me.[599]

Idiozimia is a menagerie of simultaneous negative feelings that produce in the individual who suffers from it a torment greater than each of its parts. The combination of negative memories and feelings is individual to each person, and this makes each individual's experience different. Just as each person has a unique set of memories and thoughts, so each person will experience depression uniquely. This is what makes depression vary from person to person and even vary in recurrences in the same person.

[598] William Styron, *Darkness Visible.*
[599] Editor Nell Casey, *Unholy Ghost, Writers on Depression.*

A history of a diminution or loss of the sense of self must be the most important predictive symptom of a potential suicide. This loss is a necessary precondition for suicide to become possible. Only in this state is harm to oneself possible. Yet, the development of idiozimia can be sudden and without warning. But archidiozimia or idiozimia alone is not a sufficient condition either; other elements must be present.

This is the reason why so many patients with failed attempts express or acknowledge little insight into their suicidality; they suffered a disconnect from themselves during this time. It is probable that only when they return to a state of idiozimia will they be able to remember exactly what happened, and perhaps to the exclusion of everything else. In this case, it will seem to them, that the time or events between the two suicide events have not happened. With this in mind it begins to make sense of why people with previous suicide attempts are at the greatest risk. When they fall into a state of idiozimia, only the memories of previous idiozimias are available. Certainly a highly disorienting experience to say the least. Also, it is possible that people who have experienced idiozimia without killing themselves, don't remember and therefore can truly say that they have never had any suicidal thoughts or intentions.

When idiozimia is the dominant mental state it becomes clear that skills such as problem solving, emotion regulation, distress tolerance or anger management become almost nil. Similarly, maladaptive personality traits are a product of the distortion of the self influencing both self-image and interpersonal relationships.

Idiozimia can also occur during other conditions, but generally is associated with extreme emotional states. For example, a loss of self can be experienced during extreme danger, as transpires occasionally during war, when a soldier attacks the enemy with disregard for his own safety. Idiozimia also ensues during extreme anger, when attack, assault or death of others can be the result. The term legal insanity could be defined better using this concept; at what point did the individual lose contact with him or herself and stops being responsible for his or her actions.

A second element is suicidal thoughts. The diminished sense of self (archidiozimia), combined with negative thinking, allows suicidal thoughts to emerge which otherwise would be unthinkable. The negative emotions produce intruding negative thoughts. The possibility of inflicting damage to oneself becomes less illogical. There is a huge gap between suicidal thoughts and acting on them, but once the thoughts are part of a possible solution, the gap becomes smaller. The continued intrusion of these suicidal thoughts slowly makes them seem more possible, more likely.

A plan might emerge; this is a real danger sign. The tools or methods for suicide might be perfected or put into place; a very serious sign. At this point, if idiozimia is present, it might just be a matter of time. Suicidal thoughts could have been caused by a previous idiozimia even if at the present moment the self is intact. The problem, however, is that archidiozimia or idiozimia can present itself abruptly and unpredictably. And the loss of self cannot be judged by outward appearances either.

However, suicidal thoughts can be helpful to overcome depression. The suicidal thoughts can provide an element of control in various ways, "I can end it if I can't take any more," or, "I can take this longer because I know that if it gets worse, I can end it." Suicidal thoughts are not necessarily indicative of a potential suicide, only that the suffering is bad enough to entertain suicide as a possibility. Suicidal thoughts might be a manifestation that there is a diminution of sense of self (archidiozimia) but are not in

themselves proof of anything else. Suicidal thoughts might be part of the repertoire of behaviors to help cope, giving a sense of added control to an otherwise impossibly intolerable situation.

Third element: the slow vanishing of inner strength. The intense suffering that accompanies depression and some combination of symptoms in schizophrenia and schizophreniform disorder can be so acute that ending one's life becomes a real alternative. The effort to stay alive in the face of extreme torment seems insurmountable. The struggle to continue a semblance of normalcy uses up all possible energy; only in the mildest or very moderate cases can this outward appearance be achieved to begin with. Hardly any energy remains to do anything else. The desire for calm and peace might be overwhelming but the effort necessary to achieve this seems elusive and impossible. The strength to continue living erodes slowly until death seems a welcome act.

Fourth element: hopelessness. The suffering becomes so great that the situation starts to feel hopeless. The inaccessibility of positive memories inevitably makes relief from the pain seem beyond one's grasp. That the suffering might eventually subside does not seem possible. Slowly, death becomes a longed-for relief. The renewed negative feelings, after having enjoyed a respite, can spiral out of control. Disappointment and frustration add up to all other negative feelings, promoting idiozimia. Perspective on the nature of the pain is lost, magnifying its intensity like a long-felt toothache pushing the individual slowly to a form of insanity. The seeming hopelessness of the situation needs to be obsessively ended. A quick solution becomes imperative. The wrong solution, if continued existence is considered a desired goal, is quickly equated with death. However, if ending the hopelessness of relieving the suffering is considered a necessary goal, death becomes a logical act.

Fifth element: damage to the hippocampus. Because of prolonged and intense stress, secretions of glucocorticoids damage the hippocampus. The hippocampus helps store and retrieve the memories of all related objects to an event, in this way creating a context. When the hippocampus is damaged, the emotional context will be perceived wrongly. The negative emotions, put into the wrong context, will exacerbate the effect of the first four elements. Also, the damage diminishes cholinergic impulses from the hippocampus directed to the lateral septal nucleus of the isorropic circuit and diminish the inhibitory (GABA) feedback signals that normally increase hippocampal activity, but the stress damage doesn't allow the hippocampus' activity to return to normal exacerbating the slowed down cortical conditions. Damage to the hippocampus can also lead to temporal and spatial disorientation, and therefore exacerbate archidiozimia and push it into idiozimia.

Yet, the presence of dopamine on the nucleus accumbens from the afferents from the ventral tegmental area reinforce desires by sending dopaminic signals to the prefrontal cortex (via de MD). The hippocampus' projections to the nucleus accumbens promote needs (or aversions) or desires, whereas the amygdala's projections (because of their emotional component) create or reinforce beliefs that guide responses.

Within the context of the last four elements, or because of their repetitiveness in past experience, the echoes streaming from the cortex reinforce and increase the chance that the thalamus will match these signals with external sensory signals and automatically trigger the respective emotions related to hopelessness, vanishing strength, and thus activate suicidal thoughts. The amygdala will signal the nucleus accumbens and amplify

these thoughts, and turn them into a belief, as the hippocampus simultaneously signals within this context, and turn it into an urge. With a stressed, damaged hippocampus, both the hippocampus and amygdala signal, respectively, an urge to end life, and a belief that death is welcome. This binary combination becomes an unbearable urge to commit suicide by whatever means available. This is what I call the aftoktonic switch.

Sixth element: this is so important that I have given it a special name, the phobothymic switch (from the Greek phobos=fear and thymos=wrath or anger). This element might be independent of the second, third, fourth and fifth elements just described. It is common that depression or schizophrenia is accompanied by anxiety or panic attacks. Depression and schizophrenia are states that clearly indicate that something is wrong, and the fear and anxiety associated with these states can be normal responses to a dangerous mood disorder. However, in order for the amygdala to respond to fear, the prefrontal region must be shut down; otherwise the prefrontal lobes signal the amygdala and fear slowly dissipates when danger is not present. When the amygdala is completely unchecked by the prefrontal lobes, the fear escalates and a panic attack ensues.

The first step of the fight-flight response is freezing, a strategy that helps fool predators into thinking that you are dead or makes it harder for them to detect you. At this moment the phobothymic switch can go either way, fear or aggression can be equally possible. Freezing also provides a small amount of time to evaluate the threat and determine to flee, attack, or simply return to a resting state: false alarm. This state feels strangely both like anger and fear, an eerie feeling like a shiver running down the spine, or hair raising down the back of the head to the middle of the back. In dogs, you can clearly see the hair on their backs standing up. It is a sign that either aggression or flight might be imminent. If the phobothymic switch stays balanced in this state, normalcy returns.

When the anxiety attack or the fear escalates into a full-blown panic attack, there can come a moment when the phobothymic switch is suddenly activated; the flight mechanism switches to a fight response. The uncontrolled fear turns into uncontrolled aggression. In this aggressive mode, the perceived threat, in this case an irrational panic, which is translated as a feeling of imminent death, is immediately met with an anger attack. A confrontation with the biggest known fear, imminent death, becomes not only logical but seems the only solution, the only way to win, the only way to survive. The anger is directed at the offending source of the fear; in this case, one's self. When the tiger has chased us into a dead-end canyon and there is nowhere to flee, we inevitably turn to face it and fight it to the death. There is no other choice. In a normal, healthy situation, at some point the threat is evaluated (not rationally, there is no time) by the cortex and determined that escape is impossible, or conversely, that the threat can be removed by quick action. Either way, the amygdala receives a signal from the cortex and automatically, with the help of the hypothalamus, the response changes from flight to fight mode; from fear to anger; from a panic attack to an anger attack. It is two sides of the same coin, either the left or the right prefrontal areas controlling the fight or the flight response, respectively. The phobothymic switch is an elegant engineering solution to automatically and quickly change the strategy for survival. At some point the organism is better off fighting than fleeing.

The question then becomes when, not if, the panic attack turns into a fight mode. In the case of suicide, when the individual is also experiencing idiozimia or archidiozimia, this switch into an aggressive mode becomes lethal. Each individual, according to his or her experience, will have a different point at which he or she will go from a flight mode to a full fight mode. This point is probably impossible to determine in advance. Being young and male probably increases the probability that this will happen. I suspect that the stronger, mentally and physically, an individual is, the lower the threshold for the panic attack to switch to aggression.

The phobothymic switch described is probably the reason why we lose so many young with no forewarning signs. They themselves are not even aware that this could happen. The first time they experience this is their last. If they survive this first experience, because of some distraction or interruption, they will then move into the category of potentially suicidal. Most of us don't know how we are going to react to a huge threat we have never encountered before, until we are faced with it. Similarly, the phobothymic switch will flip over to attack mode during a panic attack without warning. When this happens, the greatest possible type of aggression, the suicide, lashing out and killing the source of danger, killing oneself, the cause of the panic attack, is a response that the victim hadn't even contemplated before.

Out of the despairing darkness, a calm collectedness comes over the individual as he embarks on facing the greatest fear, death itself. He or she fights his last battle and wins. But by winning can never rise again to fight.

There are two separate, but related conditions that lead to a suicide attempt: one through the aftoktonic switch, i.e., the combination of a strong urge with a strong belief to end one's life; the other, through the phobothymic switch, where uncontrolled aggression is directed to eliminate the source of a perceived threat (the self that created the panic attack).

In some instances, mostly in the case of women, the choice of method for suicide is benevolent enough that the chances for surviving the attempt are greatly increased. Women in general choose less violent physical means to end their lives, increasing the number of suicide attempts in comparison to young men who in turn have a higher suicide rate than women.[600]

20
Is It Really Happening? Schizophrenics and Psychotics.

Schizophrenia and Schizophreniform Disorder are almost the same, except for the duration of the disorder. In Schizophrenia the symptoms should be present for at least six months with at least one month of active symptoms. In Schizophreniform Disorder, the disturbance lasts less than a month.

The essential feature of these two disorders is a mixture of two or more characteristic signs and symptoms, both positive and negative. The positive symptoms are the following: delusions, hallucinations, disorganized speech and grossly disorganized or catatonic behavior. The negative symptoms are: affective flattening (lack

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of emotional responses), alogia (poverty of speech) and avolition (inability to initiate and persist in goal-directed activities).[601]

In this group of psychotic disorders, I propose the imbalance of neurotransmitters is slightly different than in Depression and Manic Depression. Yet, running along similar lines, an imbalance between excitatory and inhibitory neurotransmitters also exists. In this case we have a complex interrelated balance between acetylcholine and dopamine. The picture that emerges here is more complicated than the glutamate-GABA relationship.

Acetylcholine works on two different types of receptors called nicotinic and muscarinic. The nicotinic receptors are of fast onset, of short duration and excitatory;[602] the muscarinic receptors are relatively slow in comparison. Dopamine, on the other hand, can act in an excitatory or inhibitory mode, depending on the dopaminic receptors of the neurons. There are five different types of receptors, known as D1, D2, D3, D4 and D5.[603] The most common and predominant are D1 and D2.[604] D1 is the most abundant and is excitatory in nature. D2, the second most abundant, is inhibitory. D3 and D4 receptors are also inhibitory. To make things more intertwined, some evidence shows that a decrease in acetylcholine excitation produces a decrease of dopamine release.

Dopamine acts in an excitatory capacity in the frontal lobes where D1 receptors are predominant. In the basal ganglia, where D2 receptors are predominant, dopamine acts in an inhibitory capacity. The basal ganglia are involved in integrating sensory information as well as coordinating movement and initiating emotions. Excessive blockade of dopamine receptors in the basal ganglia by antipsychotic medications leads to motor side effects. Dopamine receptors are mostly absent in the rest of the brain.[605]

Dopaminergic (D1) activity from the neurons in the substantia nigra pars reticulata elicit increases in striatal acetylcholine efflux.[606]

Catatonic behavior might be produced by a lack of dopamine inhibition in the limbic system.

It has been recently reported (April 24, 2000, *UMHSmedia@umich.edu*) that the cholinergic system tends to suppress positive symptoms that are exacerbated by an increase in dopaminergic activity, and that the corresponding increase in cholinergic activity then leads to an intensification of negative symptoms. In a series of experiments when acetylcholine was blocked in muscarinic receptors, researchers found significantly increased positive symptoms and lowered negative symptoms. In some circuits, as cholinergic activity is suppressed, there is an increase in dopaminergic activity.

The main evidence suggests that in Schizophrenia and Psychotic Disorders there is less release than normal of acetylcholine. This reduces dopamine levels almost in direct proportion. On the other hand, complicating matters, primarily through dopamine's inhibitory properties (D2, D3 and D4 receptors), a lessening of dopamine in some circuits increases acetylcholine release.

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[601] *Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR.*
[602] http://www.neurosci.pharm.utoledo.edu/MBC3320?acetylcholine.htm
[603] Rupinder Mann, *The Role of Dopamine Receptors in Schizophrenia*
[604] Anne Frederickson, *The Dopamine Hypothesis of Schizophrenia*
[605] Daniel C. Javitt & Joseph T. Coyle, *Decoding Schizophrenia. Scientific American*, January 2004.
[606] Elizabeth D. Abercrombie & Peter DeBoer, *Substantia Nigra D1 Receptors and Stimulation of Striatal Cholinergic Interneurons by Dopamine: A Proposed Circuit Mechanism.*

These last paragraphs do not contradict each other; they are, I suspect, looking at different aspects of the dopamine-acetylcholine balance.

A dysfunction of the mesocorticolimbic dopaminergic system has also been implicated in schizophrenia and depression.[607]

Complicating the situation further, acetylcholine and glutamate act synergistically via their actions at nicotinic ACh receptors (nAChRs) and NMDA receptors respectively. Acetylcholine rapidly desensitizes presynaptic *alfa*7nAChRs receptors and increases glutamate release onto postsynaptic NMDA receptors.[608] This finding suggests that a lowering of acetylcholine could lead to a slight decrease in glutamate excitatory activity. Also, somatically recorded perforant path excitatory postsynaptic potentials (EPSPs) may be reduced by as much as twenty-five percent by blockade of postsynaptic low-voltage-activated calcium and sodium channels. Stimulation of perforant-path synapses results in strong, rapid activation of CA3 pyramidal cells.[609] Here is another instance where lowering of acetylcholine through the action of NMDA receptors could lower the activity of calcium and sodium channels in CA3, and affect drastically the perforant-path EPSPs. This is an interesting example of the echoes being disrupted postynaptically. As a consequence of this, explicit and associative storage and retrieval of memories is disrupted. This in turn exacerbates the positive symptoms of schizophrenia.

A lower level of acetylcholine might also explain why in a study of medicated chronic schizophrenic patients, a lower level of glutamate and glutamine were found in the lower left anterior cingulate cortex. Yet, a higher level of glutamine was found in the left thalamus.[610]

The ability of phencyclidine (PCP) and ketamine to induce a broad spectrum of schizophrenia-like symptoms suggests that these drugs replicate some key molecular disturbance in the brain of schizophrenic patients. At the molecular level the drug impairs NMDA receptors which play a critical role in brain development, learning, memory and neural processing in general. This receptor also participates in regulating dopamine release, and blockade of NMDA receptors produces the same disturbances of dopamine function typically seen in schizophrenia. Thus, NMDA receptor dysfunction, by itself, can explain both negative and positive symptoms of schizophrenia as well as the dopamine abnormalities at the root of positive symptoms.[611] As we have mentioned, a lowering of acetylcholine decreases levels of glutamate, which in turn diminishes the action of NMDA receptors and thus mimics the action of PCP and ketamine.

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[607] John H. Martin, *Neuroanatomy.*

[608] Riekkinen M. & Riekkinen P. Jr., *Nicotine Selectively Enhances NMDA Receptor-Mediated Synaptic Transmission During Postnatal Development in Sensory Neocortex,* The Journal of Neuroscience, Oct 15, 1998, 18(20): 8485-8495.

[609] Nathaniel N. Urban, Darrel A. Henze, and German Barrionuevo, *Department of Neuroscience and Center for the Neural Basis of Cognition, University of Pittsburgh, Amplification of Perforant-Path EPSPs in CA3 Pyramidal Cells by LVA Calcium and Sodium Channels.*

[610] Theberg J, Al-Seeman Y, Willimason PC, Menon RS, Neufeld RW, Rajakumar N, Schaefer B, Densmore M, Drost DJ, *Glutamate and glutamine in the anterior cingulate and thalamus of medicated patients with chronic schizophrenia and healthy comparison subjects measured with 4.0-T proton MRS, Am J Psychiatry, 2003 Dec; 160(12):2231-3*

[611]Daniel C. Javitt & Joseph T. Coyle, *Decoding Schizophrenia. Scientific American,* January 2004.

Another study provides evidence that there is decreased muscarinic receptor density in the anterior cingulate cortex and no evidence for significant changes in these receptors in bipolar and depressed patients.[612]

Several studies show a reduction in both the total cell number and volume of the medial thalamic nucleus in schizophrenics. Structural abnormalities in the thalami have been observed with MRI measures, as well as a reduction in thalamic size coupled with an area of difference in subcortical white matter that connects the thalamus with the prefrontal cortex. Diminished blood flow and metabolic activity in the thalamus has also been observed.[613]

Some schizophrenic individuals also exhibit degeneration of the hippocampal formation, and a consequent increase of the lateral ventricle.[614]

The medial nucleus has extensive connections to the frontal cortex (areas 11, 47, 8, 9, 10, 44, 45 and 46) to the attentional systems (areas 40 and 7) as well as area 42 (auditory integration) and to the cingulate gyrus (area 31). The cingulate cortex (areas 23, 24, 32 and 29) has strong connections to the anterior nucleus.[615] The hippocampus and the amygdala also project to these two thalamic nuclei and their echoes also determine the ultimate regulation of thalamic activity.

Intrinsic thalamic efferent and afferent innervation is by glutamate and GABA: both corticothalamic and thalamocortical projections use glutamate as a primary neurotransmitter, whereas striatal and pallidal afferents to the thalamus are inhibitory (GABA). Further, both GABA and glutamate receptors appear to be differentially distributed in the normal human thalamus. Interestingly, intrinsic thalamic transmission is substantially modulated by other neurotransmitters, such as serotonin and dopamine. D2, D3 and D4 receptors have high affinities for a number of drugs with antipsychotic properties, although each receptor has unique pharmacological features. In particular, the D4 receptor has high affinity for the atypical antipsychotic clozpine.

The psychotogenic properties of some serotonin agonists, and the antipsychotics properties of some serotonin antagonists might implicate serotonin (5-HT) in the pathophysiology of schizophrenia. Over the last few years, a great multiplicity of serotonin subtype receptors has been identified. 5-HT2 binding has often been found to be altered in limbic regions of schizophrenic brains. Like the 5-HT2 receptors, the 5-HT6 and 5-HT7 receptors have particularly high affinities for atypical antipsychotics. The affinities of atypical agents for the 5-HT6 and 5-HT7 receptors are even higher than D4 receptor.[616]

The expression of receptors for both these neurotransmitters in the thalamus confirms that they serve a modulatory function of incoming and outgoing signals in this critical brain structure. Logically, the disruption of one neurotransmitter will disrupt other

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[612] Katerina Z, Andrew K, Filomena M, Xu-Feng H, *Investigation of M1/M4 Muscarinic Receptors in the Anterior Cingulate Cortex in Schizophrenia, Bipolar Disorder and Major Depressive Disorder.* Neuropsychopharmacology. 2003 Dec 17.

[613] James H. Meador-Woodruff, *Neurochemical Anataomy of the Thalamus in Schizophrenia*, Mental Illness Research Association.

[614] John Martin, *Neuroanatomy.*

[615] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain.*

[616] James H. Meador-Woodruff, *Neurochemical Anatomy of the Thalamus in Schizophrenia*, Mental Illness Research Association.

neurotransmitters. The abnormalities relating to serotonin in schizophrenia are probably caused by the dopamine-acetylcholine imbalance.

Animal and human studies suggest that nicotine may alleviate deficits in affective regulation and cognitive function. It is estimated that people with mental illness consume 44.3 % of cigarettes in the U.S.A. Patients with schizophrenia have very high rates of smoking (58-88 %). Nicotine withdrawal has been associated with reductions of dopamine, serotonin and norepinephrine levels in rodents and with decreased excretion of urinary catecholamines (dopamine and norepinephrine) in humans. Since most antidepressants augment dopamine, norepinephrine or serotonin, this might have relevance to the finding that stopping smoking is associated with the re-emergence of major depression in depressed smokers. Ziedonis et al (1994) found increased positive symptoms and reduced negative symptoms that varied proportionally to amount of cigarettes smoked. Hall et al. (1995) found that former smokers had less negative symptoms than current smokers. However, there is no evidence for significant changes in psychotic symptoms with smoking cessation in schizophrenia, according to studies that used the nicotine patch. Nicotine seems to make negative emotions less unpleasant and positive emotions more pleasant. Yet, positive and negative emotions should not be confused with what is called positive and negative symptoms in schizophrenia.

Nicotine alters the function of some neurotransmitter systems including dopamine, norepinephrine, serotonin, glutamate, GABA and endogenous opioid peptides. Nicotine's receptor is the nicotinic acetylcholine receptor (nAChR). Nicotine's stimulation of presynaptic nAChRs of these neurons increases transmitter release and metabolism. Unlike most agonists, chronic nicotine administration leads to desensitization and inactivation of nAChRs with subsequent up-regulation of nAChR sites.[617] This might explain why smokers often report that the best cigarette of the day is the first.

To understand schizophrenia better, it is convenient to start with Delusional Disorder. When the hippocampus is slightly impaired, instead of doing its normal job of associating sensory information to a context, its electrically fused neurons and circuits get locked into a certain configuration, and keep putting the new information into one single particular context. When it does this, it starts to categorize more and more echoes as being related to the same context, even when originally they had been encoded in different contexts. It has been shown that blocking D2 receptors in the ventral hippocampus impairs memory. Impairment of muscarinic (M1) receptors in the brain produces cognitive dysfunctions as well. Also, more dopamine (D2- inhibitory) to the hippocampus leads to more acetylcholine release.[618] This would suggest that lowering dopamine (D2 - inhibitory) to the hippocampus produces less handshakes (acetylcholine related to the glutamate NMDA receptors) to locate relevant memories and construct contexts; it locks in the particular mode in which it is functioning and doesn't switch as needed. The echoes sent to the thalamus are also locked, and this fools the thalamus to interpret that the context is constant. The result is the presence of delusions caused by the mistaken belief or wrong context being associated with the incoming sensory information.

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[617] Tony P. George & Jennifer C. Vessicchio, *Nicotine Addiction and Schizophrenia.*
[618] April 24, 2000, *UMHSmedia@umich.edu.*

All effective drugs for treating schizophrenia block the actions of a class of dopamine receptor. These binding sites, now termed D_2 dopamine receptors (which inhibit adenylate cyclase), are blocked by neuroleptics in direct relation to the antipsychotic potencies of the neuroleptics. No such correlation exists for D_1 receptors (which stimulate adenylate cyclase).[619] And drugs that increase dopamine release mimic aspects of schizophrenia.[620]

Looking at the isorropic circuit, the connections from the hippocampus to the medial septal and the diagonal band of Broca are cholinergic,[621]as well as the feedback projection from the band of Broca to the hippocampus, and the hippocampal commissure is rich in m4 muscarinic acetylcholine receptors.[622] A cholinergic malfunction in this feedback circuit might be the reason why the hippocampus remains locked in only one context and doesn't switch to other, newer, more appropriate contexts.

The projections from the substantia nigra pars compacta and the ventral tegmental area to the striatum are dopaminergic. There is evidence that schizophrenics have an increase of dopamine in the striatum. Studies show that muscarinic cholinergic stimulation dramatically influences the distribution of m2R in striatal interneurons in vivo.[623] The construction of the present is accompanied by sensory signals, which is the difference between imagined and present events. The increased activity produced by the increased dopaminic excitation of the striatal neurons mimics the accompaniment of sensory signals, and this increased activity in the striatum makes imaginary ideas and contexts be perceived as real.

In the case of Delusional Disorder, the delusions are non-bizarre, meaning that they could be conceivable in real life (e.g., being followed, poisoned, infected, loved at a distance, etc.). Apart from the direct impact of the delusions, psychosocial functioning is more or less normal, and behavior is not odd or bizarre (as long as it is consistent with the delusion). There can be mood episodes of brief duration compared to the delusions, but the particular train of thoughts brings these on during this imbalance in the brain.

This slight decrease in acetylcholine has an impact on the thalamus as well. The thalamus is receiving cholinergic inputs from the mid brain, principally from the pedunculopontine nucleus, but acetylcholine by itself cannot activate or shut down the neurons of the thalamus. Closing the hyperpolarizing potassium channel slightly

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[619] Phillip Seeman, *Dopamine receptors and the dopamine hypothesis of schizophrenia.* Synapse, Vol. 1, Issue 2., Pages 133-152. 1987.

[620] John Martin. *Neuroanatomy.*

[621] Gaykema, R.P., van der Kuil, J., Hersh, L.B., Luiten, P.G., *Patterns of direct projections from the hippocampus to the meidal septum-diagonal band complex: anterograde tracing with Phaseolus vulgaris leucoagglutinin combined with immunohistochemistry of choline acetyltransferase.*, Neuroscience. 1991;43(2-3):349-60.

[622] Levey AI, Edmund SM, Koliatsos V, Wiley RG,Heilman CJ, *Expression of m1-m4 muscarinic acetylcholine receptor proteins in rat hippocampus and regulation by cholinergic innervation.* J Neurosci. 1995 May;15(5 Pt2):4077-92.

[623] Véronique Bernard, Ouahiba Laribi, Allan I. Levey, and Bertrand Bloch, *Subcellular Redistribution of m2 Muscarinic Acetylcholine Receptors in Striatal Interneurons In Vivo After Acute Cholinergic Stimulation*, The Journal of Neuroscience, December 1, 1998, 18(23):10207-10218

depolarizes the neurons in the thalamus; in other words, acetylcholine makes the system more sensitive to sensory input.[624] Lack of acetylcholine slows down the thalamus and, as we have seen, this has a direct consequence on the attentional subsystems. In Delusional Disorder the temporal dissociation of the attentional systems produces mild visual or auditory hallucinations. On the other hand, tactile and olfactory hallucinations might be prominent, especially if they are related to the delusion (e.g., infested with insects with delusions of infestation or the perception that one emits a foul odor from a body orifice associated with delusions of reference). This reinforces the locked context.

When the hippocampus locks into a context, the sensory information is filtered through this context and is interpreted accordingly. The delusions produced by this effect fall mostly into a few categories: Erotomanic (another person is in love with one), Grandiose (having some great or unrecognized talent), Jealous (lover is unfaithful), Persecutory (being conspired against, followed, poisoned), Somatic (problems with bodily functions or odors from orifices), Mixed (various delusions together or alternating) and, of course, a category for unspecified (all others).[625]

We have seen that activation of inputs from the prefrontal cortex (PFC) can evoke action potentials in nucleus accumbens medium spiny neurons only during the UP membrane potential state, it has been hypothesized that hippocampal afferents gate PFC-nucleus accumbens information flow by setting accumbens neurons into this depolarized state. Such a gating mechanism may define the ensemble of neurons appropriate to be active in a given context, and its alteration may be responsible for pathophysiological changes in psychiatric disorders, such as schizophrenia.[626]

Patients with Delusional Disorder may develop irritable or Dysphoric Mood as a reaction to their delusional beliefs.[627] This slight slowing down of signaling in the brain can account for why a Major Depressive Episode occurs more frequently in individuals with Delusional Disorder than in the general population.

The basal ganglia circuits are continuously integrating the exterior (visual and auditory signals) space with the internal, body space. Therefore the activity of the basal ganglia influence higher order visual and auditory processing.

The basal ganglia receive input from widespread areas of the cortex, including the frontal, parietal, and temporal lobes, project both to the frontal and inferotemporal cortex. The inferotemporal cortex is critically involved in the recognition and discrimination of visual objects and is the area disturbed in prosopagnosia. But more importantly, the output nuclei of the basal ganglia – the substantia nigra pars reticulata – project via the thalamus to the cortex. Thus the inferotemporal cortex is a source of input as well as a target of the basal ganglia. Visual hallucinations are a major side effect of L-DOPA and other dopaminergic agents used in the treatment of Parkinson disease (30% have this side

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625 *Diagnostic and Statistical Manual of mental Disorder, DSM-IV-TR.*

626 Yukioro Goto and Patricio O'Donnell, S*ynchronous Activity in the Hippocampus and the Nucleus Accumbens In Vivo.* The Journal of Neuroscience, 2001, 21:RC131:1-5

627 Ibid.

effect). Pet scans have shown increased activity in the amygdala bilaterally and the right orbitofrontal cortex.[628]

The basal ganglia normally can detect the difference between imagined and real events; the real events are accompanied by sensory signals. Excessive stimulation of the dopamine receptors in these circuits might be perceived in such a way that imagined events or thoughts are perceived as if they were accompanied by "real" sensory signals, thus becoming confused with reality. In this way, thoughts will be confused with voices, and visual imagery become visual hallucinations. Pet scans reveal that when a person is hallucinating the brain undergoes activity exactly the same as when the patient is hearing an actual voice or seeing an actual object. This should not be suprising, as pet scans have also shown that imagined movments and actual movements produce the same activity in the brain.

As a consequence of the hippocampus locking or tending to one context, combined with the excessive dopaminergic stimulation in the basal ganglia circuits, most people suffering schizophrenia have delusions or hallucinations in narrow categories.

If we look at Schizophrenia as a worsening of Delusional Disorder and we continue to decrease ever so slightly cholinergic activity in the entire brain, the symptoms increase and more of them can be present. Both the positive and negative symptoms can be explained in this manner.

When the hippocampus increases its release of acetylcholine because of receiving more dopamine (D2-inhibition) beyond the levels in Delusional Disorder, Schizophrenia sets in. In this case the delusions are more extreme and can become bizarre as the context of processing sensory information is more distorted. Bizarreness, of course, can be hard to judge. Delusions are deemed bizarre if they are clearly implausible and do not derive from ordinary life experiences. The content of the delusions, as with Delusional Disorder, can be of several themes (persecutory, referential, somatic, religious or grandiose). An example of a nonbizarre delusion is the belief that one is under surveillance. Examples of bizarre delusion are a person's belief that a stranger has removed his internal organs or controls his or her thoughts (thought insertion by aliens); or, his or her thoughts have been taken away (thought withdrawal by some outside force). In Schizophrenia the misinterpretation of perceptions or experiences worsens. Smoking can increase acetylcholine release by its action on the nicotinic nAChR receptors, which neatly explains the high incidence of smokers among schizophrenics.

When the thalamus is slowed down enough, the attentional systems become disorganized and uncoordinated, and the difference between imagined and real is no longer perceived correctly. As we have seen this produces hallucinations. Interestingly, intrinsic thalamic neurotransmission is substantially modulated by dopamine (principally D2 and D4) and serotonin (5-HT). There is a whole family of serotonin receptors (5-HT2, 5-HT2A, 5-HT2C, 5-HT6 and 5-HT7) that have been linked to psychotogenic properties of serotonin agonists and antipsychotic properties of some serotonin antagonists.[629] Glutamate and GABA primarily control the corticothalamic and the thalamocortical connections. Imbalances in serotonin inside the thalamus are probably caused by too little

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[629] James H. Meador-Woodruff, M.D. *Neurochemical Anatomy of the Thalamus in Schizophrenia*.

dopamine (D2 and D4).[630] This would explain why some 70% of Schizophrenics improve their positive symptoms when treated with traditional D2 antagonists.

Hallucinations may occur in any sensory modality, but auditory hallucinations are by far the most common. They are experienced as voices, familiar or unfamiliar, that are perceived as distinct from the hearer's thoughts. Two or more voices conversing with one another or maintaining a running commentary on the person's thoughts or behaviors is particularly characteristic.[631]

Disorganized thinking ("formal thought disorder") is considered by some to be the most important feature in Schizophrenia. Because of the difficulty in developing an objective definition of thought disorder and how to measure it, in a clinical setting, inferences about thought are based primarily on the individual's speech disorders.[632]

It has been established that blocking of the muscarinic receptors exacerbates symptoms of schizophrenia.[633] By inference a lessening of cholinergic activity produces dissociations of different memory systems, even very closely related subsystems that might be used for thinking and/or speech. Manifestations of this might vary: the individual "slips off track" from one topic to another (derailment or loose associations); answers to questions might be obliquely related or completely unrelated (tangentiality); and, rarely, speech may be so severely disorganized that it is nearly incomprehensible and resembles receptive aphasia in its linguistic disorganization (incoherence and word salad).[634]

Once we have understood the causes of the positive symptoms, it becomes easier to explain the negative symptoms. Primarily for the same reasons (decrease of cholinergic activity), but in contrast to a decrease in dopamine (D2 and D4) inhibitory activity in the hippocampus, a decrease in dopamine (D1) excitatory activity in the frontal lobes affects the executive function areas in the prefrontal cortex. Disorganized behavior might present itself in a variety of ways, ranging from childlike silliness to unpredictable agitation. There can be problems in goal-directed behavior or the person might appear disheveled or dressed in an unusual manner (wearing many coats or scarves on a hot day); there might be clearly inappropriate behavior (masturbating in public) or unpredictable and untriggered agitation (shouting or swearing).[635]

This thought disorganization blocks activation of any associated emotions. The systems that so beautifully activate related emotions to certain thoughts are confused by the disorganized nature of the thoughts, and this is outwardly manifested as affective flattening. No emotions mean no emotive responses, and can clearly be seen by the person's face appearing immobile and unresponsive, with poor eye contact and reduced body language. Even though the person might smile occasionally, his or her range of emotional expressiveness is clearly diminished most of the time.

If disorganized speech is related to disorganized thought, alogia might be simply another side of the same coin, manifested by brief, laconic, empty replies. The person

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[630] Ibid.
[631] *Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR.*
[632] Harold I. Kaplan, Benjamin J. Sadock, *Synopsis of Psychiatry*.
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[634] *Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR.*
[635] Ibid.

with alogia appears to have a diminution of thoughts reflected in decreased fluency and productivity of speech.

Again, if in the prefrontal cortex executive functions are slowed down enough because of a lessening of cholinergic-dopaminic excitation, these areas will not be able to coordinate the information from the different memory systems to plan future actions. This will obviously be manifested as avolition. The individual might sit for long periods of time, show little interest in work or social activities and be unable to initiate or persist in goal-directed activities.

It is of utmost importance that when we say reduced cholinergic-dopaminic activity, we keep in mind the complex web of interactions between the dopamine (inhibitory and excitatory) and the acetylcholine (slow muscarinic, fast nicotinic) systems. Both positive and negative symptoms are linked to the dopamine-acetylcholine imbalances. Yet, the positive symptoms seem to be associated to the inhibitory dopaminergic imbalance and the negative symptoms seem to be related to the excitatory dopaminergic imbalance.

The major area for research is the specifics of the balances in each particular circuit. Keep in mind that in some circuits an increase in dopamine (through increased inhibition D2, D3 and D4) decreases acetylcholine activity, whereas in the hippocampus more dopamine (D2) increases acetylcholine release. Also, in other circuits, decreased acetylcholine activity shows increases of dopamine activity, but, overall, a reduction of acetylcholine activity means a reduced production of dopamine.[636] The fine-tuning of these imbalances is the challenge for effective therapies for psychotic problems.

21
Catatonia.

Even though, in general, catatonic behavior presents itself alongside other mental disorders, catatonia can be present on its own. Catatonic behaviors can be present with schizophrenia and schizophreniform disorder (about 15% of cases of catatonia) as well as major depression or any of the manic-depressive states (about 40% of cases of catatonia), obsessive-compulsive disorder, personality disorders and dissociative disorders (about 36% of cases of catatonia), as well as a condition present alone or caused by a medical condition (about 9% of cases of catatonia).

Catatonic motor behaviors include a marked decrease in reactivity that can reach an extreme complete unawareness (catatonic stupor), maintaining a rigid posture and resisting efforts to be moved (catatonic rigidity), active resistance to instructions or attempts to be moved (catatonic negativism), assuming inappropriate or bizarre postures (catatonic posturing), or purposeless and unstimulated excessive motor activity (catatonic excitement).[637]

Manic depression and schizophrenia are present roughly at the same rates in the general population, whereas depression is about seven times more prevalent than either of them. Since catatonia is almost three times more likely to be present with schizophrenia than with depression, most catatonic behavior has been linked to schizophrenia and

[636] http://www.med.umich.edu/opm/newspage/2000/schizo.htm
[637] *Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR.*

proportionately less to other mental disorders. Because of similarities to Parkinson's disease, an imbalance between dopamine and acetylcholine neurotransmitters is probable.

Parkinson's disease has a wide variety of disabilities, identifiable as changes in posture, appearance, walking and balance. One of the hallmarks of Parkinson's disease is a deficiency of dopamine-containing cells in the substantia nigra. In Parkinson's disease there is preservation of the striatal cholinergic interneurons and a loss or degeneration of dopaminergic projection neurons from the substantia nigra pars compacta to the striatum. Parkinson's is characterized by decreased dopaminergic activity and relatively increased cholinergic activity in the basal ganglia. The loss of the dopaminergic neurons projecting to the striatum leads to a depletion of dopamine in the caudate nucleus and putamen.[638]

The substantia nigra is reciprocally connected with the striatum (putamen and globus pallidus) and has afferent connections to the thalamus (ventral anterior, dorsomedial and the ventral lateral thalamic nuclei) as well as projections to the superior collicus. Neurons that project from the striatum to the substantia nigra are inhibitory and utilize GABA and substance P as neurotransmitters. The projections from the substantia nigra to the striatum are dopaminergic. The receptors in the putamen are both excitatory (D1) and inhibitory (D2). The putamen also receives glutamatergic signals from the thalamus and the cortex. The projections from the substantia nigra pars reticulata to the thalamus and the pedunculopontine nucleus are GABAergic.

The putamen, in turn, projects to the globus pallidus external and internal with dopaminergic (D2) and GABAergic neurons. The subthalamic nucleus receives GABAergic input from the globus pallidus. In turn the subthalamic output is glutamatergic and projects to the globus pallidus internal. The subthalamic nucleus-globus pallidus external network is the principal site of reciprocally excitatory and inhibitory neurons in the basal ganglia. Recent studies have revealed that oscillatory processes at the level of single neurons and networks of neurons in the subthalamic nucleus and external globus pallidus are associated with the operation of the basal ganglia in health and are implicated in Parkinson's disease. Under normal conditions, autonomous oscillation of subthalamic nucleus and external globus pallidus underlies tonic activity and is important for synaptic integration. In Parkinson's disease abnormal, low-frequency, rhythmic bursting in the subthalamic nucleus is expressed.[639]

Through the extensive connections of the subthalamic nucleus and the globus pallidus external (the intrinsic nuclei) to the output nuclei (globus pallidus internal, ventral pallidum and the substantia nigra pars reticulata) of the basal ganglia, this network powerfully influences the output of the basal ganglia to the rest of the brain.[640] The output nuclei also project to the pedunculopontine nucleus, which is implicated in limb and trunk movements during locomotion, and to the superior colliculus, which controls saccadic eye movements. The pedunculopontine nucleus sends cholinergic projections to the thalamus and frontal lobes. Through this pathway, a diminution of dopamine indirectly produces a diminution of acetylcholine.

The path (GABAergic and dopaminergic D2) from the striatum to the output nuclei and then to the thalamus and brainstem, known as the direct path, promotes the

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[638] Neil Wilkey, *Parkinson's Disease.*
[639] Mark D. Bevan, Peter J. Magill, David Terman, J.Paul Bolan, Charles J. Wilson, *Move to the Rhythm: Oscillations In The Subthalamic Nucelus-External Globus Pallidus Network.*
[640] Ibid.

production of movement. The path from the striatum to the intrinsic nuclei (reciprocally GABAergic and dopaminergic D2), then to the output nuclei (dopaminergic D2 and GABAergic from the globus pallidus external and glutamatergic from the subthalamic nucleus), known as the indirect path, inhibits the production of movement.[641]

The basal ganglia participate in coordinating movements at a high level, and lesions to the basal ganglia (because of Parkinson's) cause difficulty in initiating movement (akinesia), difficulty continuing or stopping an ongoing movement, rigidity and the development of involuntary movement (tremors).[642]A disturbance of function of the dopaminergic (D1 and D2) neurons projecting from the substantia nigra pars compacta to the striatum allows for greater inhibitory (GABA and D2) output to the intrinsic nuclei and output nuclei. Greater inhibitory input to the intrinsic and output nuclei translates to less inhibitory output to the thalamus. The neighboring thalamus produces excessive excitatory messages that escape and are transformed into oscillating bursts of activity that are relayed through the cerebellum and the spinal cord. This oscillation of abnormal impulses results in limb tremor. This is similar to the hypokinetic loop discussed in the section on attention deficit disorder.

Moreover, when there is reduced GABAergic (inhibitory action) from the projections from the substantia nigra pars reticulata and the output nuclei to the thalamus, the thalamus produces a continuous stream of nervous activity, primarily in the nuclei relating to motor functions. This produces a condition similar to the hypokinetic loop discussed in attention deficit disorder. The ventral anterior thalamic nuclei project to the motor area (6), the oculomotor area that controls eye movement (8) and a speech area (44). The ventral lateral thalamic nuclei projects to the primary motor and somatosensory areas (6 and 4).[643] This continuous stream of nerve impulses to the somatosensory area will produce a marked decrease in reactivity to the environment, which sometimes can reach a degree of complete unawareness. The putamen and the globus pallidus are responsible for integrating the somatosensory information with the visual information, and when the stream of information from the somatosensory area overwhelms them, the visual exterior information is not properly integrated with the motor information. Unawareness of the body is produced by the alteration of the somatosensory area. Unawareness of the environment is partially caused by loss of visual attention, as the eye movements are not responsive to changes in the visual field because of the lack of integration of the extrapersonal and intrapersonal space. The increased signals through the double connections to the motor area from the thalamus (the ventral anterior and ventral lateral)[644] override the normal motor functions and explain nicely the motoric immobility as evidenced by catalepsy (waxy flexibility) or stupor. Just like the excess of nervous activity to the motor area produces paralysis, the projections to the speech area (44)[645] when overexcited can lead to mutism.

Rigidity can be explained in terms of an excessive continuous discharge of certain nerve impulses that control muscle tone; the muscles lock and maintain a rigid posture and resist efforts to be moved.

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[641] John H. Martin, *Neuroanatomy.*
[642]Ibid.
[643] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.
[644] Ibid.
[645] Ibid.

The dorsomedial thalamic nuclei that receives GABAminergic inputs from the substantia nigra[646] projects to the frontal cortex areas involved in planning and executive functions (areas 9, 10, 11, 46 and 47) as well as to the oculomotor area (8) that controls eye movements and the speech areas (44 and 45).[647] The excess excitatory signals reaching the higher executive function areas, along with particular combinations of excess signals from the ventral anterior and ventral lateral nucleus, combine to produce unwanted or unintended motion. This can be present as the assumption of bizarre postures (catatonic posturing), stereotyped movements, prominent mannerisms or grimacing. The lack of normal executive functioning can also be manifested as extreme negativism (an apparent motiveless resistance to instructions to be moved) or the opposite, an excessive motor activity that is apparently purposeless and is not influenced by external stimuli.

Some experiments have been performed to determine if lower serotonin levels may be responsible for senility, but it seems more likely that dementia follows up on damage to brain areas responsible for serotonin synthesis – senility and lowered serotonin are separate consequences of a single cause. It appears that SSRIs do not have much influence on motor or intellectual skills that are affected by senility. Aging can reduce serotonin levels by as much as 50 percent, and Alzheimer's appears to lower this neurotransmitter level even further.[648] So it appears that even with such reduced serotonin levels, catatonic behavior does not ensue.

There are double thalamico-cortical connections to the oculomotor area (8), the primary motor area (6) and the speech area (44). The oculomotor area and the primary motor area are reciprocally connected[649] and in combination with the excess stream of signals from the thalamus can produce echopraxia (synchronization of imitating the movement one sees). The speech area and the primary motor area are also reciprocally connected[650] and in similar fashion can produce the pathological, parrotlike and apparently senseless repetition of a word or phrase just heard (echolalia).

The dopamine-acetylcholine imbalance that can be present at the pedunculopontine nucleus can also be greatly affected by the GABAergic projections from the substantia nigra pars reticulata. More inhibitory signals would mean less cholinergic output. This GABA-acetylcholine imbalance can be dependent on the dopamine-acetylcholine imbalance, but it can also be related to the glutamate-GABA imbalance we have mentioned in depression and manic depression. Cases of schizophrenia in the general populations are about one in eight compared to depression and manic depression; yet, catatonia is almost three times more prevalent in cases of schizophrenia compared to depression (unipolar plus bipolar). Because of this, catatonic behavior is more commonly produced by the dopamine-acetylcholine imbalance of schizophrenia and other psychotic disorders. However, the various manifestations of catatonia are probably related to the exact nature of the dopamine-acetylcholine imbalance (schizophrenia) or the GABA-acetylcholine imbalance (mania and depression) and possibly, and in some cases, to both.

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[646] John Martin, *Neuroanatomy.*
[647] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.
[648] Andrew Solomon, *The Noonday Demon.*
[649] Jean Talairach, Pierre Tournoux, *Co-Planar Stereotaxic Atlas of the Human Brain*.
[650] Ibid.

Moreover, in the case of Parkinson's disease, this imbalance (between the dopamine-acetylcholine) is independent of other dopamine-acetylcholine circuits, as patients with Parkinson's show no impairment in most other mental abilities.

22
Personality Disorders

Every individual is unique, particularly in non-physical attributes. Individuals present variability in a scale of energy, capacity for work, temperament, emotional responsivity, aggressiveness or passivity, risk taking, ethical sense, flexibility and tolerance to stress and change. The composite of these qualities constitutes what is known as personality. Not surprisingly, there are genetic components or tendencies (determined by studies of twins) in the more commonly accepted aspects of personality, i.e., anxiety or serenity, timidity or boldness, the power of drives and the need of satisfaction, sympathy for others and degree of disorganization resulting from adverse circumstances. Other, less commonly accepted personality traits are probably set by learning and experience.

Some traits have been recognized as early as three months and correlating with examinations made at five years of age. Among these individual differences we find activity-passivity, regularity-irregularity, intensity of action, approach-withdrawal, adaptivity-unadaptivity, high-low threshold of response to stimulation, positive-negative mood, high-low selectivity and high-low distractibility. Shyness has been recognized as early as six months.

Kernberg, a major theoretician of severe personality disorders, emphasized the role of excess (unregulated) endogenous aggression. He asserted, "The *most important* cause of severe personality disorders is severe chronic traumatic experiences, such as physical or sexual abuse, severe deprivation of love, severe neglect, unavailable parental objects as familial dispositions *that can lead* to the development of personality disorders.[651]

Sexual abuse is a weak predictor of personality disorders, but a history of neglectful and traumatic experiences co-occurs in these patients. In the case of borderline personality disorder patients, 91% report childhood abuse, and 92% report some type of childhood neglect.[652] As important as these risk factors might be for the development of personality disorders, what about those 8-9% who were not abused or neglected that developed personality disorders; or conversely, what about the ones who were abused or neglected that didn't develop personality disorders.

Careful observation and study of personality disorders have set various diagnostic criteria from which we can infer separate and distinguishable traits, that together, create what we call personality.[653] It is reasonable to assume that these traits are influenced by different circuits or modulated by different neuropeptides or neurotransmitters. Among them, we can identify several traits (or circuits). The overall interaction of the various

[651] Kernberg, O., *Interview with the developer of an object relations psychoanalytic therapy for borderline personality disorder.* American Journal of Psychotheraphy. 1988.
[652] Allan Schore, *Affect Regulation and the Repair of the Self.*
[653] *Diagnostic and Statistical Manual of Mental Disorders. DSM-IV-TR.*

circuits that control behaviors that make up the personality will lead to slight variations which serve to distinguish the various personality disorders.

Personality traits governed by different circuits:

A-) Traits related to bonding and social interactions (avoidance of abandonment; intense and unstable interpersonal relationships; need to be the center of attention; inappropriate sexually seductive behavior; lack of empathy; interpersonally exploitative; preoccupation to social rejection; fear of embarrassment; fear of retribution).

B-) Traits related to impulsivity to act (binge eating, sex, reckless driving, adrenaline junkies).

C-) Traits related to the sense of self (unstable self-image; suicidal behavior or self-mutilating behavior; grandiose sense of self; sense of inadequacy).

D-) Traits triggering emotions (affective instability due to marked reactivity of moods, irritability, anxiety, chronic feelings of emptiness, inappropriate, intense anger, frequent temper displays; envious of others).

E-) Traits related to conditions to action (can't make decisions; preoccupation with detail or organization; perfectionism; moral rigidity and stubbornness).

F-) Traits related to distortion of cognition (odd beliefs, bizarre fantasies, reads exaggerated meanings to others' comments or actions.

One example of a genetic predisposition to a personality trait, albeit to a limited degree, has been found in the expression of thrill seeking, exploration and excitability. According to Cloninger and colleagues, pleomorphism of the dopamine receptor gene on chromosome 11 accounts in a small measure for the genetic variability of this personality type.[654]

I described the isorropic activity and how the sense of self is generated in Chapter Twelve. The interaction of the isorropic circuit with various other loops generates many dimensions to the sense of self. There are genetic components that determine the exact wiring of this circuit and its interaction with other loops, circuits or brain structures. The tendency to trigger certain, specific feelings (and thus behavioral responses) as a result of detecting very particular cues could be set (genetically) lower in very specific circuits. This could explain why some people have a greater tendency to be optimistic or pessimistic, happier or sadder or have a tendency to suffer mood or personality disorders.

The multiple dimensions of the self and personality traits include cognition and affectivity and deeply influence interpersonal functioning and impulse control. The multiple interactions of the isorropic circuit with the hippocampus, the thalamus and the basal ganglia through its output to the brain stem produce specific patterns of perceiving, relating to, and thinking about the internal and external space, and of relations with the environment and oneself. The output of the basal ganglia circuits (skeletomotor, oculomotor, prefrontal and limbic loops), which perform complex integration of emotional states, body-space and visual-space, affect volition and responses to external stimuli. It is important to point out the greater effect of the limbic loop in producing behavior, or more specifically personality traits because of the cortical projections to the ventral striatum from the medial and lateral temporal lobes and the hippocampal formation, and the thalamic output of this circuit to the anterior cingulate and orbitofrontal cortex.

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[654] Allan Ropper & Robert Brown, *Adams and Victor's Principles of Neurology.*

In chaos terms, there exists a genetic predisposition to have the isorropic strange attractor drift slightly from preferred neutral calmness, which leads to the dimensional perspective that Personality Disorders represent maladaptive variants of personality traits that merge imperceptibly into normality and into one another.

The diagnostic criteria used by the *Diagnostic and Statistical Manual of Mental Disorders-DSM-IV-TR* for personality disorders reads like a description of the huge panoply of people we all know. Yet, somehow, we can distinguish when the traits are out of "normal range" leading to personality disorders. We all know someone who is somewhat paranoid, or detached from social relations and discomfort in close situations, or has a disregard for others; is impulsive, or an attention seeker; has a need for admiration or feelings of inadequacy; has an excessive need to be taken care of or a preoccupation with perfection and control. Yet these traits don't necessarily mean there is a personality disorder. A personality disorder is an enduring pattern of pervasive and inflexible behavior that deviates markedly from the expectation of the individual's culture, is stable over time, and leads to distress or impairment.

Allan Schore proposes, "The coping deficits in right hemispheric self-regulation are manifest in a limited capacity to modulate intensity and duration of affects, especially biologically primitive affects like shame, rage, excitement, elation, disgust, panic-terror, and hopeless despair. Under stress such individuals experience not discrete and differentiated affects, but diffuse, undifferentiated, chaotic states accompanied by overwhelming somatic and visceral sensations. Solms (1996) mentions a 'collapse of internalized representations of the external world' in which 'the patient regresses from whole to part object relationships,' a hallmark of early-forming personality disorders. This regressions is equated with Kohut's 'disintegration' into a 'fragmented' or 'depleted' self."

Traumatic attachment experiences negatively affect the early organization of the right brain, and thereby produce deficits in its adaptive functions of emotionally understanding and reacting to bodily and environmental stimuli, identifying a corporeal image of self and its relation to the environment, distinguishing the self from the other, and generating self-awareness. Optimal attachment experiences allow for the emergence of self-awareness (generating a richer set of echoes with a wider range of emotions related to them), the adaptive capacity (a greater tendency for the isorropic circuit to remain near neutral calm) to sense, attend to, and reflect (activate a greater range of memories and emotions) upon the dynamic changes on one's subjective self-states, but traumatic attachments in childhood lead to self-modulation of painful affect by directing attention away from internal emotional states.[655]

Needless to say, all individuals who experience traumatic experiences are not necessarily emotionally unable to adapt to the environment or regulate their internal states. It is important to maintain open the possibility of genetic tendencies in regards to personality traits or disorders.

Personality Disorders are grouped into three clusters based on descriptive similarities. Cluster A includes the Paranoid, Schizoid, and Schizotypal Personality Disorders. Cluster B includes the Antisocial, Borderline, Histrionic and Narcissistic Personality Disorders. Cluster C includes the Avoidant, Dependent, and Obsessive-

[655] Allan Schore, *Affect Regulation and the Repair of the Self.*

Compulsive Personality Disorders.[656] Others recognize a Cyclothymic Personality Disorder.[657]

Personality disorders have obvious similarities with major types of psychiatric illness, but the relation is only peripheral in the sense that the basal ganglia circuits are involved in generating behavior. In this limited sense, Cyclothymic personality is related to manic-depressive disorder. Cluster A would fall into a group with similarities with Schizophrenia. Cluster B would have in common inappropriate emotional responses based on a distorted high sense of self. Obsessive-Compulsive Personality Disorder with OCD, and the other Personality Disorders in Cluster C would share a low self-esteem.

In the case of Personality Disorders in Cluster A, traits related to the distortion of cognition are the most prominent feature.

In the particular case of Paranoid Personality Disorder, a delusional fear of malevolent intentions on the part of others is caused by a continuous cognitive misrepresentation caused by the hippocampus locking into a context of mistrust and suspiciousness. As a result of this, individuals suffering from this disorder are hypervigilant and act in guarded or secretive manner and appear to be lacking in empathy. In response to stress, people suffering this disorder may experience psychotic episodes.

In the specific case of Schizoid Personality Disorders, the lack of cognition relating to emotional transference is the most obvious feature. In this situation, mirror neurons are unable to mimic the emotional expressions of others or activate the attentional systems to perceive an emotionally competent stimulus. This leads to detachment from social relationships and a restricted range of emotional expression; likewise, the hippocampus locks into small variations of contexts dictated by this cognitive restriction. This leads to a lack of desire to enjoy close relationships and choose solitary activities; sex becomes completely secondary, and pleasure from activities becomes rare; and, response to praise or criticism is nonexistent.

In Schisotypal Personality Disorder, the lack of perception of emotional transference is worsened by particular and unusual cognitive interpretations of causal interpretations and external events. These should be distinguished from delusions. On top of paranoid ideation, inappropriate affect, lack of close friends, the situation is compounded by irrational beliefs such as strange ideas of reference, magical ideas (i.e., belief in clairvoyance or telepathy), body illusions, and can cause odd speech or thinking (i.e., vague, metaphorical, circumstantial, overelaborate or stereotyped).

In Cluster B, the isorropic strange attractor tend to lock into the positive emotional side, producing a false sense of high self-esteem, instead of the natural, neutral calmness.

In the case of Histrionic Personality Disorder, the hippocampus projections to the nucleus accumbens locks into a need for admiration (as opposed to a belief for admiration produced by the dominance of the amygdala's projections). The heightened activity produced by this tendency creates a pattern of grandiose behaviors rooted in an inflated sense of self. This promotes attention seeking behavior which results in excessive emotionality, discomfort when not the center of attention, tries to draw attention to one's self using physical appearance, excessively impressionistic speech, exaggerated

[656] *Diagnostic and Statistical Manual of Mental Disorders. DSM-IV-TR.*
[657] Allan Ropper & Robert Brown, *Adams and Victor's Principles of Neurology.*

expression of emotions, is easily suggestible, and considers relationships more intimate than they actually are.

In Narcissistic personality Disorder, this is easier to observe. The heightened activity produces grandiose behaviors based on an inflated sense of self. However, in this case, the amygdala's projections to the nucleus accumbens dominate the hippocampus' tendency to lock into the particular need for admiration, thus creating a belief for admiration and as a result a lack of empathy for others. This produces limited behavioral responses according to variations of contexts: (1) exaggerates achievements and talents; (2) fantasizes of unlimited success, power, brilliance or ideal love, as such, occasionally believes (3) they should associate with other special people; (4) promotes excessive admiration; (5) creates a special sense of entitlement; (6) exploitative of others because (7) lacks empathy, or (8) is envious of others (or others of him or her) and (9) acts arrogantly.

Antisocial Personality Disorder

Borderline Personality Disorder

Cluster C is the easiest to explain of these personality disorder groupings affecting traits related to the sense of self. In the case of personality disorders where the symptom is primarily low self-esteem, the isorropic circuit's strange attractor tends to move and remain on the negative emotional side, maintaining brain activity in both hemispheres slower than normal, perpetuating low self-esteem by triggering negative emotions. The inaccessibility of most positive memories, produced by this equilibrium, insures the continuity of these personality traits.

In the case of Avoidant Personality Disorder, as part of the low self-esteem, we have exaggerated fear of criticism, disapproval, or rejection. This leads to pervasive behaviors that guide their cognitive and affective reaction to others.

In Dependent Personality Disorder the low self-esteem is accompanied by a pervasive need to be taken care. This leads to a dependence on others for most aspects of everyday life, such as decision making, avoidance of taking care of oneself, and as a consequence, unwillingness to disagree with others, and go to excessive lengths to obtain nurturance and support from others.

From this we can infer, that brains suffering from personality disorders in cluster C lock the hippocampus inflexibly into low self-esteem contexts, creating the need to act accordingly.

In Obsessive-Compulsive Personality Disorder, the intense firing in the orbital frontal cortex causes a strong visceral sensation or anxiousness that incorrectly signals something is wrong. The interactions of the isorropic circuit with the orbitofrontal circuit, through the dorsolateral circuit, as a reaction to the anxious feelings, cause a behavioral pattern of preoccupation with orderliness and perfectionism to correct the wrongly perceived situation. The reason for the visceral sense of dread that OC Personality Disorder patients suffer is that the orbital frontal cortex and the anterior cingulate gyrus are wired directly into the gut control centers of the brain.[658]

The lateral orbitofrontal circuit arises in the lateral prefrontal cortex and projects to the ventromedial caudate nucleus. The pathway from the caudate nucleus follows the dorsolateral circuit (through the internal pallidum segment and substantia nigra pars reticulata and thence to the thalamus) and projects back to the orbitofrontal cortex.

[658] Jeffrey Schwartz, *The Mind and the Brain*.

Damage to this area is associated with irritability, emotional lability, failure to respond to social cues, and lack of empathy. OCD is also associated with disturbances in the orbitofrontal area and circuit.[659]

The threshold for release of stress hormones, which is felt as anxiety, is much lower than in the rest of the population. Tonically active neurons (TANs) in the caudate nucleus integrate emotion and thought. TANs are the neurons responsible for activating related thoughts to specific emotions and vice versa. In Obsessive-Compulsive Personality Disorder the TANs lock into certain patterns and shift the outflow in the striatum when detecting distinct environmental cues, associated with different emotional meanings, eliciting particular behavioral and cognitive responses. This produces responses within a narrow framework – such as preoccupation to details, overconscientious, inflexibility, rigidity or stubbornness—which are perceived to be needed to make things right.

The putamen, through the direct and indirect path, serves as a major center to initiate action; the caudate nucleus links thoughts with feelings. As with OCD patients, the striatum is overactive because of the lower threshold for firing of the prefrontal loops (skeletomotor, oculomotor, prefrontal cortex and limbic loops). To counterbalance the anxiety created by this, a pervasive need for mental and interpersonal control is promoted, reflected as an exaggerated preoccupation with orderliness and perfectionism.

Consonant with this, obsessive-compulsive personality sufferers create rules, trivial procedures, lists or schedules which affect behavior in various forms: (1) the main point of an activity is lost; (2) task completion becomes impossible; (3) excessive devotion to the activity itself; (4) inflexibility in questions of morality or ethics; (5) hoarding of worn-out or worthless objects, or money.

Research has revealed that patients suffering borderline personality disorder, when stressed, attribute high levels of primitive, negative ("all bad") evaluations to others (splitting), exhibit poor empathy and psychological understanding, manifest more intense negative responses to everyday life events, and show an increased sensitivity to even low-level emotional stimuli. These severe deficits in socioemotional functions are paralleled by structural defect in limbic areas involved in the processing of socioemotional information. A growing body of neurobiological research has demonstrated dysfunctions of the amygdala and the orbitofrontal cortex, in both PTSD and borderline personality disorders.[660]

23

Conclusions

[659] Eric Kandel, James Schwartz, Thomas Jessell, *Principles of Neural Science.*
[660] Allan Schore, *Affect Regulation and the Repair of the Self.*

The central nervous system connects most body parts to the brain. Using these connections, in a simplified way, following the principle that neurons that fire together stay together, a complete map of the body is created in the brain by integrating several sensory maps; the one for hot; the one for cold; the one for pressure; the one for pain; and the proprioreceptive one. All of these sensory maps, the somatosensory regions, together, when perceived by the brain, create the illusion of the body. This illusion, in turn aids the control of the movement of the body. Each body part is represented in the cortex by the equivalent of a memory of the respective part. When the brain perceives the body it feels it.

The left hemisphere controls the right half of the body and the right hemisphere controls the left half. The actual control of movement is done through an area of the brain, the primary motor cortex that sends the commands to each muscle to contract or relax. The fine-tuning and the exact timing of the sequencing of the signals are achieved with the help of several other brain areas, the premotor and supplementary motor cortices. These areas serve as memory banks, where the exact sequence of motions is stored. The cerebellum, also continuously receives information from many areas of the brain and body. The cerebellum does a fine adjusting of the movements, by comparing the intended movement with the actual result through a series of feedback loops. The cerebellum receives input from many components of the limbic system and the extraocular systems, from the brainstem and spinal cord, and from most sensory systems. The cerebellum acts indirectly in controlling movement with signals to the brainstem and the thalamic relays to the cortex. The brainstem motor pathways are mostly concerned with rapid postural adjustments and correcting misdirected movements.

Some of the outputs from these somatosensory/motor areas in the cortex, together with information from the brain stem, primarily the substantia nigra, are sent to the basal ganglia, which perform the function of creating a dynamic representation of the body in order to perceive and control movement. Likewise, a map of the external world is created and the two are integrated to create a single space in which the body is imbedded. In this elegant manner the brain can control the movement of the body through the environment.

A transfer of information occurs between the descending motor pathways and the ascending sensory pathways in the spinal cord. This serves as a short cut to confirm that the motor command is on its way, even before reaching the muscles, and closes the loop faster than waiting for the feedback signal that the actual movement was performed.

From a systems analysis's point of view, for the body to successfully navigate through the world, a spatial representation of the environment in some form must be created. There are two main visual systems. The two are laid out side by side. There are two types of ganglion cells, on-center and off-center, and both of these divide into M and P cells. The P cells have thicker axons, send signals faster and are concerned with color contrasts. Both M and P cells send their outputs to the lateral geniculate nucleus of the thalamus, but only the M cells as well as a number of miscellaneous other cells project to the superior colliculus at the top of the mid brain. This so called secondary system, because it seems to be doing less, is in control of eye movement and some aspects of visual attention. However, the colliculus is a three-layered structure. The upper regions receive various kinds of retinal, auditory and somatosensory inputs. The inputs are crudely mapped. This secondary system is the main visual system in lower vertebrates, so it must be performing some integrative functions. At a more primitive level, it must be

creating a spatial map of the environment in some crude form, and when sensory signals from the environment indicate a change, it would help direct the attention of the sensory systems on the change.

In higher vertebrates, the so-called primary visual system is located in the occipital lobes. It is the cortical site of a memory bank, where first, a spatial map of the external environment is constructed. This spatial map is mostly concerned with where everything is and perhaps with objects moving in relation to the background. Secondly, memory banks are used to aid in interpreting what is out there; at the most primitive level, determining if the object is a threat or an opportunity. In a more refined way, I see the red Corvette approaching fast down the street between the trees. Response: in relation to my body, I need to move to the sidewalk (or risk serious injury or death).

The information from the visual areas must be made accessible to various brain regions specializing in different things. At the most basic level, the spatial map of the world is sent to the basal ganglia, whose circuits proceed to integrate this map with the body map, thus producing one, single, seamless map, which is a very ingenious solution for controlling the body as it moves through the environment: the body becomes one with external space.

The circuits of the basal ganglia are in a unique position to determine small variations of the external world and/or the body. This ingenious system allows small changes in input, reflecting changes in the environment, to naturally produce slightly different output from these circuits. Since most of the output of these circuits is directed to the thalamus, it is placed in an excellent position to automatically focus the senses on these small changes through the activation of the attentional systems whenever the output signals of the basal ganglia change. Additionally, since the basal ganglia circuits are tracking the external and internal spatial maps, the thalamus is well placed to use this information to direct the senses. The information of where the body is in relation to the environment is key to directing the senses to the place of the stimulus triggered the awareness of a change.

The creation of extensive memory systems is a basic evolutionary tool to aid, in motion and creating a spatial map of the body, in seeing and constructing a spatial model of the outside world, and then to further identify what the objects in the outside world actually are.

Control of the body was co-opted for other purposes different than locomotion, reflecting a total integration of most brain systems. The internal emotional state, primarily, through the generation of facial expressions and body postures can be communicated to others. Hand, arm and facial gestures, together with body language are probably a precursor to the generation of sounds that form the basis of verbal communication. It is no coincidence that the areas relating to speech and understanding language are adjacent and reflect the fact that in many ways they aid each other.

The thalamus is the main gateway to the brain. Here all sensory and body signals converge. The extensive memory systems in the cortex produce a series of echoes that constantly stream to the thalamus. These echoes aid the thalamus in relaying the incoming signals to the appropriate areas in the cortex. The reticular nucleus achieves this by matching incoming sensory signals to echoes. When a match is found the sensory signal is mirrored to the area that generated the echo. The mirrored signals from the thalamus arrive in the cortex in layer IV, which serves as the input layer. Layers II and III

are normally used for cortico-cortical handshake signals, even through the corpus callosum from one hemisphere to another. Layers V and VI are the output layers of the cortex, and send echoes and command signals.

The memory systems establish a series of handshakes between associated memories. Common characteristics between memories strengthen the handshakes. The shared characteristics might be similarities in properties, like color, shape, taste, smell, temporal occurrence, and so on, and more importantly sharing an emotional component as well. When the sensory signals arrive at the cortex, all pertinent handshakes are activated, in turn activating other relevant areas.

Additionally, the echoes and handshake signals can have a tag that serves as a form of address to indicate where else the incoming signal should be relayed. In this way, a quick an elegant system directs incoming signals to the appropriate areas as well as activating other related areas that can aid in interpreting the signal. Each sensory system evolved memory systems to aid in interpreting the signals of each sense. Eventually, other memories evolved to aid in this process. Some of these memory systems overlap and are used to interpret signals from various senses. In general, each sense has its own channels to the thalamus and relays to specific primary sensory areas of the cortex. These in turn, activate and interrelate with secondary areas. In a hierarchical and ascending series of steps more information is extracted. In the case of vision, moving up the hierarchy, the size of the receptive fields increase and the features to which groups of neurons respond becomes more complex. The general pattern is that each “higher” area receives inputs from “lower” areas. Ultimately, there are specific areas that respond to certain categories of objects, like faces or man made objects to name a few. Ultimately the information must be presented in some coherent way to be interpreted.

The memory systems in turn, were co-opted for other uses. The visual memory system evolved into visual imagery, the ability to manipulate objects in “the mind’s eye,” create the visuals during dreaming, or even thinking in terms of vision “in one’s head.” The auditory memory systems were co-opted to construct out of sounds, words, and eventually language and prosody. These communication systems were further co-opted for thinking as “voices in our heads.”

The engineering solution evolved through natural selection concerning memory is manifold, but primarily, it is an index system using shared characteristics. The shared characteristics might be in a primordial system of such basic qualities as color, shape, or movement. Evolution evolved to more complicated memory systems to help identify and store more complex patterns, with still with more complex shared characteristics; like faces, tools, plants or words. Ultimately, even more ingenious storing systems, using even more (apparent) complicated shared characteristics -- emotions and chronology -- evolved. From a chemical point of view, these characteristics are perhaps easier to store, as the particular chemistry of an emotion becomes an integral part of the memory associated with emotion.

In this way, memory is linked to emotions, and to another fundamental evolutionary use of memory -- learning. The basic circuits for emotion, learning and memory evolved apart from the sensory and motor systems. The different sensory and motor systems are structurally and functionally independent circuits but are integrated by the basal ganglia circuits. This functional independence makes sense. For example, although perceptions are enriched when information from various modalities is

integrated, you can nevertheless identify a ball by touch alone or a dog by the sound of a bark. In contrast circuits for emotions, learning and memory are highly integrated from the start. This reflects the fact that emotions are automatically triggered according to echoes set in memory that represent an ECS when detected by the thalamus. When a match is found, the thalamus triggers the emotion, mirrors the signal to the area where the echo originated, and a cascade of handshakes is activated for further analysis of diverse sensory information.

Again, we find that two key subcortical structures, the hippocampal formation and the amygdala, form distinct neural circuits that mediate the two major limbic system functions: learning and memory, and emotions. The cortex is an expanded system that aids and promotes these processes at a much more complex level.

The integration of the attentional systems with the sensory memory systems performs two basic functions: interpreting the present and recreating the past. Short-term memory lasts only for a few seconds, maybe half a minute. Important or novel events are remembered better than routine or common occurrences. Events that have many relations and thus establish many handshakes are more easily remembered than events that have very few other associations.

To establish a durable memory, incoming information must be encoded much more thoroughly or deeply by associating it meaningfully with knowledge that already exists in memory. In other words, extensive handshakes must be established between many of the characteristics of an object or event. Attention to shared characteristics with previous memories will allow a quicker and more extensive series of handshakes to be established, and facilitates tying into the previous existing sets of handshakes. Mirroring incoming stimulus according to echoes that are similar will activate these. It is a highly efficient system to file memories away and tie them into the old ones.

There is some evidence that the cortex developed from two more primitive sources: the archicortex (the hippocampus) and the paleocortex (olfactory areas). The archicortex (hippocampus) and paleocortex (olfactory cortex) are older cortices that exhibit limited lamination, and are referred to as the allocortex. The evolutionary progression of cortical zones moves from the allocortex to the 6-layered neocortex (or isocortex). However, 2 intermediate structures are encountered. The first is the periallocortex, which consists of cortical areas immediately adjacent to the allocortex. The second is the proisocortex, which includes the paralimbic (cingulate gyrus) and parainsular (rostral insula and temporal pole) cortices.[661] This cytoarchitecture reveals the ancient origins of the hippocampus.

Originally, the hippocampus evolved to aid in spatial navigation by constructing a spatial context. This was useful for returning to particular physical locations that provided an advantage or diminished a threat: places were food could be found, a hiding spot from predators, or a safer heaven for a sexual encounter. The glutamate receptors in common with the olfactory bulb seem to suggest an associated evolutionary path between spatial orientation and smell, which makes sense to help find opportunities that emit odors (i.e., food and sex) or avoid threats (i.e., predators that emit odors).

As a result of these encounters with past previous locations, a slight chemical change in the brain ensued, reflecting the benefit or detriment to the organism. These

[661] http://www.cpa-apc.org/Publications/Archives/CJP/2000/April/Dual2.asp, *Dual Cytoarchitectonic Trends* The Canadian Journal of Psychiatry. April 2000.

chemical changes to degrees of opportunity or threat evolved into structures that could trigger emotional responses accordingly. The amygdala and the hypothalamus, evolved along with the hippocampus, and were co-opted to construct an emotional context. Thus emotions could evaluate, in the most primitive way, degrees of good and bad. As the cortex expanded, emotions could not only evaluate stimuli, but could also guide behavior by activating all related emotions. What we already know shapes what we select and encode; things that are meaningful to us spontaneously elicit the kind of elaborations that promote later recall. Our memory systems are built so we are likely to remember what is most important to us. What elicits emotions is important.

The perforant pathway seems to be sending echoes from layers II-III to the hippocampal formation. The subiculum in turn mirrors back extensive signals to layers V-VI of the entorhinal cortex, which project to the cortex, as well as an intralaminar projection back to layers I-III, to reinforce and establish echoes and handshakes to store events and memories and through their interrelations construct a context, along with the projections from the pyramidal cells of the hippocampus and the subiculum to the cortex. The double signaling strengthens the echoes and handshakes in the cortex and makes memories durable and easier to recall later. Here we see, in detail, how the handshake signals are transmitted from layers V-VI to layers I and III. If the echoes are disrupted for whatever reason, the hippocampus can't mirror signals to the cortical areas through these clusters. As an end result, the handshake signals are disrupted, and recall of memories becomes impossible.

The projections from the subiculum to the mammillary bodies and the lateral septal nucleus send information about the context in relation to the present emotion. These signals help evaluate the positive or negative aspects of the present unfolding events. Because of the various feedback connections, this evaluation depends on previous (experience) stored echoes and handshakes.

The hippocampus can alter the signaling of the entire cortex in two ways. First, the hippocampus has fused neurons that act as one. These fused neurons are GABAergic and will fire together controlling many projection cells simultaneously, in this way affecting many areas of the cortex concurrently. Second, through the extensive connections of the perforant-path between cells of layer II of the entorhinal cortex and the pyramidal cells in hippocampal area CA3, it can postsynaptically change the types of echoes emanating from the cortex and adjust the entire brain.

The hippocampus receives simultaneously many signals from the thalamus and echoes from the cortex. The thalamus, in the absence of a match between incoming signals and echoes, automatically determines this is a new and novel event, and it signals the hippocampus. With this ingenious architecture, the hippocampus, through the sodium and calcium channels, alters the echoes postsynaptically and thus can find looser matches from the echoes of the cortex and uses these to determine how to encode the novel event. The closer (not exact) matches will produce more related echoes that increase the chance of recalling the event in the future. In this way the hippocampus aids in storing and retrieving experiences.

Expert knowledge requires the setting of vast memory banks that will quickly and quietly process a lot of stimuli by establishing a set of related echoes in the cortex. These echoes have the capacity to trigger very faint emotional responses. Once these echoes are matched they will automatically trigger subtle emotional responses to matching stimuli.

The sum total of the emotional responses will serve as a guide to behavior or to intuitive knowledge, what is called a sixth sense or a gut feeling. This does not involve any drawn out thinking process, and for the most part guides our behaviors and choices.

The hippocampal response to a novel event is activated when stimuli and echoes from the cortex don't match. The hippocampus then alerts the thalamus, which automatically signal the frontal lobes (regions 9 and 10) and activates area 40 – we recognize this process as paying attention. Attention produces a series of handshakes to many other regions in the cortex searching for similarities with the present stimulus. If unable to find a match (it must be novel), the hippocampus sends impulses hoping to find more echoes from the frontal lobe activation; if a close match is found, a similarity detected, the encoding process starts. Once attention is on the stimulus, other networks may come on line, involving the left frontal inferior lobe, which in turn makes a wealth of semantic associations (area 40 and 39) and knowledge available if needed.

According to chaos theory, stabilization of reverberating circuits allows for the organization of a network that can amplify minor fluctuations over cycles of iteration and influence a system's trajectory. Even though this reexcitational activity pushes the system into a different state, it also facilitates the creation of a path (memory) trace (engram), which is part of an attractor. Attractors, as the name implies, are part of the properties of a system that under certain conditions, inevitably "attracts" the system towards that state. If the end state is always slightly different, it is called a strange attractor. The attractor is a pattern toward which all nearby patterns converge. Attractors might be thought of as either memories or as concepts held by neural circuits. From this perspective, once a part of the network is activated it tends towards the attractor (e.g., it activates the engram).

Memories have a contextual as well as an emotional component. The context and the emotion serve to establish specific handshakes that interconnect all the various elements of an episode. The memory becomes easily accessible in the future under the presence of the same emotion because the specific chemistry generated by the emotion was present during the storage of the memory, and is necessary to recreate the memory. Likewise, when sensory signals detect similarities in context in the environment, handshakes relating to context are activated, and it becomes more probable that the memories relating to that context will be activated. Unconscious memories in the Freudian sense do not exist. Memories are unconscious only in the sense that they are inaccessible for various reasons: wrong chemistry (emotion), not the right context (wrong handshakes), lost handshakes (not a very important memory, displaced by other more significant memories), and even physical trauma (an area of the brain is damaged).

Inaccessible memories are an unpleasant reality. The rate of forgetting is relatively rapid at first and then slows down with the passage of time. However, more recent time periods yield more memories and more distant time periods produce fewer memories. As time passes, we encode and store new experiences that start to interfere with our ability to recall previous ones. As more time elapses the engram becomes more "blurry" (some of the handshakes are lost), the range of cues (matching stimulus and echoes) that elicit a specific episode narrows. This means that when we suddenly and unexpectedly remember a forgotten memory, it may be because we have luckily stumbled upon a retrieval cue that matches perfectly with a faded or blurry engram. Luckily, we don't need to remember everything that has ever happened to us; memories that are never used are probably best forgotten. We are better off forgetting trivial experiences than

clogging our brains with each and every ongoing event, just in case we might want to remember one of these incidents. We do need to form an accurate picture of the general features of our world, and we are reasonably adept at doing so.

Dreaming is a process that helps store recent memories in long-term memory according to emotional content. Obviously, when dreaming, the visual system is activated to create all the visuals of the dream experience. Sounds, speech, and other sensations are integrated into the dream to establish different handshakes for the recent memories so that they can be *stored into longer-term memory in relation to emotional context.* Dreams have content of the last few days but the recent emotional context is referenced to our earliest and very most important emotions; dreaming is a cataloging process of recent important experiences (important, meaning producing an emotional response, otherwise they would not be important) indexed with previous similar emotions for quick recall when encountering an emotional competent stimulus. In the future, events that trigger emotions will activate all the relevant memories. In this elegant way, only the relevant (to an emotion) memories are stored and in the future will be activated and brought to bear on particular situations where an emotion was triggered and the context is similar to past experiences. Response will not be hindered or delayed by searching through all memories.

As mentioned, various memory systems, and different encoding and retrieval strategies evolved from our sensory systems. The reconstructive nature of memory for time is underscored by various illusions and distortions. The specific manner in which we encode an event determines what retrieval cues (echoes matched to stimulus) will later help us remember it. This has been termed source memory and can be extremely fallible. Associative retrieval is an involuntary form of remembering that is triggered automatically by an object or what somebody says. It is an automatic activation of handshakes triggered by matching a stimulus to a related echo. Procedural memory is involved in the development of learning new habits.

In addition, there seem to be three different long-term memory systems: episodic memory, which is for recollecting specific incidents from our pasts; semantic memory, part of the vast network of associations and concepts that underlies the general knowledge of the world; and procedural memory, which allows us to learn skills and know how to do things. Semantic memory is made up of various specialized areas that deal with general knowledge (i.e., objects with shared characteristics, like tools, places, words, etc.). There are also implicit and explicit memory systems. Implicit memory, similar to expert knowledge, is produced by echoes that trigger subtle emotional responses that change the internal state. These somatic changes serve to evaluate how "good" or "bad" the stimulus is. We then "know by a gut feeling."

Different echoes and handshakes are produced by the various sensory and memory systems to indicate relations. This redundancy in the brain allows various memories to operate in a seamless cooperative mode that allows recognizing words (spoken or written), and immediately becoming aware of their meaning, and when we see objects we easily recall how to use them.

Arousal is a minimum state of activity of the brain that permits the use of the senses for gathering information from the environment to aid the organism to orient in space. The reticular formation has numerous downward projections and upward projections. Its major inputs originate from the spinal cord (body state information), the

solitary complex (gastrointestinal information), vestibular information (balance and motion), the trigeminal nuclei (information from the head and neck), and projections from the tectum provide visual, auditory and tactile pattern information. The output of the reticular formation controls arousal states. The neurons can affect excitability directly through diffuse projections rostrally and caudally, or indirectly by contacting other neurons with diffuse projections. Another important path by which the reticular formation affects the excitability of cortical neurons is through connections with thalamic nuclei that have diffuse cortical connections. This has two effects: this ascending system makes the thalamus more sensitive to sensory input; and the arousal state activates the cortex to send a stream of echoes to the thalamus to begin directing the flow of sensory signals.

Awareness is the minimal processing state of sensory impulses. It involves a preliminary detection of the environment and is mostly concerned with spatial orientation. It is primarily involved with where objects are in relation to the body. For this purpose the reticular formation assists the basal ganglia circuits to integrate the external and internal spaces into one. The output nuclei send their signals primarily to the thalamus. Through these signals, the thalamus plays a central role in activating the three main attentional systems: visual, auditory and proprioreceptive. Several loops interact with each other to integrate various aspects of all stimuli. The skeletomotor loop provides information of the body state. The oculomotor loop guides the eye to aid with spatial coordinates of the environment. The prefrontal cortex loop provides assessment of the stimuli receiving information from several associative cortical areas. And the limbic loop provides emotional evaluation of the stimuli. The thalamus, using the output of these loops, can automatically detect any changes. These in turn activate the attentional systems.

Each one of the main attentional cortical areas has triple afferent and efferents with the thalamus. The thalamus, through these connections orchestrates and coordinates the various attentional systems. Attention is a constructive process in the sense that it interprets all the signals from our senses using our stored memories and experiences, and creates the present. Attention is a process that can focus externally or internally. When monitoring the external environment, attention creates the illusion of the ever-present. When attention is focused inwards it activates memory and thinking systems. If not needed it will be downgraded to awareness. Attention can also be voluntarily directed. However, the triggering of an emotion, in general, overrides the attentional systems and causes focus to shift to the ECS.

There is some evidence that the right hemisphere is more involved than the left hemisphere in visual and hearing attention. The somatosensory attention system is also more strongly represented on the right side.

The architecture of the interconnections between the different attentional areas strongly suggests that these systems are working together, particularly as there are strong cortico-cortical connections between them. In a quick and direct manner, the thalamus produces a tremendous flurry of activity as attention is brought to bear on a stimulus. With the appropriate relay of impulses, the thalamus quickly activates visual attention, auditory attention, and simultaneously brings on line the somatosensory attention of the body. Each of these attentional systems sends out its own sets of handshakes to each other to reinforce the activity initiated by the thalamus as it coordinates and integrates all the attentional systems.

Any one of these attentional systems could be activated alone for specific tasks, for example, listening to music or watching a tennis match. When one of these systems is not functioning properly, we might not be aware of this, as we can't pay attention to it.

The prefrontal lobes (areas 9 and 10) have rich connections to the thalamus and can signal it to shift attention. These areas have also been associated with executive functions, and are involved in weighing alternative possible courses of action as well as implementing them. This is where decision-making takes place, allowing you to choose from different courses of action according to what is happening in the present.

The present is at most three seconds considering how our brains work. All else is mere anticipation or reminiscence. The shortest perceivable time division – called the fusion threshold – is between two and thirty milliseconds, depending on the sensory modality. Humans consider two events as presently perceived if their temporal separation is between three milliseconds and three seconds. However, if a sensation on the skin lasts less than 500 milliseconds, an enormously long time compared to the 10-20 milliseconds of transit time required for the nerve signal to travel to the cortex, the stimulation is not consciously perceived. This does not mean that a skin shock has to be at least half a second long in order to be felt, but only that the handshake signals produced by skin shock at the cortex must last at least a half second before the skin shock can become part of the conscious experience. The thalamus tags stimuli in sequential order. If the cortical activity due to the tactile stimulus is not disrupted and is allowed to proceed for the minimum time adequate to produce a conscious sensation (about 0.5 seconds), the touch is registered as part of the ongoing flow of awareness (becomes part of conscious experience). However, the touch is not experienced 0.5 seconds later: it is instead "referred" to the previous time indexed by the initial pulse arrival at the thalamus.

Because of the phenomena called "referred in sequential time," everything was presented to our consciousness in the correct temporal sequences, and sights and sounds were synchronized to match our experience. We couldn't have been conscious in real time; however it feels like we were there, and didn't miss a thing! When the brain detects the feeling of thinking or paying attention it is interpreted as consciousness. There is a difference between a programmed, deterministic mechanical response and the mental process we call consciousness. Consciousness more than perceives and knowing; it is knowing that you know. *The brain feels conscious when it is thinking, and when it knows.*

There exist noticeable asymmetries in our brains. The brain evolved greater efficiency and speed when performing tasks that do not require bilateral pairs (i.e., language, reading, mathematics, recognizing objects, etc.) by concentrating the task to adjacent neurons in one hemisphere, and foregoing the time consuming contralateral communication. Having adjacent neurons form clusters that specialize in particular functions is more efficient than splitting the task into two areas, one on the left and one on the right. However, many functions located on one side are complemented by other functions performed on the opposite side. One of the best examples of this is speech and language, normally found on the left side and prosody, the emotional component of speech, found on the right hemisphere.

Thinking happens in many areas of the brain: the cerebellum, the basal ganglia and many areas of the cortex. It involves many systems simultaneously: sensory memory systems, attentional systems, visual imagery systems, language centers, as well as planning and coordinating systems evolved from motor systems.

Thinking in different modalities basically is an exadaptation of our auditory, visual and somatosensory systems. The memory systems that are used by these three sensory systems have been greatly expanded in Homo sapiens and are also interconnected through semantic memory and our attentional systems. Hearing memories allows us to make sense of speech sounds and build sounds into words; in turn, this gives words a syntactical and grammatical meaning, allowing us eventually to "think" (using this speech ability) in terms of a "voice in our head." In contrast, visual thinking is mostly a right hemisphere activity. The same visual memories that help us construct a map of extrapersonal space and interpret what is in our visual field allow us to "see" in our "mind's eye" and to imagine as well as to manipulate objects in "space" and "turn" them in our "heads."

Thinking, with visual imagery, is an expanded use of our vision memories. Spatial imagery in deductive reasoning activates the attentional systems during reasoning (visual attention and somatosensory attention) along with visual (area 19) and motor (supplementary motor cortex, area 6) regions as well as involving the prefrontal, area 9, involved in thought, cognition and movement planning. Moreover, the anterior cingulate gyrus (area 32) involved in emotions is also activated.

Some forms of social language probably evolved from grooming and hand-gestures as well as from unconscious reflexes and learned reactions in response to social situations and constraints, which in turn can facilitate interpersonal relationships. Gestures universally, across cultures, accompany speech, probably reflecting, from an evolutionary point of view, their older roots.

There is an emotional component to thinking and logic, as emotions can be interpreted as a reaction: when A happens, react with B. There is also a connection between movement and thinking. The intricate machinery of the brain used for coordinating sequences of movements for the whole body were co-opted for logical, step-by-step, thinking. Like over-learned motor skills, these two origins of thought, motor and hearing, allow us to integrate intentions and feelings with behaviors. Logic and deduction evolved as more powerful accessories in thinking using the same architecture and the areas of the incredibly rich memory sequences used to control movement.

Logical or deductive reasoning is more than sentential or spatial. It involves many cortical areas simultaneously, primarily in the left hemisphere, reflecting the cooperation between various abilities: language and speech, hearing, two associative areas (one auditory and one visual), emotional areas (in the left cingulate gyrus) and the left frontal gyrus (areas 8 and 9). This architecture suggests that not only do logic and deduction involve use of the memory systems of speech and vision and integration systems, but also use of areas that integrate cognition, planning behavior, thought and some aspects of eye movement with added inputs from emotions as well as use of movement routines (projections to movement planning areas 11 and 12 and the supplementary motor cortex, area 6).

Just as balance and movement require constant monitoring and the inhibition of unnecessary and distracting movements, so, in parallel ways, do memory, attention [concentration] and language. The same timing and coordination necessary for movements are necessary for sequential processing in language and thought in logic and

deductive reasoning.[662] For the process of thinking, the brain has co-opted the cerebellum to perform the tasks at which it excels: monitoring and sequencing.

The extensive connections to the limbic association cortex reflect the emotional and motivational factors involved in the decision to move. Moreover, emotions affect memories and modes of thinking by changing the chemical milieu of the brain. Emotions, naturally, also alter the functioning of the cerebellum, especially in regard to higher functions like reasoning, logic and thinking.

In general, the left hemisphere communicates its internal states via (thinking in words) linguistic means; what is possible to put into "spoken" thoughts can be expressed with words. The right hemisphere communicates its internal states via (emotions/feelings) external emotional expressions such as facial gestures, body postures and through the prosody in speech. The two hemispheres continuously modulate and complement each other's activities.

The importance of emotions and its relation to specific memories cannot be stressed enough. Small chemical changes in the brain as result of a reward or even a potential threat evolved into structures capable of generating chemical changes as a response to certain stimuli. Changing levels of neurotransmitters, hormones and neuropeptides are the means used by the brain to produce an emotion. When the brain detects an emotion it is perceived as a feeling.

The caudate nucleus is a key structure in activating memories when detecting an emotion, as well as triggering an emotion related to a specific memory. The caudate has numerous afferent and efferent connections with the thalamus. The afferent fibers arrive in matrisomes. Matrisomes are clumps of axon terminals that are also receiving signals from the lateral prefrontal cortex, the orbital frontal cortex and the anterior cingulate gyrus. There are strong efferent projections to the basal ganglia outputs.

Striosomes are clumps of axons receiving signals from the amygdala and the orbital frontal cortex. They are connected to the matrisomes via special neurons called tonically active neurons (TANs). The TANs fire with characteristic patterns when the brain senses something with positive or negative emotional meaning. The caudate nucleus, with its rich connections to the cingulate girus, the cortex, the striatum and the thalamus, activates memories, experiences, modes of thinking and behaviors associated with particular emotions. Once the caudate nucleus sends signals to activate specific memories related to the emotion, the amygdala and thalamus signal the hippocampus to put the emotion into the context of the stimulus and activate only memories that are related to this context. In this way, only memories related to the emotion and a particular context are activated.

Echo signals representing emotional competent stimuli are stored in memory. When the thalamus matches an incoming signal with one of these echoes, the pertinent emotion is automatically triggered, even without further processing of the stimuli. These types of emotions can be called primary and are specific even across species.

Secondary or social emotions are triggered by complex and specific patterns of handshakes from the sensory and other cortex areas that, when presented together, are recognized by the frontal lobes as emotional competent stimuli (ECS) through genetic and learned responses in our childhood.

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[662] Louis Cozzolino, *The Neuroscience of Psychotherapy*.

Once the emotion is triggered the stimulus is mirrored to the cortex for further processing and accordingly signals can be sent to reinforce or dampen the emotion. The frontolimbic system provides a high-level coding that flexibly coordinates sensory and somatosensory information and functions to correct responses as the conditions change, processes feedback information, and monitors and adjusts emotional responses and modulates control of goal-directed behavior. The orbitofrontal cortex is known to functions as an appraisal mechanism using cognitive as well as emotional components. It acts to integrate and assign emotional-motivational significance to cognitive impressions. The right ventromedial prefrontal cortex seems to integrate internal physiological states with important environmental cues, set as echoes, to guide behaviors in an adaptive fashion.

The brain attempts to maintain a one-to-one internal emotional landscape according to the external conditions to produce the best response. For this purpose, the brain creates a dynamic model of the external environment and generates an internal emotional representation in response.

In chaos theory vernacular, emotions represent desired attractors that maintain self-organization by perpetuating emotional equilibrium and resolving emotional disequilibrium. Chaotic variability in self-regulatory activity is thus necessary for flexibility and adaptability in a changing environment.

The purpose of emotions is to initiate certain responses to specific stimuli. They manage this in three ways: (1) the chemistry of the emotional state activates all memories related to the emotion, as this chemistry is specific to the memories; (2) they intrude on the attentional systems; and (3) they initiate certain behaviors, like fleeing or approaching the stimulus.

The nucleus accumbens might be part of the interface between emotion and movement; dopamine release in this region might play a role in goal-directed behavior. This is based on the following: (1) the nucleus accumbens receives massive dopamine inputs from the tegmentum, (2) injection of amphetamine or cocaine (they mimic dopamine) into the nucleus accumbens leads to behavioral activation, (3) the nucleus accumbens receives inputs from the amygdala and other emotional related areas, and (4) the nucleus accumbens sends output to areas involved in the control of movement.

Once an emotional habit is well learned, the brain system involved in expressing it becomes simpler. Once learned, the procedure might be transferred from the accumbens to the cortex.

The hippocampus contextualizes emotions, and if the context is appropriate or inappropriate, reinforces or defuses the emotion respectively.

Emotions do not only elicit specific, related memories and behaviors, but also, through the external expression of these emotions, communicate these emotional changes to others. What is known in psychotherapy as transference and countertransference is a continuous process of emotional information transfer between individuals. Species-specific, emotional, expressive displays in the sender activate the attentional systems of the receiver, thus becoming emotionally competent stimulus. As such, the expressive displays automatically trigger the same emotion in the receiver. When the brain of the receiver perceives the emotion, the meaning of the emotional display is felt directly. The attentional systems hover, shifting from the external sensory stimuli (the expressive displays) to the internal emerging bodily sensations (the emotions generated as an

automatic response). Thus the emotional communication is achieved by a somatic transference.

Under normal conditions, every transference of emotional information elicits a countertransference that confirms the emotional communication. These reactions are very fast, reflecting the somatic emotional changes. Transference of emotional positive changes generates positive changes in the receiver, just as transference of negative emotional changes produce negative changes in the receiver. These reciprocal transactions amplify the autonomic internal state. These transferences are very valuable in a social environment to: a) quickly spread information about how good or bad an event is; b) ease coordination of actions among a group as a response to an outside threat or opportunity; and c) facilitate adaptive behaviors such as attachment, bonding, fleeing or attacking.

There are three emotional regulation modes: 1) an interactive regulation via two or more emotionally interacting individuals, the emotional information transfer; 2) an interactive regulation through the external changing conditions that change the internal emotional state; and 3) a self-regulatory process, based on feedback and automatic tendencies to reach a neutral state of calmness.

The isorropic circuit (from the Greek, isorropia=balance) primarily comprised of the septal nuclei and the habenulas is an emotional arousal and, balancing and tuning system. Its major inputs are signals from the hippocampus and thalamus. Positive emotions are associated with a very slight increase of neural activity in the whole brain, and activation of the left anterior cingulate cortex, relative to the right. Conversely, negative emotions are linked to a slight decrease in neural activity overall and activation of the right anterior cingulate cortex, relative to the left. The isorropic circuit summarizes the activity of the entire brain, taking into account emotions, cognitive signals translated into contexts and meanings, and accordingly, fine-tunes the signals of all neurotransmitter systems in the brain stem. The primary function of this circuit is to try to balance activity in both hemispheres, continuously attempting to restore neutral calmness.

The isorropic circuit achieves five actions: 1) modulate the activity in each hemisphere by dampening or quickening activity as needed through the GABAergic interneurons and projection neurons of the diagonal band of Broca and the medial septal nucleus to the hippocampus and the GABAergic projections of the thalamus to the habenula and the habenular commissure; 2) increase overall activity of the entire cortex through the cholinergic projections to the reticular formation and the periaqueductal gray, and the interpeduncular nucleus from the medial septal nucleus and the habenula respectively; 3) determine the emotional state through the indirect connections from the amygdala; 4) determine the context of the emotion through the connections from the hippocampus; and 5) measure and compare the neural activity in each hemisphere to determine if a positive or negative emotion is present by comparing the activity of the left and right habenulas aided by the signals from the thalami, the amygdalae and the hippocampi. The overall net result of the actions of the isorropic circuit is to naturally drift, at varying rates, towards a neutral state. In essence the isorropic circuit attempts to restore balance between the activities of both hemispheres.

Thus, projections from the habenula, through the habenulointerpeduncular tract, to the interpeduncular nucleus in the reticular formation, affect most all the principal neurotransmitter systems: a) the cholinergic diffuse projection patterns are activated

through the basal nucleus of Meynert (to the cortex) and the septal nuclei (to the hippocampal formation). Acetylcholine augments excitability of cortical neurons, especially in the association areas; b) the dopamine containing neurons of the substantia nigra pars compacta and ventral tegmental area, activate the nigrostriatal dopaminergic system and mesocorticolimbic dopaminergic system through their connections to the striatum and frontal cortex, and prepare the brain for action. This is an activation-excitatory circuit. The dopaminergic systems are important in responding to natural rewarding stimuli, such as feeding and reproduction. However, dopaminergic neurons do not simply signal the hedonic value of events, because novel negative reinforcing stimuli can also activate the dopaminergic systems; c) the serotonin system through the Raphe nuclei. The actions of this system are diverse because there are many types of serotonin receptors; d) and the noradrenaline system through the locus ceruleus with projections to the thalamus, amygdala and hippocampal formations as well as medullary projections. This system plays an important role in reacting to stress, and particularly the activation of fear and anger.

The cholinergic projections of the isorropic circuit, primarily from the medial septal nucleus and the band of Broca to the hippocampal formation, the periaqueductal gray matter and the reticular formation act through muscarinic receptors. The muscarinic receptors are slow acting, consequently their effects occur with a time lag. This time lag, in chaos theory terms, allows the isorropic circuit to wander about a point, the isorropic attractor, which under normal conditions is close to the point of neutral calmness.

The isorropic attractor is the state (point) towards where the isorropic circuit's actions tend to modulate the cortex's activities (represented by a point). The subtle wandering of the isorropic attractor reflects the ability of the brain, because of the isorropic circuit, to generate and regulate a wide spectrum of emotions. Generally, this wandering activity remains within the range of chemical changes that do not affect the homeostatic balance. Potentially, this wandering permits the generation of myriad slightly differing emotions as a response to a vast array of changing internal and external stimuli. When the isorropic attractor is close to neutral calmness a wider spectrum of potential emotional responses is available, positive and negative, and by activating memories associated with the emotions, allows for activation of a greater pool of memories. The speed at which small emotional changes can be generated also allows the search for the greatest potential number of contexts. Thus the brain achieves a state that can generate the maximum variety of behaviors in the quickest time possible as response to the ever-changing environment. This places the organism in a state of maximum adaptability. When the brain detects this healthy state of maximum adaptability of the body/brain (organism) it is perceived (felt) as a sense of self.

The wider the spectrum of emotional responses that can be triggered, the more intense the sense of self is felt. Conversely, the narrower the spectrum, the less intense the sense of self is perceived. This translates into a nonverbal knowledge that many memories can be quickly activated because the brain can flutter, ever so slightly from emotion to emotion, changing from moment to moment the chemical milieu of the body and brain.

In extreme cases, when the isorropic attractor is pushed far enough from the range of homeostatic balance, the brain will no longer be able to perceive a sense of self; the organism can no longer adapt. From this point of view, the sense of self is an indirect

measure of the organism's capacity to adapt. When the organism experiences idiozimia, the ability to adapt ceases and the possibility of death increases proportionately.

The disruption of any one of the motor, sensory, memory, attentional or emotional circuits can produce devastating effects. Understanding the specifics of each circuit will obviously lead to more powerful insights and improved therapies or pharmacologies.