

THE CLAUSTRUM: BARRIER OR PORTAL?

F. Denaro¹, R.K. Holmes¹, I. Sofowora¹, Y. Liadi¹, T. Solomon¹, P. Dike¹, J. Ladow¹, J. Wachira¹,
L. R. Edelstein²

¹Department of Biology, Morgan State University, Baltimore – Maryland, USA

²Medimark Corporation, San Diego – California, USA

Corresponding author: Lawrence Edelstein, email: larry.edelstein@gmail.com

ORCID: 0000-0003-1885-4385

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INTRODUCTION

The future of claustrum research holds tremendous promise, with emerging insights into its complex role in brain function and cognition. The claustrum, a thin sheet of neurons located deep within the mammalian brain, has historically been a rather mysterious structure [1]. For many years, its function was largely unknown, but recent research has begun to unveil its fascinating potential [2, 3]. Continued work on the neurocytology of the claustrum has revealed several classes of neuron distinguished by size and morphology, each roughly correlating with its anatomical location [4]. Tracing studies serve to elucidate how these neuron classes communicate with different cortical and subcortical areas, each with broad functional implications.

UNDERSTANDING THE ROLE IN CONSCIOUSNESS

One of the most exciting areas of claustrum research is its potential involvement in consciousness. The claustrum has been thought by some to play a critical role in consciousness owing to its heterotopic, reciprocal and multimodal connectivity with nearly every region of the brain, including – most significantly – those involved in sensory processing, motor control, and higher cognitive functions. In his final paper, titled “What is the function of the claustrum?” Nobel laureate Francis Crick hypothesized that the claustrum might be central to the generation of conscious experience [5]:

“We think that a more appropriate analogy for the claustrum is that of a conductor coordinating a group of players in the orchestra, the various cortical regions. Without the conductor, the players can still play but they fall increasingly out of synchrony with each other. The result is a cacophony of sounds.”

As brain-imaging techniques improve, more sophisticated studies could make clear how the claustrum contributes to integrating sensory input, emotional states, and self-awareness, possibly providing crucial insights into the nature of consciousness itself.

EXPLORING NETWORK DYNAMICS AND SYNAPTIC PLASTICITY

The claustrum is richly interconnected with other brain regions and its role in coordinating or modulating network activity is a topic of increasing interest. Research could expand to explore the synaptic plasticity of claustral neurons – how they change and adapt in response to experiences or stimuli [2, 3]. This might not only enhance our understanding of cognition and perception but also have implications for treating neurological disorders. For example, if the claustrum is involved in integrating sensory information across different modalities, its dysfunction could contribute to conditions like schizophrenia, autism, or even certain types of epilepsy [6]. By mapping these pathways, researchers could identify targets for new therapies.

NEUROTECHNOLOGICAL ADVANCES

As neuroimaging technology advances, such as the development of more precise functional magnetic resonance imaging (fMRI) and optogenetic tools, scientists will be able to probe the claustrum with far more accuracy [7]. This would allow for a deeper understanding of how activity within the claustrum interacts with other neural circuits in real-time. Additionally, optogenetics might make it possible to selectively manipulate claustral activity, providing experimental control over its function and offering new ways to investigate its role in behavior and cognition.

IMPLICATIONS FOR COGNITIVE DISORDERS AND THERAPEUTICS

As the role of the claustrum in cognitive processes is better understood, it may become a critical target in treating cognitive disorders. Disorders like Alzheimer's disease, Parkinson's disease, and certain types of dementia could benefit from therapies that target the claustrum, especially if it plays a key role in the brain's ability to integrate sensory inputs and form coherent cognitive states [8]. Moreover, conditions such as attention deficit disorder, where sensory processing and focus are often disrupted, might also see treatments aimed at the claustral network. The ultimate goal would be to develop interventions that correct any imbalance or dysfunction within the claustrum and its connections to restore normal brain function.

ETHICAL AND PHILOSOPHICAL QUESTIONS

As researchers uncover more about the claustrum's involvement in consciousness and cognition, important ethical and philosophical questions will arise. For instance, if the claustrum is indeed central to conscious experience, would manipulating it interfere with a person's sense of self or identity? Could this knowledge lead to ethical dilemmas surrounding brain-computer interfaces, where individuals might gain control over their claustral activity? While the potential for treating disorders is significant, as the field progresses these questions will need to be carefully addressed.

INTERDISCIPLINARY COLLABORATION

The future of claustrum research will benefit from interdisciplinary collaboration between neurobiologists, cognitive scientists, engineers, and ethicists. For

example, computer models of brain networks might help simulate how the claustrum integrates signals, while behavioral neuroscientists will study how its activity correlates with changes in cognition or awareness. Combining these efforts could accelerate the discovery of novel pathways for understanding both normal and disrupted brain function.

In summary, the claustrum is poised to be one of the most intriguing and impactful areas of neuroscience in the coming decades. As new technologies and research methodologies continue to evolve, we are likely to gain a clearer understanding of this enigmatic brain structure. This could not only provide profound insights into the nature of consciousness and cognition but also open the door to new treatments for a range of neurological and psychiatric disorders.

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REFERENCES

1. Edelstein LR, Denaro FJ. The claustrum: a historical review of its anatomy, physiology, cytochemistry and functional significance. *Cellular and Molecular Biology (Noisy-le-Grand)*. 2004;50(6):675-702.
2. Hinova-Palova D, Landzhov B, Edelstein L, et al. Identification of degenerated synaptic boutons in the dorsal claustrum of the cat after electrolytic lesions of the intralaminar thalamic nuclei. *J Histotechnol* 2004, 47(3), 117–125. <https://doi.org/10.1080/01478885.2024.2335827>
3. Landzhov B, Hinova-Palova D, Fakhri K, et al. (in press). Corticoclaustral connections in the cat. *J Histotechnol* 2025. <https://doi.org/10.1080/01478885.2025.2476835>
4. Denaro F, Holmes RK, Sofowora I, et al. Neuromorphological analysis of the primate claustrum. *Microscopy and Microanalysis*, 2023, 29(Suppl. 1), 2119-2120. <https://doi.org/10.1093/micmic/ozad067.1098>
5. Crick FC, Koch C. What is the function of the claustrum? *Philosophical Transactions of the Royal Society B: Biological Sciences*, 360(1458), 2005, 1271-1279. <https://royalsocietypublishing.org/doi/10.1098/rstb.2005.1661>
6. Nikolenko VN, Rizaeva NA, Beeraka NM, et al. The mystery of claustral neural circuits and recent updates on its role in neurodegenerative pathology. *Behavioral and Brain Functions*, 2021, 17, Article number 8. <https://doi.org/10.1186/s12993-021-00181-1>
7. Beloate LN, Zhang N. Connecting the dots between cell populations, whole-brain activity, and behavior. *Neurophotonics*, 2022, 9(3), 032208. <https://doi.org/10.1117/1.NPh.9.3.032208>
8. Chen CY, Yang GY, Tu HX, et al. The cognitive dysfunction of claustrum on Alzheimer's disease: A mini-review. *Frontiers in Aging Neuroscience*, 2023, 15, 1109256. <https://doi.org/10.3389/fnagi.2023.1109256>