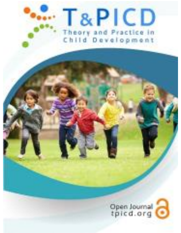

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The Role of the Claustrum in Sensory and Cognitive Development

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ABSTRACT

The claustrum is an important complex neuronal anatomic brain structure whose evolutionary process remains elucidated. The structure in question plays a key role in cognitive and sensory performances. Although it is an increasingly researched topic, especially regarding the importance of differences in children and adults with developmental differences, it is still possible to find very few publications. There are also studies arguing that claustrum is important for the risks of conditions such as autism, depression, anxiety, and Attention Deficit Hyperactivity Disorder and their response to treatment. In this short traditional review, the general anatomical structure of the claustrum and some current research results regarding this structure will be evaluated.

KEYWORDS

Claustrum; claustrum structure sensory system; cognitive development.

INTRODUCTION

The claustrum is a merged neuronal sheet located among the cortical and subcortical regions of the brain, and its relationship with sensory neurons is responsible for regulating the responses and information in the temporal and occipital areas to different stimulants such as sounds and images, independent of semantic relations (Naghavi et al., 2007). For this reason, the claustrum-insula region is especially important for the integration of stimuli.

Sensory integration processes are of great importance as children explore the world and are exposed to new stimuli every day. For example, the simultaneous processing of visual, auditory, and tactile inputs, and children's ability to understand their environment and adapt their reactions are related to colostrum development. This adaptation supports essential skills including object recognition, sound localization, and tactile perception. The claustrum enhances interactions in complex sensory environments by synchronizing sensory inputs.

Regarding cognitive development, the claustrum plays a significant role in children's learning and memory processes. It aids in regulating higher cognitive functions such as attention and awareness, which are vital for acquiring information and solving problems.

This review offers an overview of the anatomy, morphology, cellular structure, and function of the claustrum. It also presents recent research findings that emphasize the claustrum's critical role in both emotional and cognitive development, highlighting its interconnectedness with various brain functions.

Claustrum’s Anatomy

The brain is composed of two fundamental parts: gray matter (substantia grisea) and white matter (substantia alba). While white matter is located within the inner regions of the brain hemispheres, the cortex on the brain's surface and the subcortical nuclei deeper within form the gray matter. Despite being a significant structure within white matter, the claustrum has not been extensively studied (Smith et al., 2017). The claustrum is found in all mammals and was initially described as 'nucleus taeniaformis' by Azyr in 1786. However, its modern depiction and understanding stem from Eber Landau's 1936 naming of it as 'claustrum parvum.' He described it as a structure outlining the upper part of the white matter with a horizontal line, approaching the medial and lateral borders of the temporal cortex, but without continuity (Parent, 2013).

The claustrum is in the cerebral cortex bilaterally, on the inner surface of the neocortex, and deep in the insular region. The claustrum lying on the outer surface of the putamen is a thin and irregular layer (Edelstein & Denaro, 2004). This stretching situation causes the claustrum to be considered as containing both cortical and subcortical structural features, both morphologically and functionally. On the other hand, there are also publications arguing that the fact that it contains fusiform and pyramidal cells in its cell structure means that it contains more cortex structural features (Mathur et al., 2009). On the other hand, it means that the cortex does not have a layered organizational structure and its connections with the striatum and thalamus cause it to differentiate from the cortex (Braak & Braak, 1982). The neuronal structure of the claustrum is also called subcortical due to the Golgi Type 1 Neurons that express the vesicular glutamate transporter and are more frequently found in subcortical organs (Mathur, 2014). As a result, the claustrum is considered a subcortical gray matter layer or a noncortical structure located within the white matter of the cortex (Mathur, 2014).

Figure 1.
Azyr's claustrum drawings (Adapted from Parent, 2013)

Although the claustrum is derived from the insular cortex morphologically, it is a special layer separated from the multiformis lamina of the insular cortex. However, it shows that even in cases without an insular cortex in one hemisphere, the claustrum can develop fully functionally by separating from the capsula interna and putamen (Machi, 1948). Additionally, embryo studies have shown that the claustrum develops and is derived before the insular cortex. Another view mentions the claustrum is derived from the paleostriatum (Kurada et al., 2019). A third view, from a hybrid perspective, argues that this structure, which is neither cortical nor subcortical, derives from the pallial matrix and strial matrix (Arrigo et al., 2017). The claustrum's location is between the insular cortex and the putamen (Rae, 1951). The claustrum apex, which begins close to the insular cortex, extends supeo-laterally and follows the ventral and lateral edges of the putamen (Andersen, 1968).

The lower part of the claustrum extends towards the orbital gyrus. Its lower border aligns with the level of the insular cortex and putamen, while its upper border is situated at a deeper level compared to the upper border of these two structures. Its medial edge is smooth, and its lateral wing is irregular. The reason for this is that it needs to adapt to the surface it grasps (Kurada et al., 2019). This structure, with a superinferior length of 22 mm and an anterior-posterior length of 28 mm, constitutes 0.2% of the volume of the hemispheres (Kapakin, 2011; Morys et al., 1996).

Figure 2.

Localization and neighborhoods of the claustrum (Karasu, 2020:9)

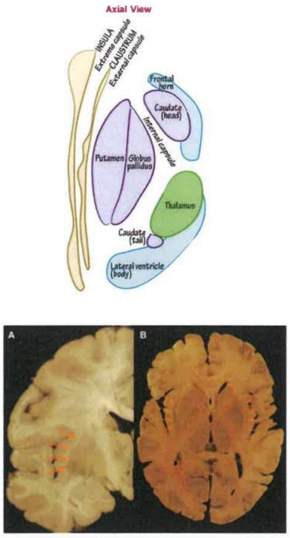
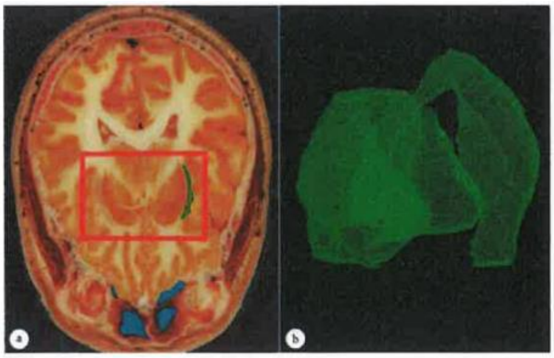


Figure 3.

3D view of Claustrum taken from Visible Human Data (NHM, 2024)

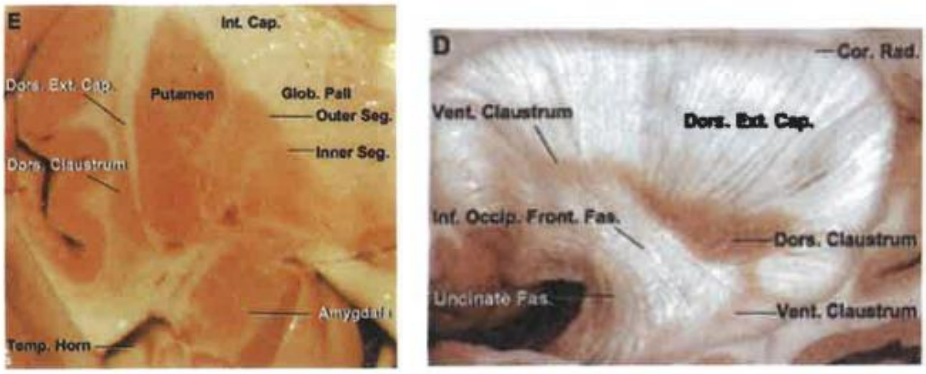


In topographic studies, the claustrum is divided into 4 basic sections: dorsal, orbital, temporal, and paraamygdalar. Another examination method divides the claustrum into two parts: a dorsal compact section and scattered gray matter. Dorsal claustrum is a gray matter layer with a triangular appearance between the putamen, from which it is separated by capsula externa, and the insular cortex, derived from capsula extrema, and forms the posterior-superior part (Kazaiawa, 2008). The ventral claustrum appears as a scattered gray matter structure segmented by the uncinate and inferior occipitofrontal fasciculus.

The claustrum has many afferent and efferent connections. Although these connections are connected to many important structures, they are mostly with the cortex. The claustrum is specifically connected to the prefrontal, cingulate, auditory, visual, and somatosensory cortex. This means that it is a structure that is closely related to vision, hearing, and the limbic system and is also in communication with subcortical structures. Especially the thalamus, hypothalamus, striatum, and hippocampus are connected to the claustrum. This means that the claustrum is in communication with many important structures that provide our sensory and cognitive functions. The claustrum can be thought of as the conductor of the cerebral orchestra in terms of its complex roles in multiple activities. The claustrum projects ipsilaterally to many cells in the cortex. These structures are called corticoclaustral and interclaustral pathways. Claustrum is the structure with the most connections according to its volume.

Figure 4.

Posterior-superior claustrum and ventral claustrum (Adapted from Kazaiawa et.al., 2008)



Sensory System and Clastrum

The bidirectional cortical connections of the claustrum underscore its role in multisensory integration, facilitating the interpretation of complex sensory inputs. Electrophysiological evidence supporting this function was provided by Segundo and Machne (1956) and later confirmed by Spector et al. (1974) in animal experiments, where 75% of claustral cells responded to multiple sensory modalities, including touch, blink, click, odor, vagal, and dental pulp stimulation. These polymodal neurons exhibited convergences such as somato-olfactory, somato-visceral, and somato-nociceptive (Segundo and Machne, 1956).

Two theories regarding multisensory integration exist. The first theory posits that clastrum occurs within multimodal regions processing specific combinations of sensory inputs, reported in various brain areas such as the arcuate sulcus, superior part of temporal sulcus, inferior and posterior parietal lobules, amygdaloid complex, hippocampus, and lastly superior colliculus (Thompson & Shaw, 1965; Ettinger & Wilson, 1990). Given the claustrum's responsiveness to multiple senses, it likely facilitates connections between these modalities. The second theory, proposed by Ettinger and Wilson (1990), suggests that no single brain structure is solely responsible for cross-modal integration; instead, a subcortical relay nucleus, potentially the claustrum, allows communication and correlation among sensory cortices. Thus, theoretically, the claustrum is in charge of synchronizing the cortical areas to enable integrated multisensory processing, although the exact mechanisms and locations of this integration remain unclear.

Another significant finding is the consistent activation of the insula-claustrum region during multisensory tasks, indicating its role in sensory integration (Hörster et al., 1989; Lewis et al., 2000; Olson et al., 2002; Naghavi et al., 2007; Kavounoudias et al., 2008).

The study of human speech encompasses two main components: auditory (heard speech) and visual (seen speech), which has been a major focus of literature. To investigate the neural representation of audiovisual integration of these two components, imaging tools such as functional magnetic resonance imaging (fMRI) have been commonly used. In a study examining synchronized and unsynchronized speech and mouth movements, as well as silent speech and viewing a static face, lip-reading primarily activated the STG/STS. Synchronized and unsynchronized audiovisual speech activated similar brain regions involved in cross-modal integration, with prominent activation near the left claustrum, a subcortical region. Region-of-interest analysis showed no differences between audiovisual conditions in STS and parietal areas, although synchronized audiovisual stimuli led to a higher signal change in the claustrum region, confirming its role in audiovisual integration.

In a 2020 intervention study by Almeida et al., music therapy applied to premature infants demonstrated significant improvements in the maturation of the external capsule/white matter. Acoustic stimulation was found to promote claustral maturation, crucial for perceiving and interpreting such stimuli. Additionally, infants who received music therapy showed larger amygdala volumes and measurements of the claustrum/external capsule and uncinate fasciculus, highlighting the therapeutic potential of music in enhancing neurological development.

Cognitive Development and Clastrum

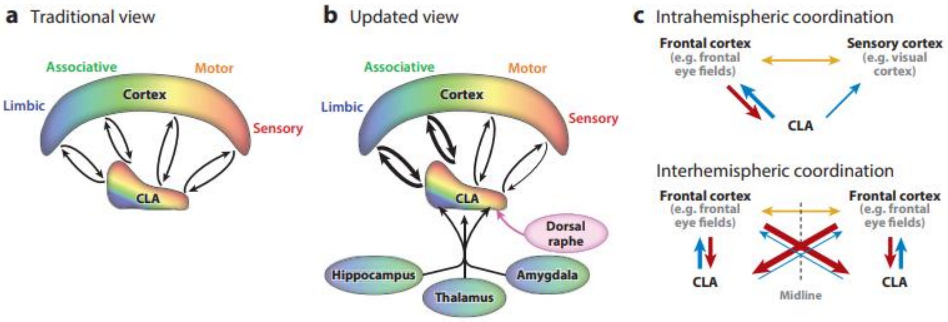
There are a few studies that reveal different opinions about the importance of colostrum for cognitive development. Further investigation is needed to elucidate the claustrum's role in stress response, learning, and adaptation to environmental changes. Current research on the claustrum's anatomical and physiological characteristics suggests its involvement in limbic functions such as attention, memory formation, emotional processing, anxiety, and alertness. It appears to relay limbic information to various cortical regions, thereby influencing perception. Specifically, the claustrum is implicated in feedforward inhibitory control over the cortex to execute these functions. However, the precise mechanism by which this inhibition influences task-related neural activity remains incomplete

Cognitive functions, including voluntary attention and executive control by the frontal cortex over subordinate structures, rely on complex circuitry mechanisms that are not yet fully resolved. Given its extensive connections with numerous cortical areas, the claustrum is believed to modulate the cortical mantle for top-down control. Yet, it remains unclear whether the claustrum itself receives top-down inputs and how it processes such inputs (White et al., 2018).

In a recent study by White et al. (2020) using fiber photometry, high claustrum activity was found to be associated with correct responses in the cognitively demanding five-choice response test compared to the less demanding single-choice version. Increased claustrum effectiveness during reward acquisition was also observed under high task demands. Moreover, optogenetic inhibition of the claustrum before responding reduced choice accuracy in the five-choice task, but not in the single-choice task, indicating the claustrum's role in cognitive control essential for optimal behavioral performance under challenging conditions. Similarly, Kersey and James (2013), when evaluating claustrum activity in writing tasks involving active and passive learning methods, found significant bilateral involvement of the insula and claustrum during active learning. This suggests that the insula and claustrum regions are particularly engaged in multitasking, observation, and execution during self-generated writing and active learning processes. No difference in fusiform gyrus activation was observed during passive learning, indicating a minor (yet significant) activation difference compared to resting conditions.

Figure 5.

Multisensory and other functions of the claustrum according to current theories (Adapted from Jackson et al., 2020)



Numerous studies have shown that claustral neuron networks become active in response to psychological stressors. Major inputs to the claustrum during stress originate from the basolateral amygdala. Additionally, single-neuron dual-projection labeling in various brain regions, such as the ipsilateral ectorhinal/perirhinal cortex, entorhinal cortex, and contralateral basolateral amygdala, underscore the claustrum's collaboration with multiple brain structures depending on stress levels (Tanuma et al., 2022).

Hedderich et al. (2021) conducted a study evaluating the developmental impact on the claustrum in prematurely born infants, highlighting deficits associated with its functions. Premature birth affects claustral development in several ways. Firstly, claustrum development appears to rely on temporal subplate neurons during intrauterine brain development, which are disrupted by prematurity. Secondly, as the most densely connected region of the mammalian forebrain relative to its volume, the claustrum's influence on pre-oligodendrocytes affects the development of white matter connections, including those involving the claustrum itself. Thirdly, due to its extensive connectivity, the claustrum contributes to general cognitive functions such as selective attention and task switching/maintenance, which are compromised in premature infants. Therefore, structural changes in the claustrum following premature birth may contribute to impaired general cognitive performance, indicating alterations in the claustrum's microstructure post-premature birth. Literature suggests abnormal claustrum development, potentially linked to abnormal subplate neuron and forebrain connectivity development due to prematurity.

Understanding the anatomical structure of the claustrum and its relationship to higher cognitive functions is essential for integrating knowledge into cognitive development. Studies have shown variability in this structure among children with specific developmental differences, such as autism spectrum disorder (ASD), which includes sensory and cognitive variations. The claustrum's complex connections are vital for comprehending the neurobiology of autism, as disruptions in related basal ganglia, limbic structures, and other cortical and subcortical regions have been implicated in the disorder. MRI comparisons between 16 children with autism and 14 typically developing children revealed smaller volumes in four claustral regions in axial and coronal planes, supporting theories of disrupted long-range circuits associated with autism (Davis, 2014)."Recent stereological studies indicate significant delays in neuronal growth within the claustrum in individuals with ASD. Research on larger autistic children and adults suggests that accelerated neuronal growth during youth partially compensates for neuronal size deficits within the claustrum. Dysregulation in claustral neuronal growth synchronization appears to significantly contribute to clinical autism symptoms, affecting interactive brain methods involving the social brain, sensorimotor systems, and memory. Smaller claustrum volumes and reduced neuronal sizes may indicate insufficient connectivity in the brains of individuals with autism, underscoring the need for further research into the claustrum's role in facilitating appropriate cognitive, emotional, and sensory development in children. Despite the limited number of studies in the literature, our understanding of the claustrum's role and its complex anatomical connections remains insufficient.

There are also studies stating that the decrease in activity observed in the claustrum may be associated with the onset of depression (Kessler, 2003). There are studies monitoring markers of claustrum activity not only in depressive disorders but also in anxiety disorders. It has been reported that prefrontal cortex, anterior cingulate, parietal cortex and amygdala region dysfunction may play a role in the development of anxiety. In a PET study conducted on 8 healthy individuals, 5 males and 3 females, following bolus injection of cholecystokinin tetrapeptide (CCK-4); An increase in cerebral blood flow was detected in the anterior cingulate gyrus, claustrum-insular-amygdala region and cerebellar vermis in people who received CCK-4 injection compared to the placebo group. As a result, it has been suggested that drug-induced or non-drug-induced anxiety in humans may be associated with increased cerebral blood flow in the claustrum-insular-amygdala region (Manstead, 2008). Similar findings are observed in ADHD findings that do not respond to treatment. Children who did not respond to treatment or had inadequate responses showed increased blood flow in the left ACC, left claustrum, right ACC, and right putamen compared to responders; while decreased blood flow was observed in the right superior parietal lobe (associated with parietal cortex attention, working memory, episodic memory access, and visual awareness). These findings suggest that patients with ADHD who respond differently to treatment may exhibit distinct patterns of blood flow in brain regions known as part of the fronto-striatal circuit and associated with the posterior attention system (Cho et al., 2007). A meta-analysis study showed that there may be structural concordance within the framework of findings from neuroimaging studies on children with relevant disorders (Cheung et al., 2010). Structural areas specific to this adaptation include the right parahippocampal gyrus, putamen, posterior cingulate, claustrum, and left thalamus (Cheung et al., 2010).

In the light of all this information, it can be said that the claustrum, whose importance has been revealed in terms of intellectual abilities, emotional competencies and healthy mood, is also important in terms of stepping into adulthood and emerging adulthood. Some of the studies based on gerontological and developmental psychology encountered the mystery of the claustrum when they examined the adulthood process of individuals between the ages of 18-29 by taking measurements in 6-month periods. Considering the studies conducted, it can be said that the literature on emerging adulthood will increase rapidly in the coming years, just like in adolescence. For example, a very recent study (Bennett and Baird 2009) comparatively examined the brain's morphometry to reveal developmental differences in adolescence and emerging adulthood. Data were obtained from 19 participants six months apart with the high-resolution T1-weighted structural magnetic resonance imaging (MRI) scans. Voxel-based morphometry was evaluated to reveal the changes. According to the results, significant energy was detected in the right midcingulate, inferior anterior cingulate gyrus, right caudate head, right posterior insula and bilateral claustrum regions of the brain. increases were observed. Additionally, no regional changes were observed in the two control groups. The results showed that there are significant differences in brain development and structure according to age, even after the age of 18.

CONCLUSION

The claustrum is an important neurological structure that performs many neurological functions that have not yet been fully elucidated in terms of its cortical connections and location. In any large organization comprising multiple modules that process incoming information and generate intelligent behavior, internal information flow is a critical challenge. Each module focuses on its own inputs and outputs, but how does one module monitor the activities of others? Moreover, how does the entire organization assess the overall situation and decide on the best course of action?

Inter-module communication often leads to information overload despite extensive direct connections and nonlinear dynamics. For instance, in military operations, individual units make decisions based on local observations of neighboring units, which may be effective locally but not necessarily aligned with broader strategic objectives. This decentralized decision-making was evident in historical conflicts like the Napoleonic Wars, where brigade commanders had to act independently while waiting for crucial information to travel from one location to another.

Technological advancements, such as wireless telegraphy during World War II, revolutionized command and control. Winston Churchill, for example, established a control room at 10 Downing Street equipped with a large map. This map displayed miniature models representing planes, ships, and tanks, which could be moved in response to real-time reports from the battlefield. This setup allowed commanders to quickly assess the entire battlefield, facilitating rapid decision-making and ensuring that strategic decisions were made based on comprehensive situational awareness.

The claustrum has connections associated with multisensory and higher cognitive functions. The claustrum has many afferent and efferent connections. Although these connections are connected to many important structures, they are mostly with the cortex. The claustrum is specifically connected to the prefrontal, cingulate, auditory, visual, and somatosensory cortex. In particular, the claustrum appears to exert feedforward inhibitory control over the cortex to perform these functions. In this respect, comprehensive experimental studies are needed to reveal the effect of the claustrum on areas such as sensory system, attention, alertness, and problem-solving and to elucidate its developmental role. Elucidating the developmental importance of colostrum may create a significant advantage in the prevention and treatment of problems such as autism spectrum disorder. In addition, it can mean a multidisciplinary field of action to support children's educational performance, affective development or emotional regulation. Therefore, it is very important to improve the neuroanatomy knowledge of child development specialists and to take initiatives to conduct multidisciplinary studies on this subject.

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