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Functional Aspects of the Human Claustrum – Literary Review

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The claustrum is an irregular and fine sheet of grey matter in the basolateral telencephalon present in almost all mammals. The claustrum is separated laterally from the insular cortex by the extreme capsule and medially from the lentiform nucleus by the external capsule. It has been the object of many studies using animal models and more recently in humans using neuroimaging. The claustrum has been involved in cognition and disease such as fear recognition, suppression of natural urges, multisensory integration, conceptual integration, seizures, multiple sclerosis. Nevertheless, the function of the claustrum still remains unclear. We aim to summarize the various scientific reports present in the literature regarding the structural and functional connectivity of the human claustrum using neuroimaging.

Key words: claustrum, functional connectivity, multisensory integration, relevant stimuli

Introduction

The claustrum is an anatomical structure enjoying high academic interest in the last decades due to its enigmatic role despite being anatomically described for a couple of centuries and hypothetically associated with a wide variety of functions or aspects of such in the scientific literature. In the last scientific work of Crick and Koch in 2005 [3], the idea developed that the claustrum plays a central role in consciousness and since then with the development of more precise scientific investigational methods and technology new data have accumulated regarding its anatomical connections and physiological properties. Out of all conducted research many widespread connections to all areas of the cerebral cortex and subcortical structures which suggests a role in the higher neurological functions and supports the Crick and Koch hypothesis. Due to extensive connections with the frontal cortex, a possible role for the guidance of executive functions and higher neurological functions including some aspects of

consciousness has emerged. Among them specific roles in the processing of salient stimuli and the fixation of attention stand out.

Literary review

Functional MRI (Magnetic resonance imaging) assays have provided evidence for simultaneous activation of the claustrum and different cortical zones such and subcortical structures such as frontal cortex, insula (evaluating stimuli), anterior cingulate cortex (controlling attention), thalamus in the different investigational paradigms.

Histologically in humans the structure consists like the neocortex of spiny projection neurons and aspiny interneurons. All of them can be stratified according to the expression of different peptides like parvalbumin, VIP (vasoactive intestinal polypeptide), somatostatin, neuropeptide Y and others. This expression being speciffic for different neuronal populations aids in specifying the embryogenesis of the claustrum. This is a contested field due to the intimate position of the structure between the putamen and the insular cortex and near the amygdaloid complex. After a 100-year debate in the scientific literature for the possible origin of the cell populations of the claustrum, the hypothesis prevails that they come from the ventrolateral dorsal pallium formed in the dorsal migratory stream from where it spreads out in the lateral pallium. As a result from over 40 years of anatomical tracer studies vast reciprocal connections with almost all parts of the cerebral cortex are observed. The most dense ones are with the frontal cortex while the ones with the sensory areas are less pronounced. The claustro-cortical connections are topographically organized on the dorso-ventral axis of the claustrum, forming modules with the different cortical areas specific for different modalities [2]. Thus a tendency is observed that cortical areas that share cortico-claustral connections also share connections from the same claustral area through claustral neurons that send out branching axonal collaterals innervating simultaneously both cortical areas. Research shows that claustral neurons have axons that branch out extensively in many cortical areas including in the contralateral hemisphere. Another interesting aspect of the cortico-claustral and claustro-cortical connections is their tendency to synapse more on interneurons which constructs a reciprocal antegrade inhibitory neuronal net. Apart from the cortical connections of the claustrum, its one-way afferent connections from many subcortical structures have also been observed. These subcortical structures belong to the lymbic system like the basolateral amygdala, hippocampus, intralaminar thalamic nuclei and others. The claustrum also receives many neuromodulatory afferences from the basal cholinergic brain centers like the substantia innominata and from the serotoninergic brain centers like the dorsal raphal nucleus as well as from the dopaminergic brain centers. These lymbic and neuromodulatory afferent connections to the claustrum through its different areas can help in activating or suppressing the excitability of large efferent claustral neuronal nets.

Despite research in the last 10-15 years forming and clarifying our understanding of the different aspects of this brain structure, the claustrum continues to be associated with a wide variety of functions without an evident key one. For example, in spite of possibly not being the only area serving as the seat of consciousness as some scientist postulate, evidence shows that the claustrum plays a role in the processing and electing of salient stimuli and the guiding of attention – functions, pertaining

to the state of increased vigilance and markers of consciousness [6,7]. On the other hand, the involvment of the claustrum in modulating the cortical activeness during sleep has also been proven [4]. A possible conclusion which emerges, considering the connection of these functions with the lymbic system is the role of the claustrum in integrating lymbic-associated information with sensory and motor cortical areas. This is supported by its position and the observed vast connections with all cortical areas. Thus a hypothesis emerges that the claustrum is a center for associating sensory and lymbic information and direct influence over attention through the frontal cortex and control of executive functions [1]. Functionally this allows the claustrum to recognize the contextual significance of a stimulus in order to guide correctly the attention and coordinate cortex activeness, directing the focus on situationally relevant stimuli. A possible mechanism through which the claustrum can accomplish this is activating of cortical interneurons which leads to antegrade inhibiting and suppressing of cortical activity to non-relevant stimuli. The role of this structure in slow-wave sleep can aid in consolidating the learned information, which is associated with relevant stimuli.

Conclusion

In conclusion, the claustrum is a highly connected brain structure hard to study due to its anatomical location and irregular form. Neuroimaging offers a powerful tool to explore its function non-invasively. The claustrum literature – including studies in animal model and in humans – has evidenced the vast anatomical connections between the claustrum and the entire cerebral cortex as well as with the subcortical structures. This helped to characterize the functional connectivity of the human claustrum, which mainly includes positive relations with insular, frontal, temporal and cingulate cortex. These findings evidence the close relationship of the claustrum with the salience network, strongly supporting its proposed role to mediate the salience value of sensory stimuli [5,8]. It has been suggested that the claustrum is central in the integration of information from multiple cortical regions into a coherent whole [3], while others have speculated that it may be central to detecting and prioritizing important external stimuli.

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