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HOT TOPICS

The paraventricular nucleus of the thalamus and its potential role in psychopathology

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The role of the thalamus extends beyond that of a relay station in the brain. The thalamus is comprised of groups of specialized nuclei each with distinct neuroanatomical connections supporting their roles in sensory processing, motor control, and emotional regulation. Given the structural and functional heterogeneity across thalamic nuclei, it is not surprising that, collectively, this brain structure has been implicated in psychiatric disorders, including addiction, depression, and schizophrenia. Although the neuroanatomical resolution of human imaging studies have, to-date, largely limited our ability to elucidate the involvement of specific thalamic nuclei in these disorders, studies emerging from the preclinical literature suggest that the paraventricular nucleus of the thalamus (PVT) is a critical component of the neural pathways underlying these disorders (see [1–3]).

The PVT is an elongated nucleus that spans the anterior-posterior extent of the dorsal midline thalamus, with extensive connections throughout the brain that are evident in rodents, monkeys, and humans [2–4]. It receives input from regions involved in arousal and emotional processing, including the periaqueductal gray, locus coeruleus, dorsal raphe, hypothalamus, hippocampus, and amygdala. In addition, it receives input from cortical "control" centers, with the most abundant afferents originating from the prelimbic cortex. The PVT has reciprocal connections with many of these regions, including the hypothalamus, hippocampus, amygdala, and prelimbic cortex; and sends dense projections to other regions involved in motivation and behavioral regulation, such as the nucleus accumbens. While its afferents and efferents are primarily glutamatergic, several neurotransmitter and neuropeptide systems are represented within the PVT, including serotonin, dopamine, norepinephrine, corticotropin-releasing hormone, orexin, and endogenous opioids. Together, its structural connectivity and neurochemical composition make the PVT ideally situated to integrate information regarding arousal, emotion and cognition, and, in turn, guide behavior [5].

The PVT initially captured the attention of behavioral neuroscientists as it repeatedly appeared as a locus of enhanced immediate early gene expression (e.g., c-Fos) in response to stimuli associated with arousal, reward, and stress [see 1–3, 5]. Of particular relevance to psychiatric symptomatology, preclinical studies have since demonstrated a role for the PVT in circadian rhythmicity, acute and chronic stress regulation, drug-taking and drug-seeking behavior, attentional processing, and decision-making [1–3, 5]. As new technologies allow us to probe the role of the PVT and its surrounding circuitry more precisely than ever before (e.g., [4, 6]), it continues to garner recognition as a critical integrator of emotional and behavioral regulation [1]. Yet, much remains to be determined, including the role of this nucleus in psychopathology. The PVT may best be described as a fulcrum between arousal, emotional, cortical, and motive circuits in the brain. Thus, when the integration and/or encoding of information from these circuits is off-balance in the PVT, affective and behavioral patterns reminiscent of psychiatric symptomatology may be more likely to emerge [see 5]. This and other hypotheses surrounding PVT function will need to be tested and refined using modern technologies; with the goal of translating findings from preclinical studies to better understand the role of this nucleus in human behavior and psychopathology.

REFERENCES

1. Barson JR, Mack NR, Gao WJ. The paraventricular nucleus of the thalamus is an important node in the emotional processing network. Front Behav Neurosci. 2020;14:598469.
2. Hsu DT, Kirouac GJ, Zubieta JK, Bhatnagar S. Contributions of the paraventricular thalamic nucleus in the regulation of stress, motivation, and mood. Front Behav Neurosci. 2014;8:73.
3. Kirouac GJ. Placing the paraventricular nucleus of the thalamus within the brain circuits that control behavior. Neurosci Biobehav Rev. 2015;56:315–29.
4. Kark SM, Birnie MT, Baram TZ, Yassa MA. Functional connectivity of the human paraventricular thalamic nucleus: Insights from high field functional MRI. Front Integr Neurosci. 2021;15:662293.
5. Iglesias A, Flagel SB. The Paraventricular Thalamus as a Critical Node of Motivated Behavior via the Hypothalamic-Thalamic-Pituitary Circuit. Front Integr Neurosci. 2021. https://doi.org/10.3389/fnint.2021.706713.
6. Engelke DS, Zhang XO, O'Malley JJ, Fernandez-Leon JA, Li S, Kirouac GJ, et al. A hypothalamic-thalamostriatal circuit that controls approach-avoidance conflict in rats. Nat Commun. 2021;12:2517.

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AUTHOR CONTRIBUTIONS

SBF wrote the paper.

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COMPETING INTEREST

The author declares no competing interests.

ADDITIONAL INFORMATION

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