Amphetamine Salts

►Stimulant Medications

Amygdala

Nava R. Silton[1], Ariel Brandwein[2]
[1]Fordham University, New York, NY, USA
[2]Long Island Jewish Medical Center, New Hyde Park, NY, USA

Synonyms

Amygdaloid nucleus; Basal ganglion; Corpus amygdaloideum

Definition

The amygdala is an almond-shaped structure located at the anterior medial portion of the temporal lobe of the brain. It is involved in the perception of emotional and affective stimuli and is therefore considered to be a part of the limbic system.

Description

The word "amygdala" derives from the Greek word for almond, the most common description given to the shape of this structure. Anatomically, the amygdala is a mass of gray matter composed of a collection of nuclei located anterior to the hippocampus and medial to the hypothalamus in the temporal lobe of the brain.

The amygdala receives input from various senses: olfactory, visual, somatosensory and gustatory. It then relays information to other areas of the brain such as the frontal and prefrontal cortex, orbitofrontal cortex, hypothalamus, hippocampus and brain stem nuclei. These connections help control the emotional and physiological responses to perceived stimuli. Some of the physiologic responses induced by the amygdala include vasodilatation of vessels in skeletal muscle, tachypnea, elevated body temperature, localized sweating, bowel hypomotility, sphincter constriction and piloerection. Neurotransmitters involved in the amygdaloid pathways include norepinephrine, serotonin, acetylcholine and dopamine.

In general, the amygdala is considered to be an inhibitory center that prevents response to irrelevant stimuli and allows habituation to repeated stimuli. More specifically, it has been theorized that the amygdala is involved in the inhibition of the activity of the periaqueductal gray (PAG), one of the major structures involved in the interpretation of fear. Normally, the PAG results in protective and defensive reactions. The amygdala suppresses these actions resulting in freezing, a manifestation of learned fear.

It has been suggested that there are two pathways directing input to the amygdala. Both pathways traverse the thalamus prior to reaching the amygdala. However, while one path courses directly from the thalamus to the amygdala, the other path is first diverted to the cerebral cortex. The purpose of this dual pathway is thought to allow two reactions to emotional stimuli to occur. The first reaction is an immediate reaction (the direct path); it allows the body to produce a quick response to potentially harmful stimuli. The delayed reaction travels through the cortex first, allowing the brain to analyze stressful situations in more detail to determine the most appropriate response. Through this combined process, the body can instantly prepare itself for potentially dangerous stimuli. Then, if the stimuli are judged to be less harmful, the initial response can be curtailed.

One of the most well-known functions of the amygdala is its involvement in the perception of fear. By incorporating input from a number of sources the amygdala is able to modulate the physiologic and emotional responses to fear. Moreover, the amygdala maintains a certain degree of plasticity which aids in the creation of short- and long-term memory for those situations. In this way, the amygdala is able to control future responses to those same fearful stimuli. In fact, it is postulated that this idea is, in part, responsible for the extinction of phobias through proper conditioning.

Research has suggested that the short- and long-term memory created by the amygdala is done so in an indirect manner. The amygdala secretes neuromodulatory substances in response to emotional situations. Adrenergic, cholinergic and glucocorticoid transmitters are thought to enhance the memory created by those situations. Gamma aminobutyric acid (GABA) and opioids tend to impair these memories. Once GABA and opioids are secreted by the amygdala, these substances influence the memory centers of the brain to either strengthen or weaken the memories for those events.

In addition to fear, the amygdala has also been implicated in the processing of stimuli involved in eating, drinking, sexual desires, aggression, reward and punishment. Unfortunately, in contrast to what is known about its function in the perception of fear, the involvement of the amygdala in other emotions has been less well studied.

According to LeDoux [4], the amygdala begins storing information relating to the body's physical state as early as three months of gestation and as late as five years old. For example, if a pregnant mother became frightened from a house fire and experienced an appropriate physiologic response (i.e. tachycardia, tachypnea, muscle tension, etc.), the fetus would experience the same physical state which would be stored as a memory by the amygdala. In the future, if that person were to be confronted with a similar situation, the frightening experience would be re-triggered.

Changes in the amygdala have been associated with a number of conditions such as post traumatic stress disorder (PTSD), attention deficit and hyperactivity disorder (ADHD), phobias, panic disorder, schizophrenia, depression and autism. More generally, it is thought that the involvement of the amygdala in these situations is related to an increased level of fear and anxiety that is often found to be a comorbidity of those disorders.

There are theories that have suggested that the involvement of the amygdala in some of the above conditions is related to its initial overactivity. The result is an overexcitation of neurons that causes the death of cells in the amygdala and a reduction in its size. As an example, this theory has been proposed as part of the mechanism in the development of depression. In fact, some researchers have postulated that anti-depressant medications may serve to reduce overexcitability thereby preventing the destruction of neurons.

Lesions of the amygdala, such as in Kluver-Bucy syndrome, have been associated with changes in emotion and appetite. Patients exhibit hyperorality, bulimia, hypersexuality and aggression. These lesions may be due to insults such as trauma, infection, seizure activity and tumors. Depending upon the cause of the lesion, the presentation of these symptoms may last only a few days or may be more permanent.

Relevance to Childhood Development

The intact functioning of the amygdala is crucial to the proper development of emotional states and their physiologic manifestations. The memories created by the amygdala early on in life allow the body to react appropriately at a later stage when posed with similar situations.

Changes in the amygdala have been linked to the development of autism in childhood. More specifically, it has been hypothesized that the amygdala plays a role in the recognition of facial expressions. Experiments focusing on monkeys with lesioned amygdalas have shown impaired social interactions in those monkeys, one of the key features of autism. However, others have argued that the lack of social interaction in these monkeys is not due to autism, but rather to a greater degree of fear which is no longer inhibited by an intact amygdala.

Additionally, Bauman et al. [1] conducted a study in which a group of juvenile monkeys had their amygdalas lesioned. They demonstrated that following one year of typical development, these monkeys began to develop stereotypical behaviors, another defining characteristic of autism. However, given the delay of one year in the development of stereotypies, it has been suggested that it is not a lesion to the amygdala itself that induces this behavior, but rather an alteration in the neural circuits involving the amygdala.

ADHD, a relatively common condition in children, has also been associated with changes in the amygdala. A study conducted by Plessen et al. [8] demonstrated that although the size of the amygdala did not differ between control and experimental subjects, the size of individual sub-regions was found to be smaller in children with ADHD. Moreover, morphologic disturbances in the amygdala may interfere with normal processing of fearful situations which may disrupt emotional learning and the drive to sustain attention to otherwise mundane stimuli.

Research has also indicated that there may be alterations in the pathways between the amygdala and the orbitofrontal cortex in children with ADHD; these pathways normally support decision-making and reward reinforcement. The disturbed connectivity of these two areas in children with ADHD may result in more impulsive behaviors and in preferences for smaller immediate rewards. Some of these pathways involve noradrenergic and dopaminergic activity. Therefore, stimulant medications which potentiate noradrenergic and dopaminergic transmission may help to enhance the cognition of children with ADHD.

References

1. Bauman, M. D., Toscano, J. E., Bebineau, B. A., Mason, W. A., & Amaral, D. G. (2008). Emergence of stereotypies in juvenile monkeys (*Macaca mulatta*) with neonatal amygdala or hippocampus lesions. *Behavioral Neuroscience, 122*(5), 1005–1015.
2. Black, H. (2001). Amygdala's inner workings. *The Scientist, 15*(19), 20.
3. Holt, D. (1998). The role of amygdala in fear and panic. *Biology, 202.*
4. LeDoux, J. (1996). *The emotional brain: The mysterious underpinning of emotional life.* New York: Simon and Schuster.
5. LeDoux, J. (2007). The amygdala. *Current Biology, 17*(20), R868–R874.
6. McGough, L. J., Cahill, L., & Roozendaal, B. (1996). Involvement of the amygdala in memory storage: Interaction with other brain systems. *Proceedings of the National Academy of Sciences of the United States of America, 93*(24), 13508–13514.
7. Pearson Education. (2008). http://dictionary.infoplease.com/amygdala
8. Plessen, K. J., et al. (2006). Hippocampus and amygdala morphology in attention deficit/hyperactivity disorder. *Archives of General Psychiatry, 63*(7), 795–807.