Subcortical Brain Structures, Stress, Emotions, and Mental Illness

We will only discuss the major subcortical structures of our mammalian animal brain. Our ancestral brain is not nearly as simple as the following short discussions might imply. In *Affective Neuroscience: The Foundations of Human and Animal Emotions*(1998), referring to the instinctual emotional processing that goes on in our subcortical brain structures, Jaak Panksepp notes the likelihood that, "in a deep evolutionary sense, many of the complex information-processing potentials of the cortex are servants (often unconscious, automatized servants) to the dictates of the affective forces that ruled behavior prior to cortical evolution."

In *An Odyssey with Animals: A Veterinarian's Reflections on the Animal Rights & Welfare Debate* (2009), Adrian R. Morrison provides a great description of just how mammalian we humans are. We humans share common subcortical brain structures with all other mammals. Morrison writes:

My cat, Buster, and I both flinch and yowl or curse at a sudden painful stimulus, and our legs both jerk in response to a tap on the patellar tendon of the knee. The spinal organization of the neurons responsible for these activities is the same in cats as it is in humans.

Moving forward into the lowest part of the brain, in both Buster and me the same neurons control basic bodily functions, such as regulation of breathing, heart rate, and vomiting. Farther forward reside the nerve cells that regulate the behaviors of sleep and wakefulness, which are identical in humans and other mammals, and where dysfunction results in similar problems, such as narcolepsy … and REM sleep behavior disorder. In this brain region in all mammals are found the neurons containing the neurotransmitter dopamine, which degenerate in Parkinson's disease.

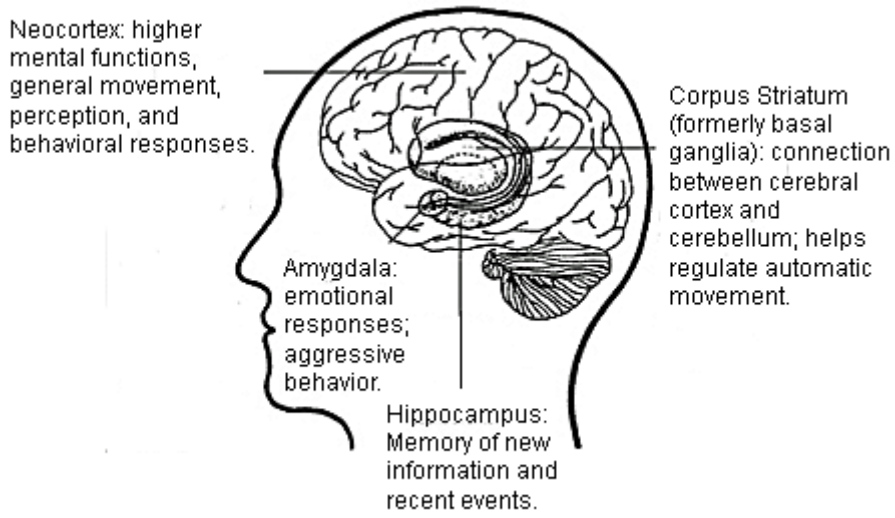
At the base of the cerebral hemispheres is the almond-shaped amygdala, where mechanisms leading to fear and anxiety in people and animals operate. Monkeys and rats have contributed much to our understanding of the amygdala. The overlying cerebral cortex is where all of us mammals analyze the sensations coming from the skin, muscles and joints via the spinal cord, or eyes and ears in the cases of vision and hearing.

Where we depart from our animal brethren is in the great development of the front part of our cerebral cortex, the frontal lobes, and the greater proportion of cerebral tissue, called association areas, which integrate the information obtained from the

regions that directly receive sensory information. These latter regions are called the primary sensory and motor areas because they receive simple, pure sensations and direct the movement of the body. It is within the frontal lobes that we humans mull over the past, prepare for the future, and reflect on its implications. Animals do not have this last capability in particular, as far as we can discern. Animals prepare for the future in a limited, instinct-driven way: Think of squirrels gathering and burying nuts for the winter. …

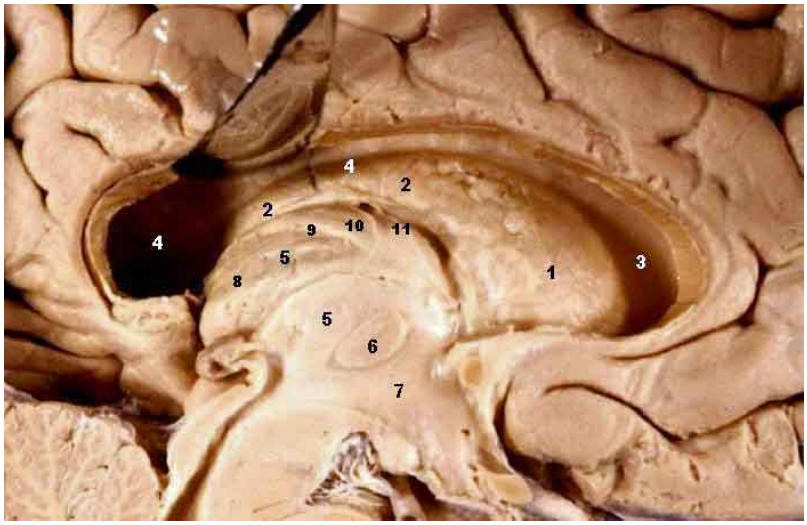
Our animal brain:

Temple Grandin and Catherine Johnson, in *Animals in Translation: Using the Mysteries of Autism to Decode Animal Behavior* (2005), recount Grandin's first encounter with real brain tissue. "The pig brain was a big shock for me because when I compared the lower-level structures like the amygdale to the same structures in the human brain I couldn't see any difference at all. The pig brain and the human brain looked exactly alike. But when I looked at the neocortex the difference was huge. The human neocortex is visibly bigger and more folded-up than the animal's, and anyone can see it. You don't need a microscope."



The illustration above links to an NIMH fact sheet on autism spectrum disorders. In the illustration, you can see the *amygdala*, *hippocampus*, and *corpus striatum*.

Remember that both the left and right hemispheres contain each of these structures, which are mirror images of each other. The pair of structures called the corpus striata has, in the past, been referred to as the basal ganglia. The corpus striata play a key role in generating obsessions and compulsions. We will discuss the corpus striata structures in more detail in Parts 2 and 3 of MyBrainNotes.com.



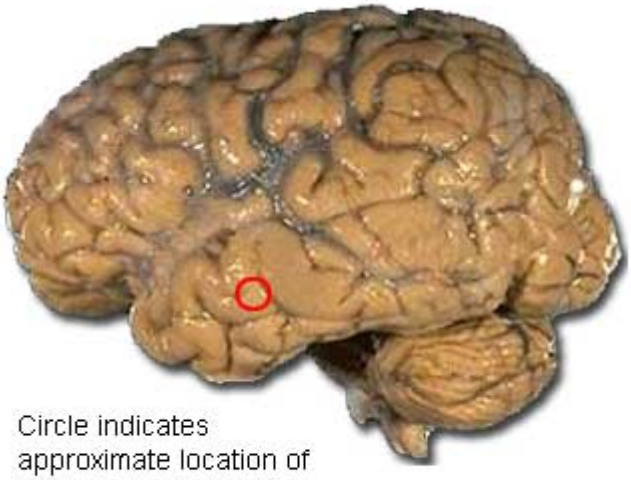
In the picture to the right, all of the strangely shaped subcortical nuclei are nestled within the much larger and more consistently formed neocortex. John A. Beal, Department of Cellular Biology and Anatomy, Louisiana State University Health Sciences Center, provides this image. What has traditionally been called the basal ganglia, and what I will call the *corpus striatum*, is labeled 1 and 2. The *thalamus* is labeled 5 and the *hypothalamus* is labeled 7. In my view, a very powerful force—whether you see it as God, evolution, or a concerted effort—stitched the subcortical nuclei together as needed to ensure the survival and continued development of animal life.

The amygdala, stress, OCD, and PTSD:

Thomas B. Czerner, in *What Makes You Tick? The Brain in Plain English* (2001), describes the amygdalae as "almond shaped" structures. The amygdalae are nestled and protected within each *temporal lobe*. The temporal lobe is located behind the temples, thus its name.

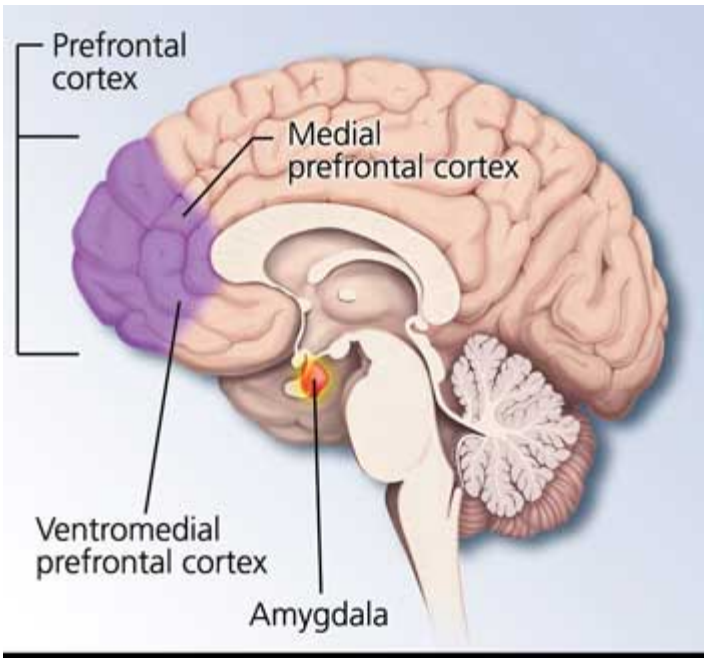
In *Descartes' Error: Emotion, Reason, and the Human Brain* (1994), Antonio R. Damasio explains that "the first hint that amygdale and emotion might be related can be found in the work of Heinrich Klüver and Paul Bucy, who showed that surgical resection of the part of the temporal lobe containing the amygdala created affective indifference, among a variety of other symptoms."

In *Evolving Brains* (2000), John Allman cites research that shows when the amygdalae are damaged, one loses the ability to discern emotions, particularly fear and anger expressed in another's face or intoned in another's voice. Allman writes: "The role of the amygdale in the perception of facial expressions was beautifully shown by Ralph Adolphs and his colleagues, who studied a remarkable patient who had suffered a bilateral amygdalar damage without significant injury to other parts of the brain. Although this patient had normal vision and could perceive faces, she was unable to discriminate the emotional content in the negative facial expressions of fear and anger. Thus all faces appeared to be smiling or neutral to her, even those which were actually frightened or angry." Damage to the amygdalae also impair one's ability to descern emotion in another's speech. Allman writes: "Sophie Scott and her colleagues found that amygdalar lesions also disrupted the ability to perceive the emotional content of speech intonation even though their patient had normal hearing. As with facial expressions in Adolphs's patient, the auditory expressions of fear and anger were the most impaired in this patient."



Circle indicates approximate location of the recessed amygdala within the temporal lobe.

The illustration below (image links to source) is borrowed from the Society for Neuroscience website. This image appears in an article on post-traumatic stress disorder (PTSD). In addition to depicting the amygdala, the illustration depicts the location of the*prefrontal cortex*. The prefrontal cortex is often referred to simply as the frontal lobe or frontal cortex. This area of the neocortex lies in front of cortical motor areas. We will discuss the frontal cortex and cortical motor areas later in this narrative. For now, suffice to say that the frontal cortex (or prefrontal cortex) is involved in executive functions and the expression of personality. The Wikipedia entry for *prefrontal cortex* explains that this area of the brain orchestrates "thoughts and actions in accordance with internal goals." The point to be made here, regarding the subcortical amygdalae, is that during normal functioning, the enlarged prefrontal cortex in humans can modulate emotional impulses generated in the amygdalae.



Brain Structures Involved in Dealing with Fear and Stress

Continued stressful circumstances, however, can potentiate amygdalae functioning, allowing it to become more powerful—some might even say willful—over time, sometimes exerting subcortical control over our human cortical reasoning. Such potentiated activity can exacerbate symptoms of mental illness, including obsessions and compulsions.

In *Why Zebras Don't Get Ulcers: The Acclaimed Guide to Stress, Stress-Related Diseases, and Coping* (2004), Robert M. Sapolsky Robert M. Sapolsky emphasizes that while the glucocorticoids released during stressful episodes may disrupt hippocampal function and the memory-forming processes, those same glucocorticoids make amygdalae synapses more excitable, allowing neurons to grow more of the cables that connect the cells to each other.

"One way to understand OCD is that the normal cortical inhibition of the amygdala is malfunctioning and that the anxiety responses induced by the amygdala therefore become more intrusive and chronic in patients with OCD. …," write Denys, Zohar, and Westenberg in "The Role of Dopamine in Obsessive-Compulsive Disorder: Preclinical and Clinical Evidence." Dopamine comes into play in response to amygdalae-generated anxiety in that dopamine drives seeking activity. Seeking activity includes not only the search for food, drink and sex but–in times of anxiety and fear–access to safety. Denys, Zohar, and Westenberg write: "When dopamine is increased, the ability of the prefrontal cortex to suppress the affective responses generated in the amygdala is attenuated." We will discuss neurocircuitry related to obsessions, compulsions, and other symptoms more fully in Parts 2 and 3 of MyBrainNotes.com.

Especially regarding PTSD, past experience is a key. Neuroscientists have found that experience shapes amygdala processing over time. You could say that the amygdala*learn*, over time, the level of danger that should be associated with any particular stimulus. In defining *incentive salience*, authors Vilayanur S. Ramachandran and Lindsay M. Oberman expertly describe the process by which

amygdalae can predict danger. In "Broken Mirrors: A Theory of Autism," *Scientific American*, November 2006, the authors write:

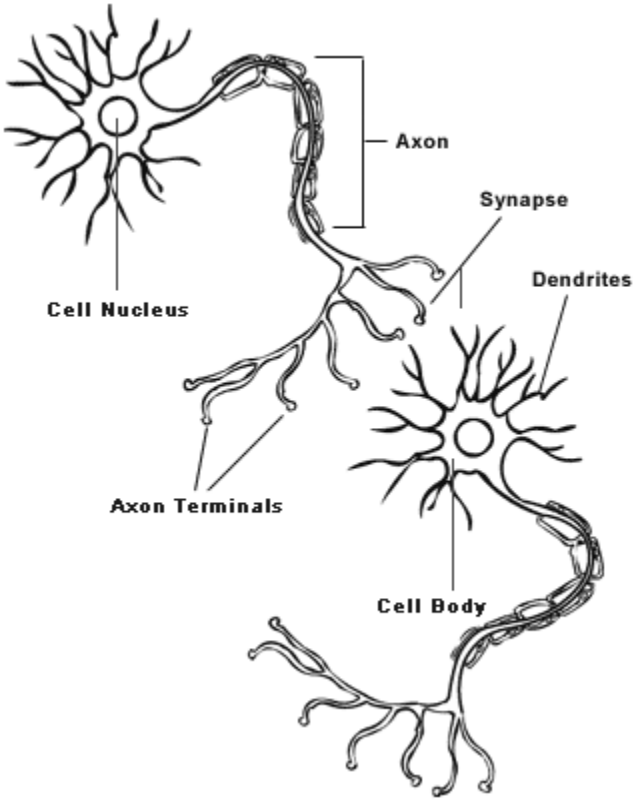
When a person looks at the world, he or she is confronted with an overwhelming amount of sensory information—sights, sounds, smells, and so on. After being processed in the brain's sensory areas, the information is relayed to the amygdala, which acts as a portal to the emotion-regulating limbic system. Using input from the individual's stored knowledge, the amygdala determines how the person should respond emotionally—for example, with fear (at the sight of a burglar), lust (on seeing a lover) or indifference (when facing something trivial). Messages cascade from the amygdala to the rest of the limbic system and eventually reach the autonomic nervous system, which prepares the body for action. If the person is confronting a burglar, for example, his heart rate will rise and his body will sweat to dissipate the heat from muscular exertion. The autonomic arousal, in turn, feeds back into the brain, amplifying the emotional response. Over time, the amygdala creates a salience landscape, a map that details the emotional significance of everything in the individual's environment.

In *The Emotional Brain: The Mysterious Underpinnings of Emotional Life* (1996), Joseph LeDoux provides an excerpt from Heinrich Klüver's and Paul Bucy's report of a monkey's behavior after removal of the temporal lobes, which include the amygdalae. Klüver and Bucy report that the monkey does not exhibit anger and fear and seems unable to recognize objects.

… The hungry animal, if confronted with a variety of objects, will, for example, indiscriminately pick up a comb, a bakelite knob, a sunflower seed, a screw, a stick, a piece of apple, a live snake, a piece of banana, and a live rat. Each object is transferred to the mouth and then discarded if not edible.

LeDoux explains that Klüver and Bucy "referred to this collection of symptoms as 'psychic blindness,' by which they meant that the animals had perfectly good visual acuity but were blind to the psychological significance of stimuli." LeDoux also notes that, after removal of the temporal lobes, the monkeys became "hypersexual, attempting to copulate with other monkeys of the same sex or with members of other species (sexual activities seldom if ever practiced by 'normal' monkeys)."

Kindling and stress—how experience affects the brain:



Is it possible that chronic stress, through a process called *kindling*, can create hard-wired, hypersensitive neural networks capable of dictating and automating symptoms from a wide range of instinctual behavior patterns? In his video course,*Biology and Human Behavior: The Neurological Origins of Individuality*, 2nd edition, Robert M. Sapolsky examines how communication between neurons is strengthened as a result of experience. When the dendritic spines of neurons are stimulated rapidly, the synapses between the communicating neurons become "hyper-responsive or potentiated" due to chemical changes within the neural environment. Subsequently, less stimulation is necessary to again prod the neuron to fire—the moment when an electrical signal bursts through the neuron's axon, prompting release of chemical messengers called neurotransmitters into the synapse between neurons, often increasing the likelihood that other neurons will fire in a sort of chain reaction. In other words, Sapolsky says, the neuron's "action potential" is increased. What's called "long-term potentiation" is thus the basis for learning and memory, possibly including injurious forms of learning such as post-traumatic stress disorder (PTSD).

In *Listening to Prozac: A Psychiatrist Explores Antidepressant Drugs and the Remaking of the Self* (1993), Peter D. Kramer writes, "Kindling rewires the brain. … the brain reshapes itself anatomically in response to small noxious stimuli. … Kindling appears to be a kind of learning, but a learning that can occur independent of cognition. … Illness, once expressed, can become responsive to ever smaller stimuli and, in time, independent of stimuli altogether. The expression of the disorder becomes more complex over time."

In "Psychosomatic disease and the 'visceral' brain: Recent developments bearing on the Papez theory of emotion" (1949), Paul D. Maclean theorized about the kindling process. "It is possible that if a certain electrical pattern of information were to reverberate for a prolonged period or at repeated intervals in the neuronal circuit, the

nerve cells (perhaps, say, as the result of enzymatic catalysis in the dentritic processes at specific axone-dendritic junctions) would be permanently 'sensitized' to respond to this particular pattern at some future time. Such a mechanism would provide for one variety of enduring memory in a way that is remotely analogous to a wire recorder. These hypothetical considerations suggest how oft-repeated childhood emotional patterns could persist to exert themselves in adult life."

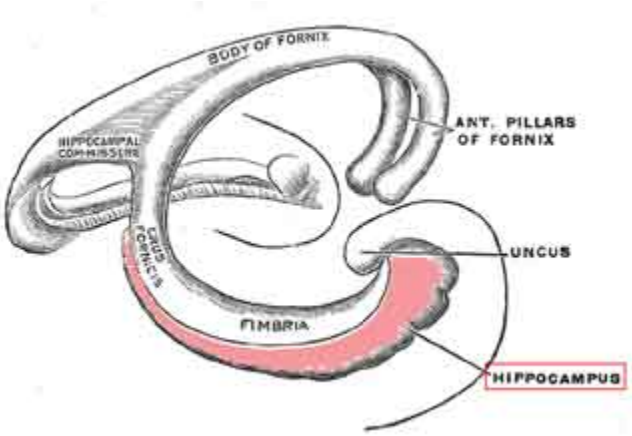
As MacLean suggests in using the term *visceral*, certain reactions are not embedded in language and intellect, they are more like "gut feelings" that can remain in primordial memory systems and that can be strengthened through kindling. Winifred Gallagher explains kindling in an article in *The Atlantic Monthly*, "How We Become What We Are" (September 1994). Gallagher writes:

Over time, repeated stressful experiences can literally, not just figuratively, alter the nervous systems of the temperamentally vulnerable. Animal research has shown that when a rat is given a small shock, it shows no marked reaction; when exposed to such stressors for five consecutive days, it shows signs of the stress response; when exposed for seven or eight days, the rat has a seizure, and thereafter this 'kindled' animal will seize with little or no provocation. Experiments of this kind are of course not done with people, but Philip Gold and other neuroscientists now think that in human beings, too, by triggering a cascade of chemical reactions, serious chronic stress, particularly in early life, causes changes in the way genes within a brain cell function, permanently altering the neuron's biology. Because they require a particular type of input to turn on or off, only some of a neuron's thousands of genes, each of which is involved in some aspect of cellular structure or communication, are activated at any given moment. When a temperamentally vulnerable person is constantly bombarded with upsetting stimuli, Gold says, the genes that get turned on are those involved in the cellular components of the stress response."

I contend that neurotransmission in the amygdalae and their target structures is sometimes *kindled* to generate dopamine-driven behaviors aimed at solving problems including restoring order, control, and most importantly–confidence. Under normal circumstances, this could be construed as a survival instinct. Under extreme stress, however, especially when an outlet for pent-up energy is not available, these behaviors may turn into obsessions or compulsions. We will discuss such neurotransmission in greater detail in Part 3 of MyBrainNotes.com. For now, I would like to point out that in*Monkeyluv and Other Essays on Our Lives as Animals* (2005), Robert M. Sapolsky describes how monkeys release dopamine in *anticipation* of a food reward. They get most excited when a light first comes on signaling that they may now perform a learned task and upon completion, will receive food. Their excitement does not peak when the food finally appears; it peaks well before that

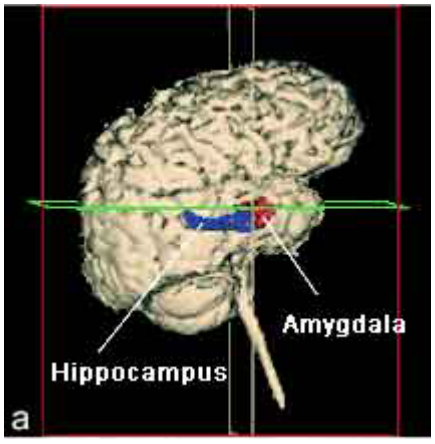
point. Sapolsky writes, **"It's about the anticipation of reward. It's about mastery and expectation and confidence."**

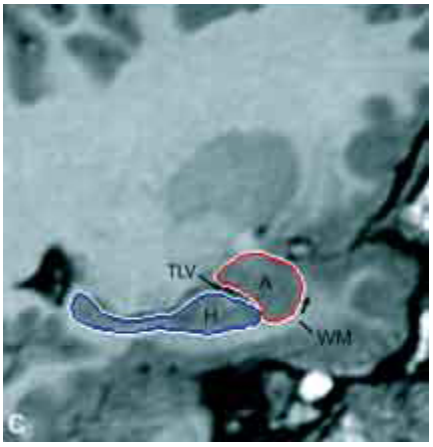
The hippocampus, memory, and depression:



The term *hippocampus* is derived from the Greek word meaning "sea-horse," which might somehow describe the shape of each hippocampal nucleus, although frankly, I do not see the resemblance. In the illustration to the left, I have added pink color to the hippocampus for clarity. You can see that it adheres to the curve of nerve fibers that curve once again to become the body of the fornix nerve pathway. This image links to its source, which includes a YouTube video on the anatomy of the hippocampus and surrounding structures. You may need to download the latest version of Adobe's Flash Player to watch the YouTube video. Be sure to click on your browser's BACK button to return to MyBrainNotes.com.

The hippocampi—one in each hemisphere, extending to meet the amygdalae within the temporal lobes—are crucial for "forming, storing, and processing memory," according to the *MedlinePlus Dictionary*. I should note here that the hippocampi are two of the first regions of the brain to suffer atrophy in Alzheimer's disease. In the illustration to the right from the *Journal of Neuroscience* (links to source), the amygdala is colored red and the hippocampus is colored blue.

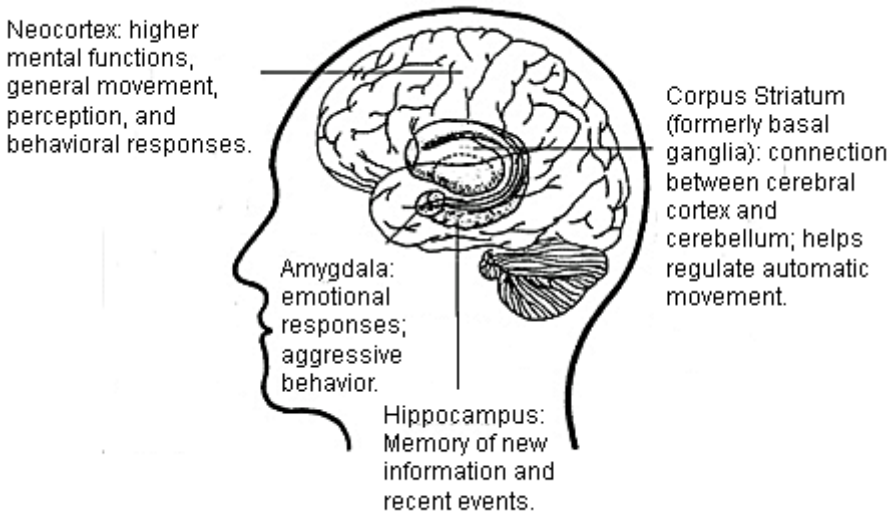




The MRI sagittal view to the left (links to source) shows the amygdala (labeled "A") and the hippocampus (labeled "H"). In *Brainscapes: An Introduction to What Neuroscience Has Learned about the Structure, Function, and Abilities of the Brain*(1995), Richard M. Restak explains that "Fibers from all four lobes, along with association fibers uniting these separate connections into one unified experience, converge into the hippocampal region." Restak writes: "Thanks to extensive two-way connections, with other brain areas the hippocampus and its immediate connecting structures integrate and coordinate both our outer- and inner-world experiences into a unity." The hippocampi and other structures—such as the amygdalae—that process and integrate stimuli provide input to the autonomic nervous system (ANS; see ANS—the autonomic nervous system). So one can experience all the autonomic consequences of fear at the mere memory of a traumatic event.

Restak writes: "Damage to the hippocampus on both sides of the brain deprives the victim of the ability to learn new things and thus suspends the person in a time warp composed of the distant past, a present as thin and sharply etched as a knife blade, and an uncertain and fearful future. This happens because under normal circumstances we are able to maintain our sense of identity—who we *are*—only by forming new memories from moment to moment and accessing old ones at a leisurely command."

Another example of kindling, which we discuss above, is the effects of stress on the hippocampi. In his 1995 *New York Times* article titled, "Severe Trauma May Damage the Brain as Well as the Psyche," Daniel Goleman explains that studies in rats and primates suggest that glucocorticoids are the culprit. Goleman quotes Robert Sapolsky, who explains that glucocorticoids "may be neurotoxic to the hippocampus at the massive levels that are released under extreme stress or during trauma. I'm talking about the levels you would see in a zebra running from a lion, or a person fleeing a mugger—a real physical life-and-death crisis—if it is repeated again and again as time goes on."



If the glucocorticoids released during extreme stress and trauma damage the hippocampi, it is no wonder that, according to Sapolsky in *Why Zebras Don't Get Ulcers*, "there is atrophy of the hippocampus in long-term depression. The atrophy emerges as a result of the depression (rather than precedes it), and the longer the depressive history, the more atrophy and the more memory problems."

Sapolsky points to the work of psychologists Martin Seligman and Steven Maier who exposed animals to "pathological amounts" of stress. "The result is a condition strikingly similar to a human depression." Sapolsky explains that it is "repeated" stress that generates depressive symptoms combined with "a complete absence of control on the part of the animal." In other words, the animal has no outlets that can be used to vent frustration. "When it comes to what makes for psychological stress, a lack of predictability and control are at the top of the list of things you want to avoid," Sapolsky writes.

Sapolsky calls attention to the work of Joseph LeDoux of New York University, "who pretty much put the amygdala on the map when it comes to anxiety." In a way that only he can do, Sapolsky sums up the paradox between severe, traumatic stress and its effect on the hippocampi versus the amygdalae. "Suppose a major traumatic stressor occurs, of a sufficient magnitude to disrupt hippocampal function while enhancing amygdaloid function. At some later point, in a similar setting, you have an anxious, autonomic state, agitated and fearful, and you haven't a clue why—this is because you never consolidated memories of the event via your hippocampus while your amygdala-mediated autonomic pathways sure as hell remember."

<="" a="">The hippocampus, epigenetics, and PTSD:

<="" a="">

In "Determining Nature vs. Nurture," *Scientific American Mind* (Oct/Nov 2006, p12), Douglas Steinberg provides a great explanation of how the environment can affect neurons, including those in the hippocampi. Steinberg writes:

A field called epigenetics has finally begun to address some of these issues. Its practitioners study how tiny molecules stick to, or become unstuck from, two main targets in a cell's nucleus: the DNA in and around a gene and the histones—the proteins around which chromosomes spool. These tiny molecules are known as methyl and acetyl groups and their presence or absence at target sites controls whether particular genes can generate proteins, the workhorses of most physiological processes.

Until a couple of years ago, the conventional wisdom in biology held that such molecular changes occur in primitive cells, usually during embryonic and fetal development, not in mature cells such as a child's or adult's neurons. Then researchers proved that epigenetic changes are indeed at work in mature cells. Now studies are starting to show how environmental cues can stimulate epigenetic changes that could contribute to several psychiatric diseases. Systematic measurement of those changes could eventually indicate how the environment influences the genetic chemistry underlying many human behaviors.

<="" a="">Steinberg points to the work of Eric J. Nestler, psychiatry department chair at the University of Texas Southwestern Medical Center at Dallas. Nestler has proposed a model of depression that includes "epigenetic changes in the hippocampus, a memory-storing brain region that actually shrinks in some cases of human depression."

The image to the right links to a BBC News story about the work of Michael J. Meaney, a psychiatry professor at McGill University. Steinberg explains that Meaney "has found that when a rat pup receives less licking and grooming from its mother, it is more fearful and more reactive to stressors as it matures." Steinberg reports:

The team found that a hippocampal gene sheds methyl-group molecules during the first week of a [rat] pup's life if its mother is a 'high licker.' Pups of low lickers do not

prune the molecules. An adoption experiment proved that licking triggers these events: when the team entrusted pups born to mothers of one licking type to mothers of the other type, the genes' methyl status reflected the licking type of the adoptive parent. Licking is believed to exert its effect by raising the pups' thyroid-hormone production and activity of the neurotransmitter serotonin. … The findings suggest that a mother's parenting style can have very different effect on the activity of a child's genes. … Epigenetics may indeed unveil what is happening at the intersection of genes and environment.

Steinberg calls attention to the work of Dr. J. Douglas Bremner who does research on Post-traumatic Stress Disorder (PTSD). In an on-line article Bremner writes: "Recent studies have shown that victims of childhood abuse and combat veterans actually experience physical changes to the hippocampus, a part of the brain involved in learning and memory, as well as in the handling of stress. The hippocampus also works closely with the medial prefrontal cortex, an area of the brain that regulates our emotional response to fear and stress. PTSD sufferers often have impairments in one or both of these brain regions. Studies of children have found that these impairments can lead to problems with learning and academic achievement." Bremner goes on to say: "Memory problems play a large part in PTSD." He explains that PTSD patients report deficits in declarative memory, such as being able to remember facts or lists, fragmentation of memory, and dissociative amnesia, which involves gaps in memory lasting from minutes to days.

To see video from a PBS special on epigenetics, link to NOVA Science Now. Be sure to click the BACK button on your browser (or the Backspace key in some browsers) to return to MyBrainNotes.com.

Click on this link to read "Epigenetics: The Science of Change" (2006), published in*Environmental Health Perspectives*.

Epilepsy, temporal lobe epilepsy (TLE), the amygdala, and the hippocampus:

In temporal lobe epilepsy (TLE), rather than convulsive seizures or loss of consciousness, patients usually have extraordinary subjective experiences. They my experience *autoscopy*, the sensation of leaving one's body. They may also present with hypergraphia, an overwhelming urge to write, religiosity, or both. The subcortical structures in each temporal lobe thought to be responsible for these kinds of rich and dramatic feelings are the amygdalae and the hippocampi.

Before we discuss TLE symptoms including hypergraphia and religiosity, a note about epilepsy in general is in order. The National Institute of Neurological Disorders and Stroke provides the following information: "Epilepsy is a brain disorder in which clusters of nerve cells, or neurons, in the brain sometimes signal abnormally. In epilepsy, the normal pattern of neuronal activity becomes disturbed, causing strange sensations, emotions, and behavior or sometimes convulsions, muscle spasms, and loss of consciousness." Regarding consciousness, the Epilepsy Foundation identifies another symptom of epilepsy, an "absence seizure," which is "a lapse in consciousness with a blank stare that begins and ends within a few seconds."

The abnormal neural activity that causes epileptic seizures can have several causes—brain damage including developmental abnormalities, physical injury to the brain including head trauma and stroke, and infectious illnesses such as meningitis. A family history of epilepsy is considered a risk factor for the illness. According to the Epilepsy Foundation, "Brain function—from cell membrane to level of neurotransmitter substances to other biochemical mechanisms—is controlled by individual genes that, if damaged or mutant, may lead to seizures. The search is on for genes which may be directly linked to a specific type of epilepsy."

Hypergraphia, religiosity, and anatomic loci:

As mentioned above, *hypergraphia* is an overwhelming urge to write. Such copious writing could be construed as compulsive but this classification does not adequately explain symptoms. *Religiosity* can be defined as overly developed piety or religious zeal and is sometimes linked together with hypergraphia as a complex symptom. One of my goals in creating MyBrainNotes.com is to clarify how neural activity over which we have little control can dictate our behavior–including such obsessive activity as hypergraphia and religiosity. In some cases, such as an epileptic seizure, the link between neural activity and abnormal behavior is well accepted. Other behaviors, however, such as hypergraphia and religiosity, are not so easily attributed to neural activity because they often appear to be rational and well thought out. A person beset with hypergraphia or religiosity often considers his or her behavior as being willful.

In *Seized: Temporal Lobe Epilepsy as a Medical, Historical, and Artistic Phenomenon*(1993), Eve LaPlante notes the observations of Norman Geschwind, a twentieth-century Harvard neurologist. In evaluating some of his epileptic patients, Geschwind found that hypergraphia often occurred among patients who imbued their experiences with religious and moral significance. (I should note here again that the amygdala and hippocampus are nestled within the temporal lobe.) LaPlante adeptly explains Geschwind's theory that over-activity within the temporal lobe "enhances the

tissues' normal functions of emotion and memory, causing patients to feel experiences unusually deeply, to imbue those experiences with religious or moral significance, and to record them compulsively in drawing or writing."

Waxman and Geschwind, in Hypergraphia in Temporal Lobe Epilepsy" (1974), report:

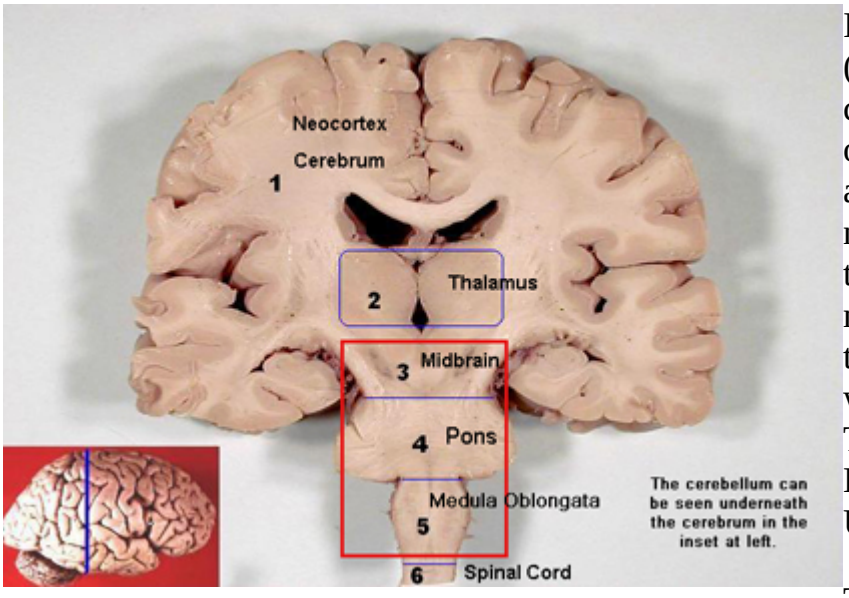
The phenomenon of hypergraphia, or the tendency toward extensive and, in some cases, compulsive writing in temporal lobe epilepsy is described in seven patients, in each of whom there was electroencephalographic demonstration of a temporal lobe focus. Unusually detailed and strikingly copious writing was evidenced in each patient. Six patients provided documentation of their extensive writing, which often was concerned with religious or moral issues. A seventh patient claimed to have written extensively, but refused to exhibit his writings. Aggressiveness, religiosity, and changes in sexual behavior in temporal lobe disorders have been described previously. The hypergraphia of temporal lobe epilepsy appears to be part of a specific behavioral syndrome of special interest because of its association with dysfunction at specific anatomic loci.

An important thing to remember is that Geschwind and his colleagues, although criticized at the time, were correct in suggesting that the unusual behaviors associated with TLE might have, as LaPlante puts it "a distinct anatomical base." Again, the temporal lobe structures most likely to contribute to highly-charged emotional behaviors like hypergraphia and religiosity would be the amygdalae and the hippocampi. In "Norman Geschwind's Contribution to the Understanding of Behavioral Changes in Temporal Lobe Epilepsy: The February 1974 Lecture" (2009) Devinsky and Schachter discuss Geschwind's progress in revealing that it was an abnormality or *lesion* in the limbic system (which includes the amygdalae and hippocampi) that accounted for the unusual symptoms of TLE. They write: "This neurobiology accounted for the overarching increased interictal [between seizures] emotionality that underlay the increased religious interests, hypergraphia, increased aggression, increased moral and philosophical concerns, viscosity, and seriousness (lack of humor). Hyposexuality was the exception, although it was consistent with a discharging lesion altering this emotion-driven behavior."

Grandin and Johnson, in the Notes section of *Animals in Translation*, point out that "There are at least three different lines of evidence that religion is basic to the human brain: (1) religion is universal to all cultures, (2) identical twins separated at birth have the same degree of religiosity as adults, and (3) there is a 'God part' of the brain in the temporal lobes that makes you feel the presence of God when it's stimulated." The BBC produced a story called God on the Brain which references several scientists and their work in this area.

The thalamus and OCD:

In *The Tangled Wing: Biological Restraints on the Human Spirit* (1982), Melvin Konner calls the thalamus "the major way station of incoming sensation." In *What Makes You Tick?*, Czerner explains that the thalamus "is the gateway for virtually all of your sensations and directs impulses generated by each of your sensory neurons to its appropriate area in the cortex." For example, the thalamus directs visual information to the primary visual cortex, which we will discuss later in this narrative.



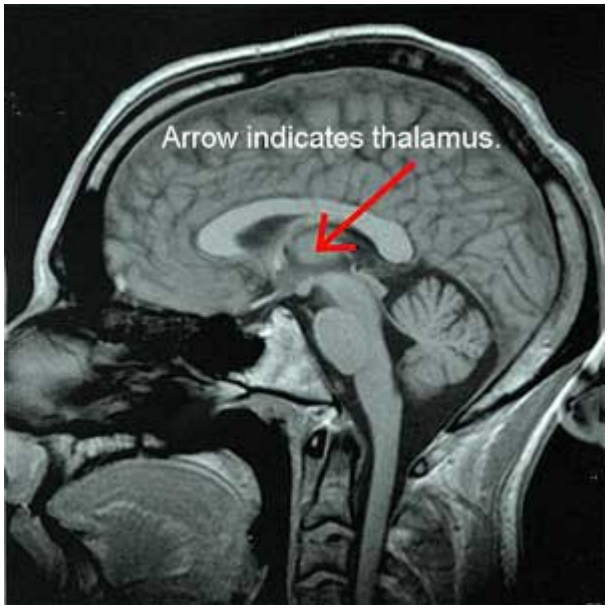
In the photograph to the left (image links to source), you can see that the thalami occupy a central location among the subcortical nuclei. As previously noted, the thalami are actually two mirror-image ovoid masses that occupy each lateral wall of the third ventricle. This image is from John A. Beal of the Louisiana State University.

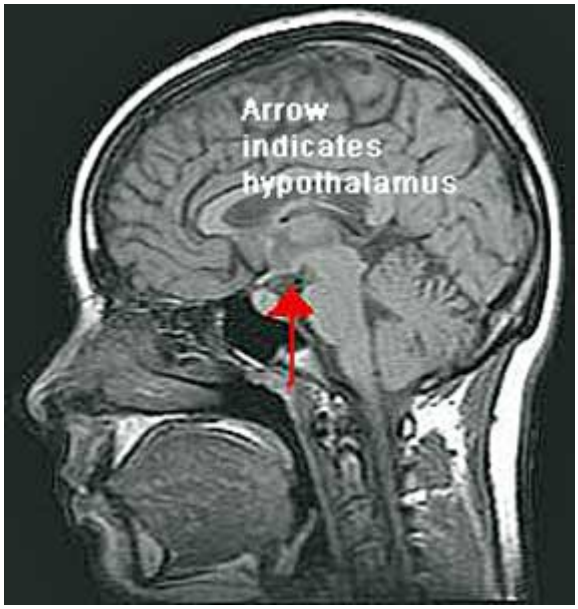
The thalami are of primary importance in relaying messages from subcortical nuclei to the neocortex. The thalami are integral to what we will call *cortical-subcortical circuits*, which we will discuss at length in Part 3 of MyBrainNotes.com. These circuits possibly shift, in certain situations, into what I call *autonomous processing* mode whereby one circuit supports cognitive processing while another separate circuit supports more automatic processing and behavior, what we would call compulsions. Building on information in Parts 1 and 2, we extensively discuss the neurocircuitry of obsessions and compulsions in Part 3 of MyBrainNotes.com.

The hypothalamus and seeking behavior:

Note in the MRI image below right (image links to source) the small size of the*hypothalamus* when compared to the size of the thalamus in the image below left (image links to source). In *Brainscapes*, regarding the hypothalamus, Restak explains that "… despite its diminutive size it is responsible for regulating such critical functions as body temperature, hunger, sexuality, and via connections with the nearby pituitary gland (the 'master gland of the body'), the endocrine system and the

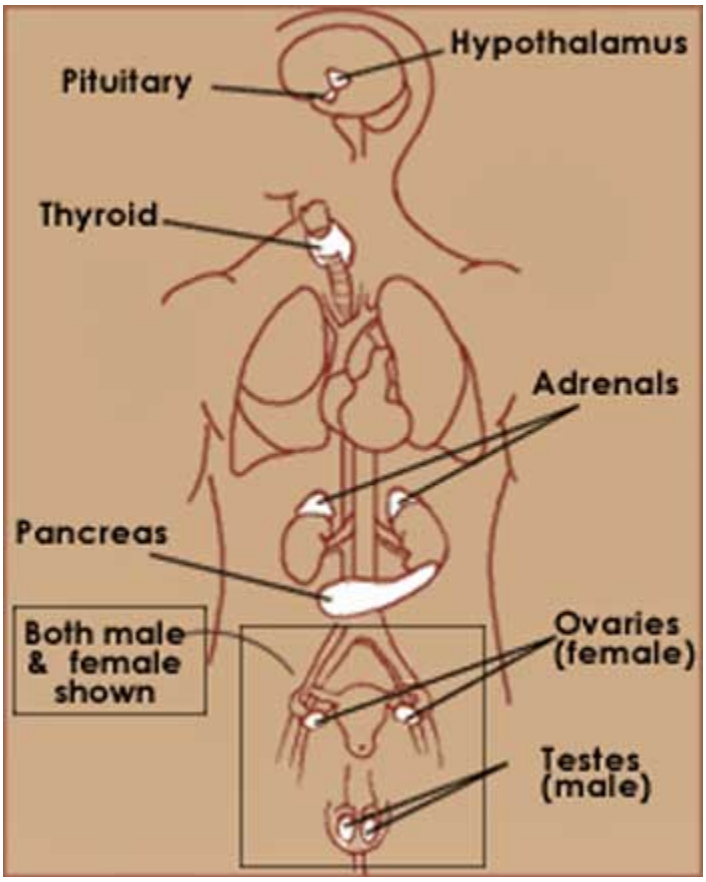
composition of the blood and fluid compartments, that internal symphony of circulating chemicals in our bodies aptly described by French physiologist Claude Bernard as the 'internal milieu.'"





The on-line *MedlinePlus Dictionary* defines the hypothalamus as "a basal part of the diencephalon that lies beneath the thalamus on each side, forms the floor of the third ventricle, and includes vital autonomic regulatory centers (as for the control of food intake)." If you remember the previous discussion on neural tube development, the "diencephalon" develops from the forebrain portion of the neural tube. Also, in our discussion of the autonomic nervous system, we examine the critical role of the hypothalamus in governing sympathetic nervous system reactions including fear, flight, fight, and sexual reactions.

In *Descartes' Error*, Damasio writes, "The innate neural patterns that seem most critical for survival are maintained in circuits of the brain stem and hypothalamus. The latter is a key player in the regulation of the endocrine glands—among them the pituitary, the thyroid, the adrenals, and the reproductive organs, all of which produce hormones—and in the function of the immune system." Damasio adds, "In turn, the hypothalamus and interrelated structures are regulated not only by neural and chemical signals from other brain regions, but also by chemical signals arising in various body systems."



The illustration to the right (links to source) depicts the major components of the endocrine system. In *What Makes You Tick?*, Czerner very eloquently writes: "Deep within your brain but well above the brain stem, neurons in your pituitary and hypothalamus evolved from cells that enabled your chordate ancestors to sense the chemical perfume of an unseen mate in a distant meadow and initiate a courtship. Now the sense and regulate the hormones in your blood. They lie deep in the subcortical, central region of the brain, which could be called the seat of your animal soul. This area, truly the heart of your brain, includes several important nuclei that produce and regulate your degree of arousal, the tone and depth of your feelings, and your emotionally directed behavior. The behavior produced in this middle portion of the brain is often labeled instinctual and unthinking because it is less easily modified than the more deliberately planned, finely turned responses generated in the newly acquired cerebral cortex above it."

I would like to note that the words Czerner uses to describe the behavior arising from activity in the subcortical nuclei—"less easily modified" and "instinctual and unthinking"—are particularly appropriate when referring to obsessions and compulsions. We discuss the role of subcortical nuclei in producing OCD symptoms in Part 2 and then, more extensively, in Part 3 of MyBrainNotes.com.

Grandin and Johnson, in *Animals in Translation*, elaborate on one of the ideas Jaak Panksepp develops in *Affective Neuroscience*. Grandin and Johnson write: "Animals and humans share a powerful and primal urge to seek out what they need in life. We depend on this emotion to stay alive, because curiosity and active interest in the environment help animals and people find good things, like food, shelter, and a mate, and it helps us stay away from bad things, like predators." Grandin and Johnson point out that the hypothalamus regulates sex hormones and appetite, which or course leads to the seeking of food and mates. So the authors see the hypothalamus as integral to

what Jaak Panksepp, in *Affective Neuroscience*, calls the SEEKING system. We will discuss the SEEKING system and the neurotransmitter that powers this system, dopamine, in greater detail in Part 2 of MyBrainNotes.com.

Hypothalamus, appetite, attachment, and anorexia:

I had not intended to discuss eating disorders on MyBrainNotes.com given that I have not read much about them specifically. During my work on the site, however, I found that the ventromedial hypothalamus in responsible for energy regulation (the intake of food) and that this same area also controls female sexual receptivity. Also, as with illnesses diagnosed as OCD, it seems that frustration over attachment issues and dopamine dysregulation may play a role in eating-disorder symptoms. We discuss dopamine in both Parts 2 and 3 of MyBrainNotes.com. We also discuss attachment issues in Depression, Obsessions, and Compulsions: Concepts in Ethology and Attachment Theory, in part 3 of MyBrainNotes.com. Also in Part 3 is a page called OCD Treatments Including Antipsychotic Medications which includes a subsection particularly relevant to the treatment of eating disorders called Antipsychotics and eating disorders

In *Affective Neuroscience*, regarding the hypothalamus and appetite, Panksepp eloquently writes: "The essence of energy regulation is well hidden from scientific view, apparently in the deep metabolic recesses of the hypothalamus." He later describes experiments that illustrate the role of the hypothalamus in consummatory behavior. In these experiments, researchers joined two rats together in a "parabiotic union," a state that sometimes occurs in human identical conjoined twins whose bodies are fused together during development in the uterus. In the experiments, the two conjoined rats thereafter share each other's blood supply. Panksepp writes: "Each of these normal animals gradually ate less, and eventually each contained only half the body fat that a normal rat contains. … The critical area of the brain that probably receives this signal is the ventromedial hypothalamus… ."

Panksepp points out that lesions in the ventromedial hypothalamus "have long been known to produce overeating and eventual obesity,… ." When researchers joined an animal lesioned in this way with a nonlesioned partner, the lesioned animal overate and became obese. In contrast, the animal with a normal hypothalamus detected the abundant nutrition the lesioned animal consumed, and thus lost its appetite completely and became emaciated. The hypothalamus is not, however, a simple on-off switch. Panksepp explains that the ventromedial hypothalamus contains "a long-term metabolic detector by which overall energy balance is regulated."

The ventromedial hypothalamus "also controls female sexual receptivity," notes Panksepp. He explains that "reproduction is generally reduced by starvation" since, metabolically speaking, "it is not wise to have children when food is scarce!" He points out that the "onset of female puberty is also triggered to some extent by weight" since from a metabolic viewpoint, "if one has abundant food, one should begin to reproduce earlier." This dual function reveals, explains Panksepp, "how closely energy detectors and female sexual receptivity systems are coupled in the brain."

Regarding anorexia and other eating disorders, the University of Maryland Medical Center provides patients with helpful educational material. According to the material, the hypothalamus-pituitary-adrenal axis and associated neurotransmitters—including serotonin, norepinephrine, and dopamine—that regulate stress, mood, and appetite are being investigated for a possible role in eating disorders. It is interesting that the educational material also cites what I call attachment issues as a possible cause of eating disorders. Regarding attachment and anorexia, an observation Panksepp makes in*Affective Neuroscience* takes on additional meaning. He writes: "One long-term emotion that is especially incompatible with normal appetite is separation distress. When young animals are socially isolated, they typically lose weight even if they have free access to lots of food. When the young are reunited with their kin, and a mood of apparent contentment is reestablished, appetite returns." We discuss separation distress specifically in Part 2 of MyBrainNotes.com in PANIC/LOSS: an Innate Brain System.

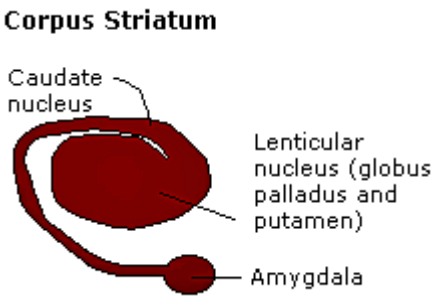
Scientists have found that damage to another very specific area of the hypothalamus, the lateral hypothalamus, severely reduces feeding behavior. Panksepp explains how this area of the brain was at first thought to contain a "feeding system." Research has shown, however, that neurons in this area of the brain, as Panksepp puts it, "elaborate seeking strategies, which require a great deal of sensory and motor integration" and that resulting routines "are governed by interactions with the basal ganglia [corpus striata complex]… ." We will discuss the corpus striata complex in the next subsection. Panksepp points out that massive lesions in the lateral hypothalamus produce animals that have difficulty doing anything. He writes: "They typically have an abnormally high metabolic rate and proceed on a downhill course toward death unless they are given extended nursing care."

The corpus striata (basal ganglia) complex:

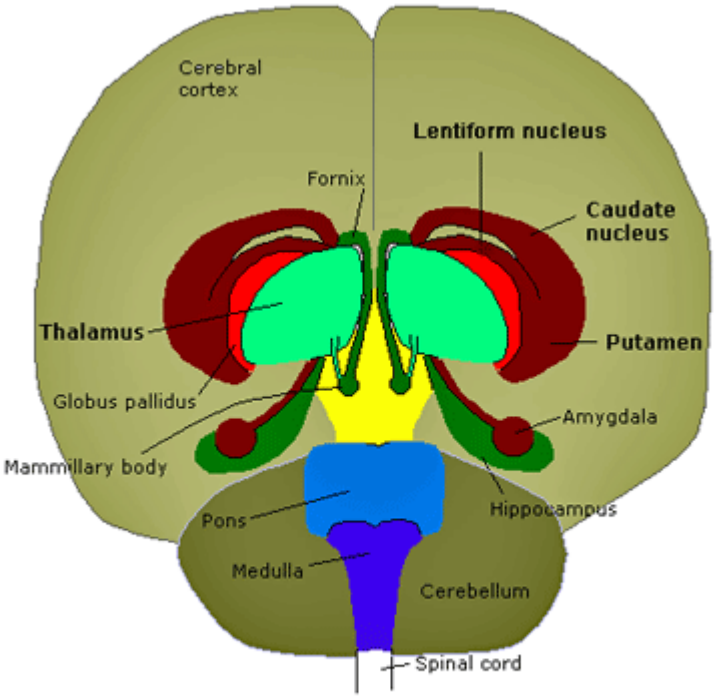
An essential component of MacLean's protoreptilian brain and often referred to as the*basal ganglia*, the *corpus striata* "are most closely linked with the initiation,

smoothness, and precision of movement," writes Restak in *Brainscapes*, "and are responsible for the automatic movements we make without thinking."

Regarding the older terminology, the term *basal* generally means situated at or forming a base. *Ganglion* is the singular of *ganglia* and means "a mass of nerve tissue containing cell bodies of neurons that are located outside the central nervous system," according to*MedlinePlus Dictionary*. So the term *ganglia* is a misnomer. *Nuclei* would be more accurate since the structures are in the brain, the primary component of the central nervous system. The *basal nuclei* then are a collection of interconnected brain structures deep within the brain. However, more specific terms, such as *corpus striatum*, seem to be increasingly employed so I will discuss the structures using the more precise terminology.



The anatomical meaning of the term *corpus* is any mass of tissue in the body that has a distinct structure or function. As you can see in the illustration to the right (image links to source), the*corpus striatum*, which includes the structures labeled *caudate nucleus, lentiform nucleus,* and*putamen,* is indeed an oddly shaped and distinct structure. The corpus striatum's function, as we will discuss, is certainly distinct. The nuclei that make up each corpus striatum are located, as mirror image masses, in each hemisphere to the outside of the more centrally located thalami. Referenced in the plural, these structures are called the *corpus striata*. Components of the corpus striatum, the caudate nucleus and the lentiform nucleus are, according to *MedlinePlus Dictionary*, "separated by sheets of white matter to give the mass a striated appearance" when dissected into sections. Thus, the name *corpus striatum*.



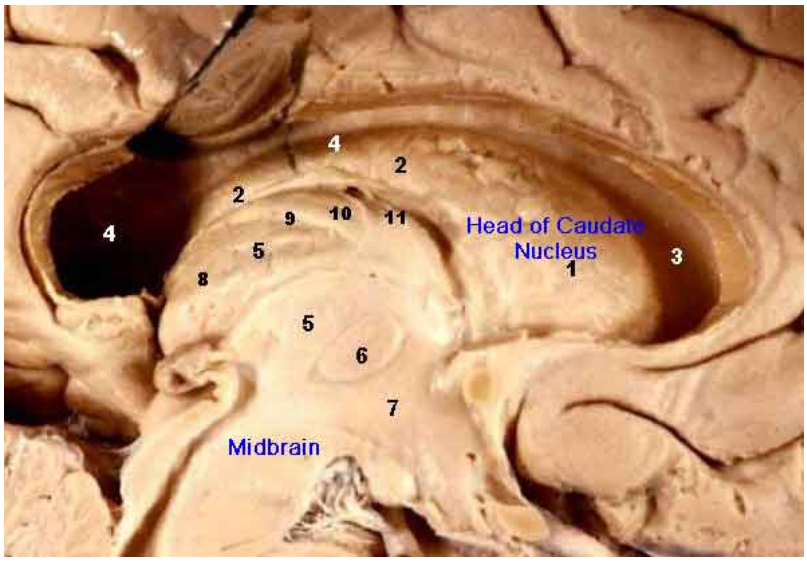
The brain as viewed from the underside and front. The thalamus, corpus striatum (putamen and caudate nucleus), and amygdala have been splayed out to show detail.

The term *caudate* is derived from *caudal*, which in this case means "of, relating to, or being a tail." The term *lentiform* is taken from *lenticular*, which*MedlinePlus Dictionary* defines as "having the shape of a double-convex lens." Nestled within the curve of each lentiform nucleus is a pale yellow globular mass constituting the *globus pallidus*, also called the *pallidum*. These structures are colored bright red in the illustration to the left (image links to source).

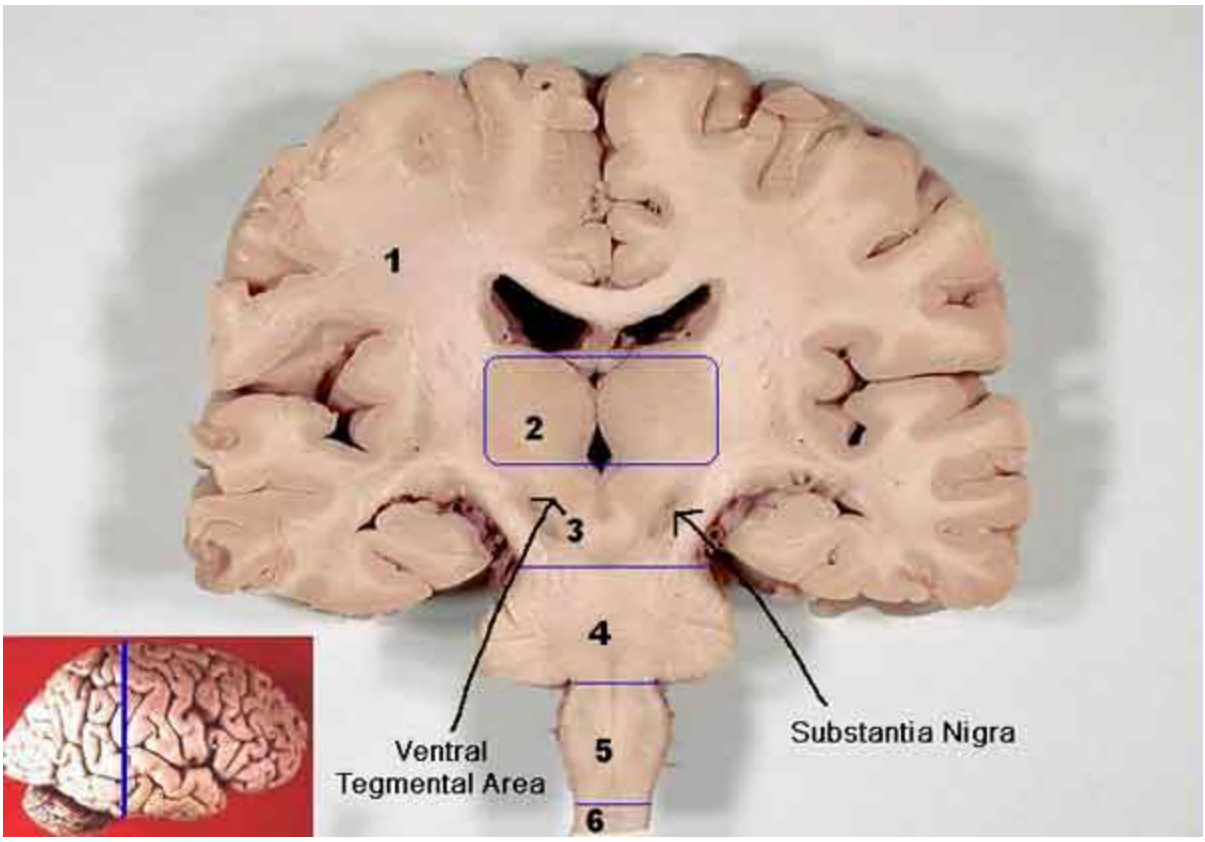
In the brains of persons afflicted with Huntington's Disease, which has a genetic etiology, "excessive levels of endogenous glutamate may gradually destroy the basal ganglia [corpus striata]," writes Panksepp in*Affective Neuroscience*. "Although these patients eventually exhibit severe motor disabilities, their mental status is initially compromised by a schizoid type of disorder characterized by disjointed cognitive activity. For instance, a person may remember all the steps in a favorite recipe but not be able to sequence them into a final product. Apparently, the flow of information through striatal-thalamic-cortical loops helps solidify behavior sequences based on various component parts. The cortex contains the component parts, but the striatum welds them into a coherent plan."

John A. Beal, Department of Cellular Biology and Anatomy, Louisiana State University Health Sciences Center, provides the following two images of anatomical specimens (link to source). In the first picture below right, the right brain hemisphere has been removed. You can see the left hemisphere head of the caudate nucleus, labeled 1, and part of the caudal, tail-like portion of the nucleus, labeled 2. The

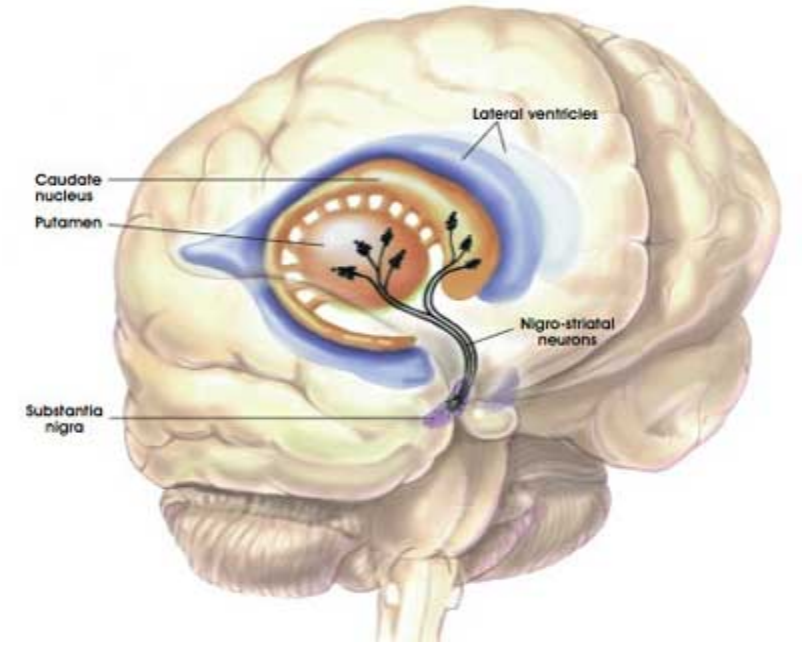
lentiform nucleus is hidden behind the thalamus, labeled 5, and the interthalamic adhesion, labeled 6.



Additional structures work with the corpus striata to manage movement. The*subthalamic nucleus*interconnects with the globus pallidus, which remember is nestled within the curve of the lentiform nucleus. Also, the *substantia nigra*, a group of cells named for their dark color, located in the midbrain, connect with the corpus striata by way of axonal fibers called the*nigrostriatal pathway*. The substantia nigra is, according to *MedlinePlus Dictionary*, "a layer of deeply pigmented gray matter situated in the midbrain and containing the cell bodies of a tract of dopamine-producing nerve cells whose secretion tends to be deficient in Parkinson's disease." You can see the substantia nigra clearly in the image below.



I will note here that in addition to the striated nuclei, associated structures including the globus pallidus, nucleus accumbens, entopeduncular nucleus, ventral tegmental area (VTA), and substantia nigra are all considered part of a system that manages movement. (You can see the approximate location of the VTA in the image above.) Grouped together, these structures are sometimes referred to as the *striatal complex*. Given that not all of the structures included in this complex have a striated appearance, I prefer not to use the adjective "striatal," so I call this complex the *corpus striata complex*. Regarding this system, Panksepp writes: "Both cognitive and emotional information converges here before coherent behavior can occur." Later, he explains that "it seems likely that basal ganglia [corpus striata] circuitry elaborates a primitive feeling of motor presence, which may represent a primal source of 'willpower.' The more highly evolved brain regions must still utilize this system as a final output pathway for behavior."



Neural feedback networks connect the corpus striata to the surrounding neocortex, with primary connections to the cerebral motor areas. To enable finely controlled, smooth movements, neural networks within the corpus striata rapidly manage the interplay of both excitatory and inhibitory signals, integrating input from the environment with information related to body position. Imagine you're at an elegant dinner party, lifting to your lips a fine china cup filled to the brim with coffee into which you've poured too much cream. Not too fast! Certainly you feel the inhibitory signals, the micro-movements necessary to raise the cup without spilling a drop, especially after having two glasses of wine with dinner. The balance of excitatory and inhibitory signals necessary to execute smooth movements depends on neurotransmitters, including dopamine. This explains why Parkinson's disease—marked by a slow, rigid, shuffling gait—develops when dopamine supply from the substantia nigra to the corpus striata is deficient. Corpus striata networks are also responsible for managing memorized movement—those we undertake without forethought. Thus, an excess of dopamine in these networks may help explain the unwanted repetitive, stereotyped movements seen in OCD and Tourette syndrome.

I first learned about the corpus striata from Thomas Aird's article titled "Functional Anatomy of the Basal Ganglia," which appeared in the October 2000 issue of *Journal of Neuroscience Nursing*. Aird explains that some of the more common OCD symptoms are indicative of an organic brain disorder, rather than a psychological disorder. He writes: "Unlike Parkinson's disease, which has historically been seen as an organic brain disorder, movement disorders (dyskinesias) often play out in normal human routines—such as hand washing, counting, or sorting. Thus, people with such symptoms have often been incorrectly construed as having a 'psychological' disorder."

We will discuss dopamine functioning in the corpus striata complex and this system's role in generating symptoms in more detail in Parts 2 and 3 of MyBrainNotes.com. To give you some indication of the importance of the corpus striata complex in

generating normal versus dysfunctional behavior, I will mention here that Graybiel and Rauch reports, in "Toward a Neurobiology of Obsessive-Compulsive Disorder" (2000), that lesions in the corpus striata and/or the globus pallidus can produce "striking OCD-like behavior."

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