International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 02 Issue 11 November 2022

Page No: 1270-1275

DOI: https://doi.org/10.47191/ijmscrs/v2-i11-20, Impact Factor: 5.365

The Functional Implication of the Amygdala in Relation to Fear

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ABSTRACT

Fear is a basic, universal, and primary sensation; its function is to protect against risk situations; without fear, people would act recklessly and endanger their lives. Fear acts as a regulator of our behavior, warning us of dangers and avoiding them when detecting a threat, this is interpreted as such when damage to physical integrity is involved as well as damage against reputation self-esteem, self-concept, or security, depending on the idea and beliefs about it. The amygdala is the structure responsible for this sensation. Hereunder, this text will show a review about the location, structure, functioning and importance of the amygdala, as well as the relationship between this structure and fear through studies carried out in animals and humans.

ARTICLE DETAILS

Published On:
14 November 2022

Available on:
https://ijmscr.org/

GENERAL ANATOMY OF THE TONSIL

The amygdala is a brain structure also known as the tonsillar complex or body discovered in the 19th century by the German physiologist Karl Burdach[1]; It receives that name because of its resemblance to an almond, because of its name in Greek, "amýgdalo". The tonsillar body is located inside the uncus[1] cortex, in the anterior region of the temporal lobe, between the temporal horn of the lateral ventricle and the lentiform complex. It is part of the limbic system, a set of interconnected brain structures that fulfill several basic functions related to instincts and the survival of the species, such as hunger, thirst, sex, memory, and the most primitive emotions. (Figure 1). It receives input from the inferior temporal association cortex, as well as from the thalamus, septal area and olfactory tract, with their respective catecholaminergic and serotonergic projections from the brainstem.[1]

The amygdala is made up of different groups of neurons organized into nuclei, each with different roles. These nuclei are: corticomedial (NC), central (CE), and basolateral (BLA); the BLA receives sensory input and is necessary for anti-fear conditioning; the EC receives information from the BLA and is involved in emotional stimulation. It sends information for the activation of the sympathetic nervous system to the reticular nucleus for the activation of reflexes, to the trigeminal and facial nerves for facial expressions of fear, to the ventral tegmental area, as well as to the locus coeruleus and dorsolateral tegmental nucleus for the release of norepinephrine, dopamine, and epinephrine; the NC is involved in the processing of smell and pheromones.[2]

The connections of the amygdala are predominantly bidirectional and follow three different pathways: the uncinate fasciculus, the stria terminalis, and the ventral amygdalofugal pathway. Connections to cortical areas pass through the uncinate fasciculus, which runs anterior to the tonsillar complex. Projections to the septal area and hypothalamus follow the stria terminalis. The fibers that form the ventral amygdalofugal pathway project to the thalamic nuclei and various structures of the brainstem and telencephalon.[3,4]

The amygdala presents variations depending on the sex (female or male). This explains why slight differences are observed between men and women in emotional memory and sexual responses, since the amygdala has receptors for sexual hormones such as androgens and estrogens, and it has been observed that a greater or lesser amount of these substances can cause long-term changes in the size of the amygdala and in its neurotransmitters. In fact, it seems that men have a larger amygdala than women, but it has not been clearly determined whether this affects the different behavior between men and women.[5]

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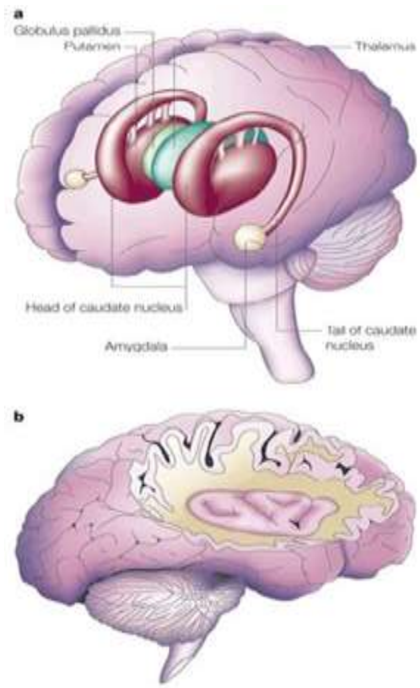

Figure 1. a) Location of the amygdala and basal nuclei in the human brain. b) View of the right hemisphere of the human brain with the superior temporal lobe and sections of the frontal and parietal lobes removed to reveal the insula9.

GENERAL FUNCTIONS OF THE AMYGDALA

This structure is crucial for some functions, and investigations of specific elements of neural circuitry have been carried out over the years. Mentioned below[5]:

Perception of Emotions

Stimulation of the amygdala causes aggression or fear and is even related to aversive memory.

Behavioral Responses to Fear

They occur from the first contact with a threatening factor and produce its memorization, which allows its assimilation as an experience. The responses depend on their connections to the hypothalamus, which in turn activates the autonomic nervous system, producing increased attention to danger, immobilization, or the flight response. The amygdala emits projections to areas that control the facial muscles, such as the facial and trigeminal nerves, which explains the facial expression typical of fear, characterized by wide-open eyes, raised eyebrows, tense lips and an open mouth.

Regarding the response to threatening factors, according to Méndez-Bértolo, C. et al.[3] it is believed that there is a fast subcortical pathway directed towards the amygdala, which has evolved and allowed the rapid detection of the threat. Electrophysiological data of this pathway in humans were recorded, finding rapid amygdala responses in situations of fear. After presenting participants with happy, angry, and fearful gestures, the latter produced shorter latency activation.

This pathway is essential for understanding nonconscious emotional responses. However, it has come to be questioned due to the paucity of evidence for short-latency fear-related responses in the primate amygdala, including humans.[1,3] As a second point, the amygdala appears to be part of a general system for memory. of an emotional type, which allows us to remember which clues in the environment are associated with a dangerous or beneficial event. Thus, when these keys appear in the future, an automatic response of fear or rapprochement can be generated, with the aim of promoting our survival. The activation of the amygdala in the face of stimuli that cause fear causes an enhancement of our memory, that is, we better remember things that happen to us when intense emotions arise simultaneously, thus, emotional arousal or activation is what makes it easier for memories are consolidated.[5]

The study by Kensinger, E. and Corkin, S.[1,4] shows how words associated with high emotional arousal, such as negative words, are better remembered. For this reason, animals and humans learn very quickly to move away from a potentially dangerous stimulus that has caused them great emotional arousal. This argument was examined thanks to the implementation of 6 small experiments on a sample of people where 280 words were selected as stimuli. Half the words were neutral, and the other half were negative. The negative words were selected by be low in valence and high in arousal. The magnitude of the response was presented mostly for negative words.

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Emotion Recognition

One of its functions is to recognize emotions based on the facial expression of others. It is believed that there is a connection between the amygdala and the inferior temporal cortex, where recognition of faces and gestures is processed. Thus, the amygdala gives the emotional meaning to the facial expression and allows us to relate appropriately with others, enhancing social relationships.[5]

Pleasure Responses

The amygdala doesn't just focus on fear; it also links data from the environment with both appetitive and non-appetitive elements of a stimulus. Feeling good in certain places is due to the association of the place with positive events, in contrast to one related to negative events. Thus, we reduce the time we spend in dangerous environments and make our survival likely.[5]

CORRELATED ANATOMOFUNCTIONAL OF THE AMYGDALA AND FEAR

Fear and anxiety are defined as brain states caused by external or internal stimuli that underlie a specific set of measurable behavioral, physiological, hormonal, and autonomic reactions, with the aim of increasing the probability of survival, either by activating fighting functions, escape or immobilization. Fear is generated from acute and objective sensory information.

The amygdala has been shown to be strongly related to fear signal processing and conditioning.[6]

Most of what we understand about fear comes from studies using Pavlovian fear conditioning. In this paradigm, an initially neutral stimulus (also known as a conditioned stimulus) like tone, it evokes fear through association with an aversive event, known as the unconditioned stimulus. For example, a blow to the foot.[1]

ANIMAL MODELS

The close anatomical conservation of the amygdala across species (Figure 3), medial hypothalamus, and periaqueductal gray (PAG) nuclei suggests that similar circuits exist for different classes of fear in different mammals, including humans. Animal studies demonstrate the relationship of the amygdala with fearful emotions. This was seen in monkeys with bilateral amygdala injury when levels of fear and aggression decreased. The amygdala and related areas have been shown to interfere with the acquisition and expression of various indices such as conditioned fear and ongoing behavioral disruption.[7] There is functional conservation of these circuits across species. For example, electrical stimulation of the medial hypothalamus in fish can elicit aggressive behavior. In humans, electrical stimulation of the ventromedial hypothalamic nucleus elicited a feeling of panic and impending doom, and people subjected to electrical stimulation of the dorsolateral PAG showed tachycardia and reported a feeling of uncertainty and being chased by someone. Although the significance of these findings in humans remains unclear, it is speculated that the predator fear circuit in humans may be activated under conditions of severe physical threat or fear of death, and that panic attacks may reflect an extreme behavioral response. predator related.[8]

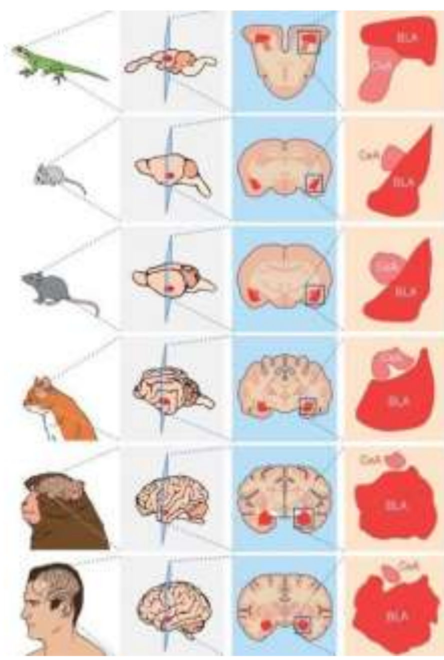

Figure 2. Hexagon of Emotions test for recognition of facial expressions.
The image shows facial expressions. In the first row the expressions are of happiness and surprise; second row: expressions of surprise and fear; third row: expressions of fear and sadness; fourth row: expressions of sadness and disgust; fifth row: expressions of disgust and anger; last row: expressions of anger and happiness9.

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STUDIES IN HUMAN

In humans, the relationships between the amygdala and fear have been predominantly studied using fMRI (Functional Magnetic Resonance Imaging) in face-viewing paradigms showing rage or terror. A fast, subcortical pathway to the amygdala has evolved to enable rapid detection of threats[3]. Adolphs et al.[1] carried out an investigation to address the preferential involvement of the amygdala on facial expressions generated during fear, having as participants a patient with bilateral lesions of the amygdala (patient SM), in addition to six others with damage unilateral (right or left tonsil). The participants had to rate six examples of images with different facial expressions: happiness, sadness, anger, fear, disgust, and surprise, as well as neutral expressions on emotional scales. The SM participant showed abnormal ratings of facial expressions of fear, and to a lesser extent, anger, and surprise. In contrast, patients with damage to the right amygdala did not show significant alterations; and patients with lesions in the left amygdala showed abnormal evidence, without association with fear.[1]

Subsequently, researchers used an adapted version of the activity used by Adolphs that was carried out in a larger group of patients, who suffered from right unilateral lesions secondary to anteromedial temporal lobectomies[9]. These patients showed abnormal processing of faces for sadness, happiness, fear, and disgust.

On the other hand, a method was developed to analyze the perception of fear according to facial expressions, in which some patients presented problems in the functioning of the amygdala complex [9].

In two facial recognition tests, deficiencies were shown in the expressions of sadness and fear. Calder et al.[9] studied two participants with bilateral lesion of the amygdala (patients DR and SE) with an activity that consisted of transformed facial expressions which are illustrated in Figure 2. According to the authors, the lesions of patient DR they were due to a series of operations for intractable epilepsy, which were directed first to the left amygdala and then to the right. While the lesions of the SE patient were caused by encephalitis that caused the destruction of the temporal lobe corroborated with an MRI. The results showed that the DR patient had difficulty recognizing the expressions of disgust and in both patients (SE and DR) the identification of the expressions of fear and anger were deficient. These results complement the results of the Adolphs et al. study, by showing that bilateral damage to the amygdala affects the recognition of facial expressions. Reports from other patients have also shown similar deficiencies in recognition of fear expressions when looking at images of facial gestures. Although these patients have difficulty identifying fear, there is no deficiency in understanding the concept, so they understand the sensation, but cannot perceive it.[9]

Figure 2. Anatomical conservation of the amygdala among different species. 13

PATHOLOGICAL SITUATIONS OF THE TONSIL

Dysfunctions of the tonsil have been related to various neurodevelopmental disorders and to neurocognitive and behavioral alterations. Multiple studies focused on the tonsillar complex have allowed us to understand pathophysiological aspects and formulate new hypotheses in relation to its generation.

There are various circumstances in which the amygdala is the protagonist of mental disorders, such as anxiety disorders, panic attacks, post-traumatic stress disorder or phobias, as well as in alterations associated with the consumption of drugs such as marijuana, according to the panorama that It implies its alteration in hormonal levels and/or the release or inhibition of neurotransmitters, when exposed to these factors (such as

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continuous stress or addictive substances) and considering the constitution and sensitivity (size and development per se) of the amygdala to these.[10]

Depending on the size of the amygdala, (observed both in intrinsic factors, such as genetic predisposition, expressed from various psychiatric disorders, or gender, as well as in extrinsic factors, such as the consumption of addictive substances) it is possible to establish addictive behaviors or express defined disorders from their links between behaviors or events and pleasurable sensations, causing said behaviors to become repetitive. The abuse of certain substances can cause alterations in the amygdala, affecting its proper functioning.[1]

Following the topic on the consumption of addictive substances, the amygdala has a high number of cannabinoid receptors, therefore, it is very susceptible to cannabis producing some change in its functioning. Studies show that the consumption of this substance with its consequent changes in the amygdala, enhance depressive behaviors, as well as a decrease in their reactivity in threatening situations, which represents a lower fear response. It was shown that adolescent female marijuana users were more likely to have abnormal development of the amygdala, manifesting with symptoms of anxiety and depression, coupled with the fact that in adolescence there seem to be a greater number of cannabinoid receptors in this structure. On the contrary, it is known that the prolonged use of cocaine sensitizes the amygdala, so that it is activated more easily.[5]

It can be stated that the amygdaloid complex is involved in numerous psychiatric processes, both due to structural damage to said complex and functional damage. In a study that focused on the amygdala during different processes, it was shown that an altered amygdala complex is observed in common psychiatric disorders, its maximum expression being the Klüver-Bucy syndrome.[11] The Klüver-Bucy syndrome discovered by Heinrich Klüver and Paul Bucy, is a set of symptoms associated with the destruction of certain brain area.

The main symptoms of this disorder are lack of fear, lack of risk assessment, meekness, and obedience together with indiscriminate hypersexuality, hyperphagia, a tendency to explore everything with the mouth, a tendency to become overexcited at any visual stimulus and to imitate it, lack of visual recognition or agnosia and memory disturbances. It has been observed that this syndrome occurs as a direct consequence of the removal or bilateral injury of the tonsillar complex and part of the temporal lobes where the hippocampus and uncus are generally affected. This destruction explains the existence of symptoms linked to affectivity, the emission or inhibition of emotional responses, the management of aggressiveness and sexuality, among many others.[12]

Speaking specifically about disorders, fear in phobias becomes something maladaptive: they are learned just like any other fear, but plasticity changes occur that are produced in an accelerated way in the BLA, being very resistant to extinction, so that the organism interprets that its survival would be at stake if the fear ceased. It has been assumed that lesions in the amygdala could give rise to these phobias, since they make it impossible to generate an unconscious emotional response, especially when the stimulus is emotionally charged with what constitutes fear.[1] Currently, they are being carried out clinical and experimental studies that try to obtain diagnostic and therapeutic information on the role of the tonsillar body in different states of phobia, anxiety and prevalent disorders in young people and adults.[1]

In patients with mood disorders such as depression and bipolar disorder, a certain tendency is observed to present a left amygdala complex of smaller volume. Schizophrenia is a disorder that has been associated with anatomical and functional alterations of the amygdala. has observed a reduction in the volume of the tonsillar body, bilateral in men and unilateral in women, suggesting a greater number of morphometric alterations in schizophrenic men[2]. On the other hand, regarding autistic disorder, it has been observed that, in the same way, the amygdala complex was increased in autistic children, (this is not the case in autistic adolescents, where it has been observed that it is equal to the volume of any healthy adolescent or adult)., preserving only pathology at the microscopic level)[11]. Finally, regarding neurodegenerative disorders, alterations in tonsillar volume have been observed in groups with frontotemporal dementia and Alzheimer's disease in relation to the control group, observing a predisposition to increased tonsillar atrophy.[10]

CONCLUSION

The amygdala is a fundamental structure for different functions in relation to the interpretation and memory of emotions. Fear is a vital sensation for human beings because it promotes a state of alertness in the face of a threat to protect the individual in situations of risk. Evidence in animals and humans proves that there is a relationship between this sensation and the tonsillar complex. The amygdala, along with its nuclei and connections with different structures of the nervous system, are creators of the sensation and memory of fear, and it is closely related to several disorders of great importance such as schizophrenia, autism, and mood disorders, among others.

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