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| RESEARCH ARTICLE

Evolution, Morphology and Function of the Amygdala: Focus on Schizophrenia

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| ABSTRACT
The etiopathogenesis of schizophrenia to date appears unclear. Multiple types of research have focused attention on the possible etiological role of the amygdala. The amygdala is involved in emotion processing, cognitive function, and social cognition; these aspects appear severely impaired in schizophrenia. In this brief review, we will look at studies that have correlated morpho-functional aspects of the amygdala with the psychopathological domains of schizophrenia.

| KEYWORDS
Schizophrenia, amygdala, Evolution, Morphology, etiopathogenesis

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1. Introduction
Lesions of amygdala have resulted in different types of emotional deficits, for example, facial affect impaired recognition, which is correlated with schizophrenia (Fotiadis et al., 2008).

The amygdala has been identified by Burdach in the last nineteen century as the almond shape gray mass of matter visible in the brain (Sava et al., 2020). According to the research made by Porter & Mueller (2020), in the form of mammals, the amygdala is visible in the segregated group of nuclei topography that is situated in the ventrolateral caudal temporal lobe. Amygdala is an almond-shaped structure, and it consists of a total of four components: two of the component receive input from the olfactory system, one component is pallial, which receives different types of cortico-thalamic sensory input, and where the last one is closely associated with the autonomic nervous system. As stated by Perathoner et al. (2016), the presence of the amygdala is seen across the tetra-pods, with the different types of shapes as well as sizes that are gathered from the tetra-pods studies. The homologous structure of the amygdala in zebrafish, an animal model for neuroscientific studies, allowed us to elucidate the role of the amygdala in emotional and cognitive processing (Mueller, 2022). The amygdala is the specific multi-nuclear component that consists of a total of 13 nuclei which are divided among four individual groups, namely basolateral, centromedial, cortical-like, and dorsal (Rhomberg et al., 2018).

2. Anatomy of the amygdala
The amygdala nuclei are divided into four subfields:

1. The basolateral amygdala (BLA), usually or basolateral complex which, includes: the lateral nucleus (LA), the basal nucleus (BA) and the accessory basal or basomedial nucleus (BM) (Blume et al., 2019).
2. The cortical-like group (CoA) consist of the lateral olfactory tract and of the cortical nuclei (Cersosimo, 2018).
3. The centromedial (CM) group that contains both medial olfactory as well as central autonomic nuclei (Ilyas et al., 2019).
4. The dorsal amygdala, also known as the extended amygdala, includes the bed nucleus of the stria terminalis (BNST) and the substantia innominate. This structure contributes to cognitive reward (Fudge and Emiliano, 2003).

According to the research made by Felix-Ortiz et al. (2013), the BLA group is divided into the anterior basolateral amygdala (BLa) and posterior part (BLp) (Yang et al., 2016).

LA nucleus relates to sensory areas, and it is the gateway of sensory input; the LA nucleus is interconnected with the others amygdala nuclei. LA represents the hub of fear conditioning memory (Yang and Wang, 2017). BA nucleus is involved in anxiety and in social behavior (Yang and Wang, 2017). BM nucleus receives afferents from LA and projects to the central nucleus, which represents the output port of most amygdala projections (Yang and Wang, 2017).

The CoA is an area of integration of sensory input and has widespread connections with cortical and subcortical areas (Vàsquez et al., 2018). The CM is connected with the hypothalamus, and it is involved in autonomic and endocrine responses (Mosher et al., 2010).

3. Function of the amygdala

The amygdala plays a crucial role in the integration of autonomic, endocrine and behavioural systems and ensures the adaptation of living organisms to the environment (Rasia-Filho, 2000). The amygdala contributes to regulating emotion and, at the same time, encodes different types of memories under the severe condition when it comes to particular emotions remembrances (De Macedo Rodrigues et al., 2015). The main role of the amygdala is related to analyzing and assigning saliency to sensitive information that has emotional and social importance (Adolphs, 2010). Some of the common emotions which trigger the response are fear, anxiety, and depression. On the other hand, Pagliaccio et al. (2015) stated that the amygdala is the particular brain structure that detects stress stimuli and then provides the signal to the HPA axis for responding by detecting both the emotional as well as biological stressors.

Interestingly BLA and hippocampus are interconnected and regulate the association between emotion and memory (Yang and Wang, 2017).

4. Amygdala and Schizophrenia

Schizophrenia has been associated with particular impairments in social functioning that include difficulty in the decision-making process (Henry et al., 2016). Social cognition is compromised in schizophrenia because of the reduced connection between the insula and the amygdala (Mukherjee et al., 2013). According to the research made by Stevens & Jovanovic (2019), one of the most important key brain-based regions that are fully associated with the emotional aspects of face processing is the altered function of the amygdala. The altered resting-state-based functional connectivity of the amygdala has been evaluated to be impaired in patients with schizophrenia (Walther et al., 2021). As stated by MacKay et al. (2018), schizophrenia is closely associated with brain disconnection syndrome, which involves the abnormal interconnection between the different brain networks, such as the prefrontal cortex, orbitofrontal cortex, insula, fusiform girus, hippocampus and sensory associative cortical regions (Mukherjee et al., 2013).

Specifically, the altered connection between the amygdala and the prefrontal cortex impairs emotion recognition and expression; moreover, this disconnection leads to flat affect, a core negative symptom of schizophrenia (Aleman et a., 2005). The extended amygdala integrates external and internal stimuli; in addition, BNST is connected with the substantia nigra. Through the extended amygdala-nigral pathway, the amygdala modulates dopaminergic pathways (Fudge and Emiliano, 2003). Furthermore, alterations of glutamatergic and GABAergic neurons in amygdalocortical neural pathways have been observed in the brains of schizophrenics (Benes, 2010). It has also been observed that the amygdala is connected through glutamatergic pathways with the anterior cingulate cortex. Inhibition of this pathway has been associated with typical symptoms of schizophrenia, such as motor stereotypies, deficits in social cognition and cognitive dysfunction (Huang et al., 2022). Visual hallucinations are underpinned by a hyperconnectivity between the amygdala and visual cortical areas (Ford et al., 2015), while auditory hallucinations are related to an abnormal connection between auditory cortical areas and the amygdala (Horga et al., 2014). As stated by Green et al. (2015), the altered function of the amygdala during the acute stage of schizophrenia affects the recognition of negative emotions from faces and social judgments. Hyperactivation of the amygdala, measured by the increase of cerebral blood flow, has been observed in paranoia (Pinkham et al., 2015). Moreover, an aberrant computation between external data and internal representation of reality, which leads to delusion, is determined by the disrupted fronto-striatal-parietal-amygdaloid circuit (Corlett et al., 2010). In addition, as reported in several meta-analyses, the amygdala has reduced size in patients with schizophrenia (Barth et al., 2021), and the reduced volume of the amygdala is associated with a higher violence risk (Tesli et al., 2020). Ultimately, recent transcriptome studies focused on long-non-coding RNA associated with synaptic neurotransmission protein and with immune response have been identified in the tissue of amygdale (Tian et al., 2018).

5. Conclusion

Based on the above analysis, it has been stated that patients with schizophrenia show structural and functional abnormalities in the amygdala. The amygdala has a key role in the pathogenesis of schizophrenia, and it can represent, with other brain structures, as the hippocampus, the pathological base of schizophrenia.

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