# The Thalamic Bridge to Cognition and Consciousness

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## Abstract

From an evolutionary perspective, deeper brain structures are postulated as being more primitive than those that were developed later on. As such, the thalamus, being a deep brain structure, is generally believed to occupy one such primitive role: that of a 'sensory relay station'. Recent evidence, however, suggests that the thalamus is in fact responsible for more complex and higher order functions involving cognition and consciousness, processes previously attributed solely to the cerebral cortex. This review examines several of these emerging theories through the lens neural pathways, with particular focus placed on how the complex circuitry of the thalamus allows for the intricate connectivity between itself, the cerebral cortex, and other subcortical structures.


## Introduction

The thalamus remains a mysterious structure in neurobiology: arising from the diencephalon and playing numerous essential roles in human physiology. The diencephalon can be divided into four parts: the epithalamus, the dorsal thalamus, the ventral thalamus, and the hypothalamus. This review will focus primarily on the dorsal division, as this is the portion that innervates the cerebral cortex, which is most relevant to this discussion. The thalamus is a paired gray matter structure composed of an array of different nuclei each serving a specific purpose. It is conveniently located between subcortical structures and the cerebral cortex, which facilitates its relay function, filtering information about sensory inputs (i.e. taste, touch, sound, etc.) between the brain and the body. The thalamus' advantageous location and specialized nuclei has given rise to speculation of whether the structure serves a more intricate function, one involved in cognition and consciousness.

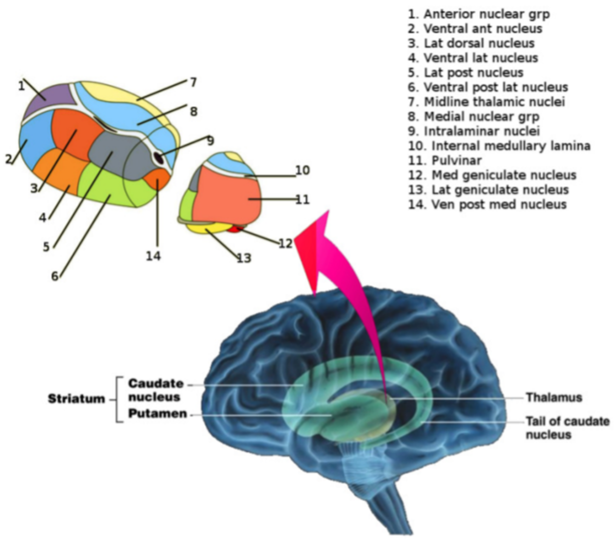


Figure 1: Thalamic nuclei. Image courtesy S Bhimji MD.

## First Order and Higher Order Nuclei

The anatomy of the thalamus is one of great complexity. Brain nuclei, such as that which the thalamus is composed of, are collections of neuronal cell bodies and thus are classified as gray matter. Thalamic-specific nuclei can be further classified as either 'first-order' (FO) or 'higher-order' (HO). 'First-order' thalamic nuclei correspond with earlier proposed functions of the thalamus, that is, with relaying sensory information from subcortical structures. Alternatively, 'higher-order' thalamic nuclei receive inputs from cortical layer 5 instead of the periphery and are thus being implicated as potentially carrying out higher order function, as their name implies. This theory is also supported by the role of HO nuclei in cortico-thalamo-cortical pathways, as they allow communication between cortical areas. This information has given rise to speculation that HO nuclei play a more integrative role while FO nuclei solely facilitate sensory relay function. However, these theories are being challenged by new evidence suggesting that both system's purposes are more complex and are both involved in higher order functions. Both HO and FO nuclei may in fact represent a 'thalamic bridge', in which the thalamus occupies an integrative role between sensory perception and cognition.

## Modulatory vs. Driver Input

The differential properties of synapses also contribute a great deal to thalamic activity. It is postulated that two distinct forms of synaptic inputs exist: 'driver input' and 'modulatory input'. Drivers carry the message whereas modulators modify how driver inputs are processed through processes such as attenuation or amplification. This further promotes categorization of thalamic nuclei as either 'first-order' (FO) or 'higher-order' (HO) based on where they receive their driving input from. FO nuclei receive driver input from subcortical structures while HO nuclei are mainly innervated by descending corticothalamic inputs from layer 5. Layer 6 cells provide modulatory feedback input to all thalamic nuclei, projecting to thalamic regions and providing thalamocortical input to the same cortical region from which they originate. Modulatory inputs from the cortex thus reach both HO and FO thalamic nuclei and affect the functionality of thalamocortical neurons.

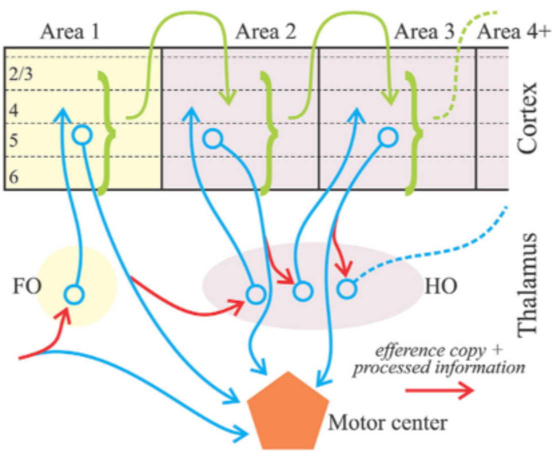


Figure 2: Thalamocortical circuitry (Usrey & Sherman, 2017.

The implications of this set-up are that sensory signals relayed via FO nuclei are processed in the cortex and then transmitted via HO to different cortical areas. This phenomena promotes a functional aspect of HO nuclei in trans-thalamic communication, one that allows cortical areas to communicate with each other outside of the direct connections between different cortical areas. It is also important to recognize that the inputs to both 'first-order' and 'higher-order' nuclei arrive via branching axons with extra thalamic branches innervating a motor center carrying a message that can be interpreted as an efference copy (an internal copy of an efferent). Efference copies are neural representations of motor outputs that predict reafferent sensory feedback. This phenomena is observed in tickling, where efference copies are created when you attempt to tickle yourself, which allows for the prediction of the sensory consequences of the movement. Yet, when other people tickle you, it is not predicted, and the sensation is much more intense.

## The Cognitive Thalamus

The circuitry between the thalamus and cortex gives rise to a cognitive function of the thalamus, particularly in memory and learning. The link between the thalamus and memory has long been speculated in accordance with evidence indicating that damage to the thalamus invariably occurs in Korsakoff syndrome, a chronic memory disorder. One prominent thalamic nucleus assumed to be linked to memory is the anterior nuclei of the thalamus (ANT) which is located at the rostral end of the dorsal thalamus. The ANT is a key component of the hippocampal system for episodic memory, connecting the anterior cingulate (which is implicated in complex cognitive function) and orbitomedial prefrontal cortex (which is involved in decision-making). Early evidence shows a specific role of the anterior thalamus in Pavlovian conditioning, a learning procedure that involves the pairing of a potent stimulus with a neutral one to ultimately elicit a potent response in the subject to the neutral stimulus. Data indicate that the ATN is specifically involved in the acquisition phase of Pavlovian learning. One study on rats demonstrates that acquisition of contextual fear memory is delayed after ATN lesions. Another prominent thalamic nuclei involved in memory and learning is the mediodorsal nucleus of the thalamus (MD).

The MD has been implicated in executive functions (involving planning, working memory, and decision-making) because of its significant interconnectivity with the prefrontal cortex (PFC) which is ultimately responsible for cognitive control functions. As discussed previously, the involvement of 'higher-order' thalamic nuclei in distributing efference copies of the cerebral cortex signals to other cortical areas through a mode termed transthalamic communication gives insight into the significance of thalamic connections.

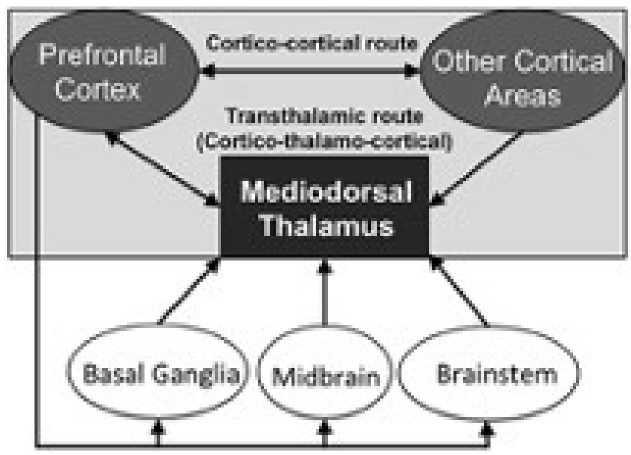


Figure 3: Corticocortical and transthalamic routes of transmission via the mediodorsal thalamus (Ouhaz et al., 2018)

Thus, using the example of the mediodorsal thalamic nucleus previously discussed, lesions to this structure would disrupt connections between the thalamus and cortex. As a result, the direct connections via different cortical areas and the transthalamic connections of different cortical areas would no longer be aligned, ultimately altering our internal perception of sensory stimuli. Our senses of sound, taste smell, etc. would no longer properly feed into subsequent processes which rely on accurate information, consequently impacting mental processes such as thinking and learning. An evident manifestation of this pathology would be people demonstrating unexplained behaviors or verbalizing nonsensical thoughts. Thus, it is evident that the mediodorsal nucleus of the thalamus is essential in this higher order cognitive scheme.

## The Thalamus and Consciousness

In addition to the role of the thalamus in cognition, studies have shown that this structure may also be heavily affiliated with consciousness, which is also dependent on thalamocortical and corticocortical interactions. The higher-order thalamic nuclei which facilitate cortical communication may play a role in modulating corticocortical interaction across different conscious states. One specific region of the thalamus that has been highlighted in relation to consciousness is the central lateral thalamus (CL). Consciousness is thought to involve feedforward and feedback interactions between cortical layers and areas and the CL is connected to both deep and superficial cortical layers. A study done on macaques shows promising evidence for CL function in consciousness. Electrical stimulation of the CL in two anesthetized macaques produced behavioral indications of arousal.

It was also shown that sleep and anesthesia were associated with less activity in the CL, whereas CL stimulation reversed these changes. This finding can be explained by thalamic circuitry, one of these circuits carries sensory information from the thalamus to the cerebral cortex and another carries feedback about predictions, attention, etc., all of which are needed to facilitate consciousness in organisms.

## Conclusion

From this brief overview we can see that the thalamus is not a simple, crude structure but is instead involved in many dynamic processes that significantly alter the nature of the information relayed to the cortex. The distinct cell groups/nuclei in the thalamus provide insight into how such a structure is able to perform these broad range of functions. Specifically, it is the 'higher-order' nuclei that allow for the cross talk between different cortical areas. As for the 'first-order' nuclei, they provide a path for the outside world and the various subcortical structures to communicate with the cerebral cortex. This review also highlighted some key thalamic nuclei that have been specifically implicated in cognition and arousal. Altogether, although a myriad of recent research is emerging looking at the thalamus and its sophisticated circuitry, we still have a long way to go to truly understand all the roles this alluring structure takes on.

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