Thalamic Connectivity System Across Psychiatric Disorders: Current Status and Clinical Implications

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**ABSTRACT**

The thalamic connectivity system, with the thalamus as the central node, enables transmission of the brain’s neural computations via extensive connections to cortical, subcortical, and cerebellar regions. Emerging reports suggest deficits in this system across multiple psychiatric disorders, making it a unique network of high translational and transdiagnostic utility in mapping neural alterations that potentially contribute to symptoms and disturbances in psychiatric patients. However, despite considerable research effort, it is still debated how this system contributes to psychiatric disorders. This review characterizes current knowledge regarding thalamic connectivity system deficits in psychiatric disorders, including schizophrenia, bipolar disorder, major depressive disorder, and autism spectrum disorder, across multiple levels of the system. We identify the presence of common and distinct patterns of deficits in the thalamic connectivity system in major psychiatric disorders and assess their nature and characteristics. Specifically, this review assembles evidence for the hypotheses of 1) thalamic microstructure, particularly in the mediodorsal nucleus, as a state marker of psychosis; 2) thalamo-prefrontal connectivity as a trait marker of psychosis; and 3) thalamo-somatosensory/parietal connectivity as a possible marker of general psychiatric illness. Furthermore, possible mechanisms contributing to thalamocortical dysconnectivity are explored. We discuss current views on the contributions of cerebellar-thalamic connectivity to the thalamic connectivity system and propose future studies to examine its effects at multiple levels, from the molecular (e.g., glutamatergic) to the behavioral (e.g., cognition), to gain a deeper understanding of the mechanisms that underlie the disturbances observed in psychiatric disorders.

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The thalamus is a subcortical structure that is the center of the thalamic connectivity system, through which most of our brain’s neural computations flow, with multiple connections to cortical, subcortical, and cerebellar regions (1). As the node of this extensive system, the thalamus plays a pivotal role in the processing of sensory inputs and is an essential hub for cognitive processing, such as working memory, attention, flexible goal-directed tasks, sleep, and sensory perception. Recent investigative methods in neuroimaging have presented the thalamic connectivity system as a unique network of high translational and transdiagnostic utility in mapping the neural alterations that may potentially contribute to symptoms and deficits in psychiatric patients (2–5). Unlike the traditional neuroimaging approaches in which the thalamus was delineated and investigated, advancements in technology have enabled modern approaches to leverage the key pivotal properties of the thalamus: this structure is composed of multiple nuclei topologically arranged with respect to the cortex, each with distinct inputs and outputs, and therefore, thalamocortical connectivity patterns are, to a great extent, segregated. However, even with much effort, it is still debated how the thalamic connectivity system contributes to psychiatric disorders.

This narrative review aims to assess how currently available evidence reveals the contribution of thalamic connectivity system abnormalities to psychiatric disorders, as well as to evaluate the nature and characteristics of the components of the thalamic connectivity system. This article provides an overview of the structure and function of the thalamus, followed by evidence of thalamic connectivity system abnormalities in patients with schizophrenia, bipolar disorder, major depressive disorder (MDD), and autism spectrum disorder (ASD) by integrating studies across multiple levels of the system. We identified markers of disease-specific and general psychopathology in the thalamic connectivity system and assessed their nature and characteristics. Specifically, this review assembles evidence for the hypotheses of 1) thalamic microstructure, particularly in the mediodorsal nucleus, as a state marker of psychosis; 2) thalamo-prefrontal connectivity as a trait marker of psychosis; and 3) thalamo-somatosensory/parietal connectivity as a possible marker of general psychiatric illness. Finally, the article explores potential underlying mechanisms of thalamocortical dysconnectivity in psychiatric disorders. We discuss the current views on the downstream effects of cerebellar-thalamic connectivity on the thalamic connectivity system and propose future studies to examine its...
effects at multiple levels, from the molecular (e.g., glutamatergic) to the behavioral (e.g., cognition) levels. Gaining a deeper understanding of the underlying mechanisms of the thalamic connectivity system, as well as the identification of markers of disease-specific and general psychopathology, will facilitate the use of this network as a novel strategy for better treatment and even earlier prevention of psychiatric disorders.

THE THALAMUS AND THE THALAMIC CONNECTIVITY SYSTEM

The thalamus is a walnut-sized, paired structure that sits in the middle of our brain. It consists of approximately 60 topographically arranged nuclei, each of which has distinct inputs and outputs to cortical, subcortical, and cerebellar regions. The nuclei are largely segregated, with the exception of the thalamic reticular nucleus. Thalamic nuclei, predominantly organized in reciprocal feedback loops, receive input from layer 6 of largely nonoverlapping cortical areas. Thus, thalamocortical connectivity patterns have unique characteristics in that they are topographically arranged and segregated, and with the exception of the thalamic reticular nucleus and midline nuclei, the connectivity patterns are mostly confined to a single hemisphere and provide a major source of excitatory input to the cortex (Figure 1).

The functions of thalamic nuclei are defined by their inputs, and based on these inputs, thalamic nuclei can be categorized into two groups: first-order and higher-order (HO) nuclei (6). First-order nuclei relay driver input from the subcortex and relay the primary sensory information to the cortex. Such nuclei include the lateral geniculate nucleus, the medial geniculate nucleus, the ventral posterior nucleus, and parts of the ventral anterior/lateral nuclei, which relay visual information from the retina, auditory information from the inferior colliculus, somatosensory input from the medial lemniscus, and motor input from the deep cerebellar nuclei, respectively. In addition to receiving input from cortical layer 6 in reciprocal feedback loops as first-order nuclei do, HO nuclei receive additional input from layer 5 that is organized in a feedforward structure. Thus, HO nuclei receive driver input from layer 5 of upstream cortical areas and relay it to other cortical areas, forming cortico-thalamo-cortical, or transthalamic, pathways; in this manner, they work to relay information from one cortical area to another (7,8). Such nuclei in the brain include the medial dorsal nucleus (MD), which receives inputs from the amygdala, limbic system, basal ganglia, midbrain, and brainstem and has reciprocal connections with the prefrontal cortex (PFC) and pulvinar, which receives inputs from the superior colliculus and has reciprocal connections with the PFC and temporal, parietal, and occipital cortices. Through transthalamic pathways, HO nuclei send information based on activity in lower cortical areas to the target (higher) cortical areas, and while doing so, they can modulate or even block the message (9), selectively gating the information and positioning themselves as a key player in cortical processes such as cognitive functioning (Figure 1).

Lesion studies have revealed that different nuclei are associated with different behavioral changes, including cognitive functions and psychiatric symptoms [ventral lateral nucleus: sensory processing impairments, synesthesia (10); pulvinar: social cognition and attention impairments (11); MD: PFC-dependent abilities (12)]. The involvement of the MD and

![Figure 1](https://www.sobp.org/GOS)

**Figure 1.** Schematic diagram of the thalamic connectivity system at the neural and systemic levels. (Left) Schematic diagram showing the neural transmission of first-order (FO) and higher-order (HO) thalamic nuclei. (Right) Schematic diagram of pathways between the frontal and parietal cortices to the thalamus. AMY, amygdala; BG, basal ganglia; BS, brainstem; DCN, deep cerebellar nuclei; LD, lateral dorsal nucleus; LGN, lateral geniculate nucleus; LP, lateral posterior nucleus; LS, limbic system; MB, midbrain; MD, mediodorsal nucleus; MGN, medial geniculate nucleus; ML, medial lemniscus; PFC, prefrontal cortex; Retina IC, retina and intercollicular pathways; SMC, somatosensory cortex; VA, ventral anterior nucleus; VI, ventral intermediate nucleus; VL, ventral lateral nucleus; VP, ventral posterior nucleus; VPL, ventral posterolateral nucleus; VPM, ventral postero medial nucleus.
PFC in cognitive functioning is being examined in detail across various species. In mice, an optogenetic study reported distinct roles of afferent and efferent projections between the mediodorsal PFC and MD in supporting goal attributes (13). The differential roles of the PFC and MD in cognitive control were further investigated in monkeys, and unlike MD neurons, which specialized in decision making and response selection, PFC neurons specialized in preferential encoding of the environmental state (14). In humans, a recent neuroimaging study revealed an association between improved cognitive abilities and increased thalamocortical connectivity in the pulvinar, MD, intralaminar nucleus, and nuclei of the lateral group (15).

**THALAMIC CONNECTIVITY SYSTEM ABNORMALITIES IN PSYCHIATRIC DISORDERS**

**Schizophrenia**

Schizophrenia is a severely debilitating disorder characterized by positive and negative symptoms and cognitive deficits. Abnormalities involving thalamic deficits have been extensively investigated in schizophrenia. Multiple large consortium and meta-analytic studies have reported reduced thalamic volume in patients with chronic schizophrenia, as well as those with first-episode psychosis (FEP) (16–18). The significance of the region to schizophrenia pathophysiology has been extensively demonstrated. Thalamic volume is the strongest classifier distinguishing between patients with FEP and healthy control subjects (19); furthermore, an increased thalamic volume is associated with improved cognitive functioning in patients with schizophrenia (20).

HO nuclei, such as the MD and pulvinar, are heavily implicated in schizophrenia pathophysiology. As revealed by postmortem studies, patients with schizophrenia have reduced neuron counts, density, and total volume in the MD, anterior nucleus, and pulvinar (21). Abnormalities in density and volume in the MD and pulvinar have also been confirmed in vivo in multiple neuroimaging studies [for a review on the thalamus in schizophrenia, see (22,23)]. Furthermore, it is suggested that these structures could be a hub of not only cognition but also cortical structural changes in schizophrenia, with their progressive loss of volume being associated with structural abnormalities of the cortex (24). Moreover, their densities show state-like characteristics, and they are reduced only in patients with FEP and not in their unaffected relatives (2,25).

The most commonly used method to evaluate the thalamic connectivity system in schizophrenia calculates the connectivity between the thalamus and 5 or 6 cortical regions (3,4,26). Interestingly, when applied to diffusion tensor imaging (DTI)-based structural connectivity and task-free functional connectivity studies, regardless of magnetic strength [e.g., 3T or 7T (27)], this method yields consistent results of reduced thalamo-prefrontal and increased thalamo-somatosensory/parietal connectivity patterns in patients with chronic schizophrenia, patients with FEP, and individuals at clinical high risk for psychosis, as well as patients with early-onset schizophrenia (28). Furthermore, it has been reported that task-free functional connectivity does not show a progressive deterioration in schizophrenia (29). Currently, thalamocortical dysconnectivity consisting of reduced thalamo-prefrontal and increased thalamo-somatosensory/parietal connectivity is considered a core neurobiological abnormality in schizophrenia [for further reading, see (23,30,31)]. Recently developed methods to investigate the interconnectivity of the thalamus, cerebellum, and cortex revealed dysconnectivity among the thalamus, cerebellum, and temporal cortex (32–34), which highlights the widespread involvement of the thalamus in brain activity and suggests the cerebellum as the next key region to investigate.

**Bipolar Disorder**

Bipolar disorder is characterized by cycles of mania and depression. The volume of the thalamus is reduced in bipolar disorder in postmortem and neuroimaging meta-analysis studies (35,36). However, when thalamic volume was investigated in individuals with prodromal bipolar disorder, the individuals showed no reductions (37). Similarly, in a recent voxel-based meta-analysis, the anterior thalamic radiation, a white matter structure that is also associated with emotion regulation difficulties in this disorder (38), was compared between patients with bipolar disorder and prodromal individuals. While patients with bipolar disorder showed reduced fractional anisotropy and increased radial diffusivity, no such deficits were seen in individuals at risk for bipolar disorder (39), suggesting that disruptions in the thalamic connectivity system do not occur or are too subtle to be detected in the very early stages of bipolar disorder.

Another intriguing aspect of thalamic connectivity system abnormalities in bipolar disorder is that thalamic volume abnormalities in bipolar disorder tend to be weaker than those in schizophrenia, which is suggested to relate to the increased neurodevelopmental disruption in schizophrenia relative to bipolar disorder (18,36). Interestingly, a similar trend was also shown in thalamocortical connectivity deficits in bipolar disorder. In a meta-analysis of task-free functional connectivity studies, bipolar disorder showed similar patterns of thalamocortical dysconnectivity to schizophrenia, and as with thalamic abnormalities, it showed a similar or lower degree of deficits in thalamocortical dysconnectivity relative to schizophrenia (31). Furthermore, the recent evidence of significant associations between decreased thalamo-prefrontal connectivity and increased thalamo-somatosensory/parietal connectivity suggests that these dysconnectivity patterns could be a part of a common mechanism shared by schizophrenia and bipolar disorder.

**Major Depressive Disorder**

MDD is characterized by substantial impairments in emotional and cognitive processing. Accumulating evidence suggests deficits in the thalamus in MDD. MD in particular has been reported to show increased metabolism and blood flow (40). Patients with MDD showed reduced thalamic volume (41), and clinical implications have been reported for its negative association with symptom severity (42). Further studies using electroconvulsive therapy showed improvement in thalamic volume and its positive associations with clinical improvements in patients with MDD after electroconvulsive therapy (43–45).
In addition to the clinical associations, studies have also demonstrated treatment-responsive characteristics of the thalamic connectivity system in MDD. When task-free functional connectivity between the thalamus and the mood-regulating cortical areas is compared between patients with treatment-resistant and non-treatment-resistant MDD, treatment-resistant patients show reduced connectivity and greater spontaneous thalamic activity (46). Higher thalamic activity has also been reported to be correlated with lower clinical improvement in response to antidepressants in MDD (47), indicating its heavy involvement in MDD pathophysiology.

Similar to the schizophrenia literature, the thalamocortical connectivity of patients with MDD has been investigated using 5 or 6 cortical regions of interest. DTI-based anatomical connectivity and task-free functional connectivity studies have reported decreased thalamo-prefrontal connectivity and increased thalamo-temporal and thalamo-somatosensory/parietal connectivity patterns (5,48–52). Among these, thalamo-temporal connectivity has been reported to have particular clinical significance in MDD. Task-free thalamo-temporal connectivity has been shown to have a positive correlation with symptom severity (49) and to occur irrespective of age of onset, unlike thalamo-prefrontal functional connectivity, which is significantly reduced in adult-onset MDD (48). To date, thalamo-temporal connectivity is one of the most clinically implicated connectivities in MDD.

**Autism Spectrum Disorder**

ASD is a highly heritable neurodevelopmental condition associated with impairments in reciprocal social communication and patterns of rigid or repetitive behavior. There is substantial evidence supporting structural and functional thalamocortical connectivity deficits in ASD. Structurally, increased DTI-based thalamo-somatosensory connectivity and decreased DTI-based thalamo-prefrontal, thalamo-parietal, and thalamo-temporal connectivity patterns have been reported (53,54). Functionally, studies have demonstrated reduced task-free thalamo-prefrontal connectivity and increased task-free thalamo-temporal connectivity (53,54). A recent study using a large dataset from the Autism Brain Imaging Data Exchange reported increased task-free thalamo-prefrontal, thalamo-temporal, and thalamo-sensorimotor functional connectivity patterns, with more pronounced effects in temporal cortical areas, including the temporoparietal junction (55). Further corroborating the notion of thalamo-temporal hyperconnectivity in ASD, a study reported that the pathophysiology of ASD is more likely related to thalamocortical hyperconnectivity (i.e., temporoparietal and posterior cingulate cortices) than to amygdala-cortical hypoconnectivity (56), as well as reduced effective connectivity (57). However, despite the strong findings supporting thalamo-temporal connectivity deficits in ASD, the meaning or clinical relevance remains to be elucidated because studies have yet to reveal significant correlational relationships.

**STATE-VERSUS TRAIT-RELATED THALAMIC CONNECTIVITY SYSTEM DEFICITS IN PSYCHIATRIC DISORDERS**

Among psychiatric disorders, schizophrenia is one of the most comprehensively studied disorders in terms of investigating individuals in different phases of the course of illness, which includes individuals at clinical high risk for psychosis, patients with FEP, and patients with chronic schizophrenia, as well as individuals at genetic or familial high risk. This approach has enabled investigating and elucidating trait-/state-related markers and thus has provided information regarding potent endophenotypes and biomarkers. As described in the previous sections, thalamic connectivity system deficits are currently being reported at multiple levels of analysis across multiple psychiatric disorders, with some of the patterns being shared across some disorders, such as altered thalamo-prefrontal and thalamo-somatosensory/parietal connectivity patterns and microstructural reductions in the MD (Figure 2).

**Thalamo-Prefrontal Connectivity: A Trait Marker of Psychosis?**

Reductions in thalamo-prefrontal connectivity are shared to different degrees, both structurally and functionally, among schizophrenia, bipolar disorder, and MDD, implicating this as a

![Figure 2. A diagram of multiple levels of the system leading to thalamic connectivity system disruptions. The proteins and genes highly implicated in psychiatric disorders are often essential in glutamatergic transmission in the brain, particularly within the thalamic connectivity system, which comprises the thalamus and thalamic connectivity patterns. These effects are taken up to show disease-specific or general psychopathology characteristics within the system. Schizophrenia and bipolar disorder share reduced thalamo-prefrontal connectivity and increased thalamo-somatomotor/parietal connectivity. Major depressive disorder (MDD) is characterized by reduced thalamo-prefrontal connectivity and increased thalamo-temporal and thalamo-somatomotor/parietal connectivity patterns, and autism is characterized by increased thalamo-temporal and thalamo-somatomotor/parietal connectivity patterns. Shaded blue, red, pink, green, and gray areas indicate the prefrontal cortex, somatomotor/parietal cortex, temporal cortex, thalamus, and cerebellum, respectively. GABA, gamma-aminobutyric acid; NAA, N-acetylaspartate.](https://www.sobp.org/GOS)
transdiagnostic connectivity feature in psychosis (5,52,58–61). Considering the strong implication of the relevance of thalamo-prefrontal connectivity in cognition, which has been supported by animal and human studies, it may be a fair view to attempt to understand these differences in terms of cognitive functioning deficits, in particular executive functioning, which are seen across disorders and prodromal states (62–65). Indeed, thalamo-prefrontal connectivity has been shown to be associated with cognition at rest in psychosis (59), dependent on cognitive demand during tasks in schizophrenia (66), and can also be increased by cognitive remediation training (67). Together with the DTI-based structural connectivity study reporting the association of thalamo-prefrontal connectivity with working memory (68), the current literature implicates thalamo-prefrontal connectivity in cognitive function in psychosis.

However, further evidence demonstrating reductions in both structural and functional thalamo-prefrontal connectivity in early-stage psychosis, individuals at clinical high risk for psychosis, and those with high genetic risk for psychosis may require the current interpretation of this phenomenon to be re-evaluated (26,69–75). Notably, asymptomatic relatives/siblings of schizophrenia share decreased thalamo-prefrontal connectivity but not increased thalamo-sensorimotor connectivity (72,74), suggesting that this biological phenotype may be considered a useful intermediate phenotype in linking genetic effects to schizophrenia pathophysiology. Indeed, schizophrenia-related genes have been confirmed to be associated with MD–dorsolateral PFC connectivity (76,77). Taken together, current evidence suggests that reduced thalamo-prefrontal connectivity may represent a heritable trait and vulnerability factor for psychosis. Thalamo-prefrontal connectivity has also been reported to be reduced in ASD. However, no study has yet compared deficits with schizophrenia, bipolar disorder, or MDD. Such studies, together with longitudinal studies, will help fully corroborate this notion.

**Thalamo-Somatomotor/Parietal Connectivity: A Marker of General Psychiatric Illness?**

Studies have consistently reported increased thalamo-somatomotor/parietal connectivity across psychiatric disorders. For example, studies have reported that increased thalamo-somatomotor/parietal connectivity is shared across schizophrenia, bipolar disorder, and MDD (5,52,58–60) but is not seen in asymptomatic relatives/siblings of patients with schizophrenia (72,74); however, the relevance of this deficit remains unclear because it is one of the understudied components in the thalamic connectivity system. Notably, thalamosomatosensory/parietal connectivity has been shown to be modulated by electroconvulsive therapy in MDD and schizophrenia (45,69). Studies on this phenomenon are limited, but it is currently postulated to reflect the expression of these mental illness phenotypes or related secondary factors (72). Interestingly, reports have consistently demonstrated, as previously described, significantly increased thalamo-somatomotor/parietal connectivity in ASD. Furthermore, it has been reported that thalamocortical connectivity deficits are shared genetically across psychiatric disorders (78).

Although further studies are needed, it is possible to speculate based on current knowledge that this observation of increased thalamo-somatomotor/parietal connectivity may be reflective of a factor that is present in various psychiatric disorders (i.e., a general psychopathology factor, or p factor) or perhaps underlies them (i.e., a general psychopathophysiological factor). Previous studies have found that a higher p factor was associated with structural disturbances within the cerebello-thalamic-cortical circuit (79). If this truly is the case, it could explain our rather slow advancements in gaining deeper understanding of this deficit, even with the rigorous performance of correlation analyses with multiple measures, such as clinical scores and cognitive function. It could be, as suggested in a review study by Giraldo-Chica and Woodward (30), that we are not testing the correct measures and need to broaden our perspective to find other, perhaps new, measures.

**Thalamic Microstructure in the MD: A State Marker of Psychosis?**

Recent neuroimaging methods have enabled in vivo segmentation of the thalamus into nuclei using the topographic properties of the thalamus. This new and exciting method has yet to be applied across multiple psychiatric disorders but has already shown promising results in the study of psychosis. Current neuroimaging findings, together with postmortem findings in schizophrenia, suggest that the most strongly implicated thalamic nuclei are the MD and pulvinar (2,80), which are also strongly implicated across psychiatric disorders (81). Studies have revealed volumetric reductions in the MD and pulvinar in psychosis and youths with psychosis spectrum symptoms (80) and microstructural reductions in FEP (2). Several studies investigating genetic associations have reported that unless multivariate analyses are applied to detect very subtle changes, volumetric integrity is preserved in healthy relatives of patients with schizophrenia despite their high genetic loading (82,83). A study further investigated thalamic microstructural integrity in a sample of unaffected relatives of those with psychosis, in whom reduced thalamo-orbitofrontal connectivity was previously reported (71), to elucidate whether such disruptions were associated with the thalamic microstructure; however, the microstructure was intact and volumetric integrity was preserved (25). Further examinations are required, but the current line of evidence suggests state-like characteristics of the MD and pulvinar, which may provide a foundational basis for a new avenue of reverse-translational studies related to the thalamic connectivity system for developing better treatments and better detection strategies.

**IN Volvement OF THE CerebellUM IN thalamocortICAL DYSCONNECTIVITY**

There are yet a limited number of studies postulating the common source of thalamocortical dysconnectivity, particularly in thalamo-prefrontal and thalamo-somatosensory/parietal connectivity patterns observed in schizophrenia and bipolar disorder. However, recent findings have indicated that the impact of cerebellar neurons on different thalamic nuclei varies substantially and highlight the possibility that cerebellar
output differentially controls various parts of the thalamocortical network (84–89). Manipulating cerebellar output affects sensorimotor integration by somatosensory and motor cortices and thereby directs thalamocortical activity related to voluntary movements (90–92). Furthermore, emerging evidence has supported the functional topography of sensorimotor, cognitive, and affective subregions in the cerebellum, with each distinct process linked to different processing regions across the brain (e.g., anterior cerebellum: sensorimotor areas; posterior cerebellum: PFC and parietal association cortices).

Studies have also reported cerebellar-thalamic connectivity deficits. In schizophrenia, it has long been postulated via the cognitive dysmetria theory that cerebello-thalamo-cortical circuitry disruptions lead to impairments in the coordination of mental processes (93). In addition to the structural circuitry having reduced integrity (94), being associated with cognitive functioning (95), and being disrupted from preclinical to chronic stages of schizophrenia (96), cerebell-thalamo-cortical circuitry holds value as a strong classifier between patients with first-episode schizophrenia and healthy control subjects (97). Functionally, it is hyperconnected and is a robust state-independent neural signature for psychosis prediction and characterization (98) and a heritable trait in schizophrenia (99). Similarly, the critical role of the cerebellar circuitry and the presence of disruptions in this circuitry have also been reported in bipolar disorder (100), MDD (101), and ASD (102). Evidence has demonstrated that connectivity between the thalamus and cerebellum is a common biological mechanism underlying multiple psychiatric disorders, particularly psychotic disorders (103).

**Downstream Effects of Cerebellar Circuitry on the Thalamic Connectivity System**

Studies elucidating detailed relationships between the thalamus and cerebellum can reveal the downstream effects of disruptions in the cerebellum and cerebellar circuitry on the thalamus, providing evidence for consequential downstream effects of thalamic disruption on the cortex. However, it is very difficult to explore these causal relationships in humans because 1) current neuroimaging methods are insufficient for the task, 2) invasive measures are needed, and 3) these relationships must be examined in longitudinal studies with long follow-up durations. Nonetheless, it is crucial to aim to provide information on these fundamental mechanisms in our brain. Particular study designs (such as translational and reverse-translational designs) and powerful, high-precision technologies show significant promise, potentially enabling such questions to be addressed with previously unattainable spatial and temporal resolution. To date, only a small number of studies are available, but in one recent study with a reverse-translational design, dysfunctional delta rhythms in the medial frontal cortex during an interval timing task were explored in an animal model. Both frontal and cerebellar neurons were modulated, and subsequent optogenetic cerebellar stimulation in mice normalized the dysfunctional frontal networks, which has also been observed in patients with schizophrenia, highlighting the direct impacts of the cerebellum on frontal networks, particularly in cognitive processing (104). Neuroimaging studies, although they cannot address direct causality, have revealed that cerebellar gray matter reductions may be associated with modulation of cerebellar-thalamic connectivity and the frontoparietal network (105). When investigating whether thalamic dysconnectivity patterns were shared with other nodes in a larger system, the corticostriatal-thalamic-cerebellar circuit, cerebellum, and striatum showed similar patterns of disruption, highlighting that thalamic connectivity deficits may not be focal disruptions but may be understood as a part of disturbances in a larger system, such as the corticostriatal-thalamic-cerebellar circuit, or perhaps in the context of a brain-wide level of NMDA receptor disruptions (106). Future studies are warranted to explore the effects of NMDA receptor disruptions in the cerebellar circuitry on the thalamic connectivity system.

**CONCLUSIONS**

Overall, there are shared and distinct patterns of deficits in the thalamic connectivity system across schizophrenia, bipolar disorder, MDD, and ASD. The disease-specific deficits include reduced thalamo-prefrontal connectivity in schizophrenia and bipolar disorder and increased thalamo-temporal connectivity in MDD and ASD. However, we do not yet know the relative degree of deficits across illnesses or, due to methodological differences across studies, the differential localization of deficits within the system. More exploration into sources causing thalamic connectivity system disruption needs to be conducted, although in this review, we provide the possibility that the cerebellum and cerebellar circuits would be a fruitful model to study. Furthermore, current evidence supports thalamo-prefrontal connectivity as a heritable trait and a marker of vulnerability to psychosis, and additional studies may be required to fully substantiate this notion, but thalamo-somatotor/parietal connectivity is a possible general psychiatric illness marker. Taken together, current evidence supports the transdiagnostic validity of the thalamic connectivity system, and future studies elucidating further details of this system are highly warranted.

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REFERENCES

1. Sherman SM, Guillery RW (2006): Exploring the Thalamus and Its Role in Cortical Function, 2nd ed. Cambridge, MA: MIT Press.

2. Cho KIK, Kwak YB, Hwang WJ, Lee J, Kim M, Lee TY, Kwon JS (2019): Microstructural changes in higher-order nuclei of the thalamus in patients with first-episode psychosis. Biol Psychiatry 85:70–78.

3. Woodward ND, Karbasforoushan H, Heckers S (2012): Thalamocortical disconnection in schizophrenia. Am J Psychiatry 169:1092–1099.

4. Kubota M, Miyata J, Sasamoto A, Sugihara G, Yoshida H, Kawada R, et al. (2013): Thalamocortical disconnection in the orbitofrontal region associated with cortical thinning in schizophrenia. JAMA Psychiatry 70:12–21.

5. Sheffield JM, Huang AS, Rogers BP, Giraldo-Chica M, Landman BA, Blackford JU, et al. (2020): Thalamocortical anatomical connectivity in schizophrenia and psychotic bipolar disorder. Schizophr Bull 46:1062–1071.

6. Guillery RW (1995): Anatomical evidence concerning the role of the thalamus in cortico-cortical communication: A brief review. J Anat 187:583–592.

7. Sherman SM (2017): Functioning of circuits connecting thalamus and cortex. Compr Physiol 7:713–739.

8. Mo C, Sherman SM (2019): A sensorimotor pathway via higher-order thalamus. J Neurosci 39:692–704.

9. Sherman SM, Guillery RW (2011): Distinct functions for direct and transthalamic corticothalamic connections. J Neurophysiol 106:1088–1077.

10. Ro T, Farnè A, Johnson RM, Wedeen V, Chu Z, Wang ZJ, et al. (2020): Intact thalamic microstructure in asymptomatic relatives of schizophrenia patients with high genetic loading. Schizophr Res 230:111–113.

11. Cho KIK, Shenton ME, Kubicki M, Jung WH, Lee TY, Yun JY, et al. (2016): Altered thalamo-cortical white matter connectivity: Probabilistic tractography study in clinical-high risk for psychosis and first-episode psychosis. Schizophr Bull 42:723–731.

12. Hua J, Blair NIS, Paez A, Choe A, Barber AD, Brandt A, et al. (2019): Altered functional connectivity between sub-regions in the thalamus and cortex in schizophrenia patients measured by resting state BOLD fMRI at 7T. Schizophr Res 206:360–377.

13. Zhang M, Palaniyappan L, Deng M, Zhang W, Pan Y, Fan Z, et al. (2021): Abnormal thalamocortical circuit in adolescents with early-onset schizophrenia. J Am Acad Child Adolesc Psychiatry 60:479–489.

14. Bergé D, Lésh TA, Smucny J, Carter CS (2020): Improvement in prefrontal thalamic connectivity during the early course of the illness in recent-onset psychosis: A 12-month longitudinal follow-up resting-state fMRI study [published online ahead of print Dec 16]. Psychol Med.

15. Giraldo-Chica M, Woodward ND (2017): Review of thalamocortical resting-state fMRI studies in schizophrenia. Schizophr Res 180:58–63.

16. Ramsay IS (2019): An activation likelihood estimate meta-analysis of thalamocortical connectivity in psychosis. Biol Psychiatry Cogn Neuroimaging 1092–1109.

17. Alcaraz F, Fresno V, Marchand AR, Kremer EJ, Coutureau E, Wolff M (2020): Functional topography of the thalamo-cortical system during development and its role in cognition. Neuroimage 59:617–647.

18. van Erp TGM, Hibar DP, Rasmussen JM, Glahn DC, Pearlson GD, Andreasen OA, et al. (2016): Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. Mol Psychiatry 21:585.

19. Faria AV, Zhao Y, Ye C, Hsu J, Yang K, Cifuentes E, et al. (2021): Multimodal MRI assessment for first episode psychosis: A major change in the thalamus and an efficient stratification of a subgroup. Hum Brain Mapp 42:1034–1053.

20. Ramsay IS, Fryer S, Boos A, Roach BJ, Fisher M, Loewy R, et al. (2018): Response to targeted cognitive training correlates with change in thalamic volume in a randomized trial for early schizophrenia. Neuropsychopharmacology 43:590–597.

21. Dorph-Petersen KA, Lewis DA (2017): Postmortem structural studies of the thalamus in schizophrenia. Schizophr Res 180:28–35.

22. Pergola G, Selvaggi P, Trizio S, Bertolino A, Blasi G (2015): The role of the thalamus in schizophrenia from a neuroimaging perspective. Neurosci Biobehav Rev 54:57–75.

23. Steuillet P (2020): Thalamus-related anomalies as candidate mechanism-based biomarkers for psychosis. Schizophr Res 226:147–157.

24. Cobia DJ, Smith MJ, Salinas I, Ng C, Gado M, Csaemansky JG, Wang L (2017): Progressive deterioration of thalamic nuclei relates to cortical network decline in schizophrenia. Schizophr Res 180:21–27.

25. Hwang WJ, Cho KIK, Kwak YB, Lee J, Kim M, Lee TY, Kwon JS (2021): Intact thalamic microstructure in asymptomatic relatives of schizophrenia patients with high genetic loading. Schizophr Res 230:111–113.

26. van Erp TGM, Hibar DP, Rasmussen JM, Glahn DC, Pearlson GD, Andreasen OA, et al. (2016): Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. Mol Psychiatry 21:585.

27. Alcaraz F, Fresno V, Marchand AR, Kremer EJ, Coutureau E, Wolff M (2020): Functional topography of the thalamo-cortical system during development and its role in cognition. Neuroimage 59:617–647.

28. van Erp TGM, Hibar DP, Rasmussen JM, Glahn DC, Pearlson GD, Andreasen OA, et al. (2016): Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. Mol Psychiatry 21:585.

29. Bergé D, Lésh TA, Smucny J, Carter CS (2020): Improvement in prefrontal thalamic connectivity during the early course of the illness in recent-onset psychosis: A 12-month longitudinal follow-up resting-state fMRI study [published online ahead of print Dec 16]. Psychol Med.

30. Giraldo-Chica M, Woodward ND (2017): Review of thalamocortical resting-state fMRI studies in schizophrenia. Schizophr Res 180:58–63.

31. Ramsay IS (2019): An activation likelihood estimate meta-analysis of thalamocortical connectivity in psychosis. Biol Psychiatry Cogn Neuroimaging 4:859–869.

32. Culbrett A, Wu Q, Chen S, Adhikari BM, Hong LE, Gold JM, Waltz JA (2021): Temporal-thalamic and cingulo-opercular connectivity in people with schizophrenia. Neuroimage Clin 29:102531.

33. Ferri J, Ford JM, Roach BJ, Turner JA, van Erp TG, Voyvodic J, et al. (2018): Resting-state thalamic connectivity in schizophrenia and relationships with symptoms. Psychol Med 48:2492–2499.

34. Fryer SL, Ferri JM, Roach BJ, Loewy RL, Stuart BK, Anticevic A, et al. (2021): Thalamic connectivity in the psychosis risk syndrome and early illness schizophrenia [published online ahead of print March 15]. Psychol Med.

35. Bielau H, Trüben K, Krell D, Ageklin MW, Bernstein HG, Stauch R, et al. (2005): Volume decrease of the thalamus in schizophrenia patients with high genetic loading. Schizophr Res 230:111–113.

36. van Erp TGM, Hibar DP, Rasmussen JM, Glahn DC, Pearlson GD, Andreasen OA, et al. (2016): Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. Mol Psychiatry 21:585.
38. Linke JO, Stavish C, Adleman NE, Sarljs J, Tewbin KE, Leibenluft E, Brotman MA (2020): White matter microstructure in youth with and at risk for bipolar disorder. Bipolar Disord 22:163–173.

39. Hu R, Stavish C, Leibenluft E, Linke JO (2020): White matter microstructure in individuals with and at risk for bipolar disorder: Evidence for an endophenotype from a voxel-based meta-analysis. Biol Psychiatry Cogn Neurosci Neuroimaging 5:1104–1113.

40. Drevets WC, Bogers W, Raichle ME (2002): Functional anatomical correlates of antidepressant drug treatment assessed using PET measures of regional glucose metabolism. Eur Neuropsychopharmacol 12:527–544.

41. Bora E, Harrison BJ, Davey CG, Yucel M, Pantelis C (2012): Meta-analysis of volumetric abnormalities in cortico-striatal-pallidial-thalamic circuits in major depressive disorder. Psychol Med 42:671–681.

42. Webb CA, Weber M, Mundy EA, Killgore WDS (2014): Reduced gray matter volume in the anterior cingulate, orbitofrontal cortex and thalamus as a function of mild depressive symptoms: A voxel-based morphometric analysis. Psychol Med 44:2833–2843.

43. Jehna M, Wurm W, Pinter D, Vogel K, Holl A, Hofmann P, et al. (2021): Do increases in deep grey matter volumes after electroconvulsive therapy persist in patients with major depression? A longitudinal MRI-study. J Affect Disord 291:908–917.

44. Takamiya A, Kishimoto T, Hirano J, Nishikata S, Sawada K, Kurokawa S, et al. (2020): Neuronal network mechanisms associated with depressive symptom improvement following electroconvulsive therapy. Psychiat Med 51(16):1–8.

45. Wei Q, Bai T, Brown EC, Xie W, Chen Y, Ji G, et al. (2020): Thalamocortical connectivity in electroconvulsive therapy for major depressive disorder. J Affect Disord 264:163–171.

46. Lui S, Wu Q, Qiu L, Yang X, Kuang W, Chan ROK, et al. (2011): Resting-state functional connectivity in treatment-resistant depression. Am J Psychiatry 168:642–648.

47. Yamamura T, Okamoto Y, Okada G, Takashii Y, Takamura M, Mantani A, et al. (2016): Association of thalamic hyperactivity with treatment-resistant depression and poor response in early treatment for major depression: A resting-state fMRI study using fractional amplitude of low-frequency fluctuations. Transl Psychiatry 6:e6754.

48. Brown EC, Clark DL, Hassel S, MacQueen G, Ramasubbu R (2018): Intrinsic thalamocortical connectivity varies in the age of onset subtypes in major depressive disorder. Neuropsychiatr Dis Treat 15:75–82.

49. Brown EC, Clark DL, Hassel S, MacQueen G, Ramasubbu R (2017): Thalamocortical connectivity in major depressive disorder. J Affect Disord 217:125–131.

50. Greicius MD, Flores BH, Menon V, Glover GH, Solvason HB, Lui S, Wu Q, Qiu L, Yang X, Kuang W, Chan ROK, et al. (2011): Resting-state functional connectivity in treatment-resistant depression. Am J Psychiatry 168:642–648.

51. Jia Z, Wang Y, Huang X, Kuang W, Wu Q, Lui S, et al. (2014): Impaired thalamocortical connectivity in schizophrenia. Brain Imaging Behav 8:429–437.

52. Tu PC, Bai YM, Li CT, Chen MH, Lin WC, Chang WC, Su TP (2019): Identification of common thalamocortical dysconnectivity in four major psychiatric disorders. Schizophr Bull 45:1143–1151.

53. Nair A, Tramer JM, Shukla DK, Shih P, Müller RA (2013): Impaired thalamocortical connectivity in autism spectrum disorder: A study of functional and anatomical connectivity. Brain 136:1942–1955.

54. Nair A, Carper RA, Abbott AE, Chen CP, Solders S, Nakutin S, et al. (2015): Regional specificity of aberrant thalamocortical connectivity in autism. Hum Brain Mapp 36:4497–4511.

55. Woodward ND, Girado-Chica M, Rogers BP, Cappellini S, Cusack CJ (2017): Thalamocortical connectivity in major depressive disorder: An analysis of the Autism Brain Imaging Data Exchange. Biol Psychiatry Cogn Neurosci Neuroimaging 2:76–84.

56. Idiaka T, Kogata T, Mano Y, Komeda H (2019): Thalamocortical hyperconnectivity and amygdala-cortical hypoconnectivity in male patients with autism spectrum disorder. Front Psychiatry 10:252.

57. Chen H, Uddin LQ, Zhang Y, Duan X, Chen H (2016): Atypical effective connectivity of thalamo-cortical circuits in autism spectrum disorder. Autism Res 9:1183–1190.

58. Anticevic A, Cole MW, Repovs G, Murray JD, Brambua MS, Winkler AM, et al. (2014): Characterizing thalamo-cortical disturbances in schizophrenia and bipolar illness. Cereb Cortex 24:3116–3130.

59. Woodward ND, Heckers S (2018): Mapping thalamocortical functional connectivity in chronic and early stages of psychotic disorders. Biol Psychiatry 79:1016–1025.

60. Skåtun KC, Kaufmann T, Brandt CL, Doan NT, Alnæs D, Tannenes E, et al. (2018): Thalamo-cortical functional connectivity in schizophrenia and bipolar disorder. Brain Imaging Behav 12:640–652.

61. Cui Y, Dong J, Yang Y, Yu H, Li W, Liu Y, et al. (2020): White matter microstructural differences across major depressive disorder, bipolar disorder and schizophrenia: A tract-based spatial statistics study. J Affect Disord 260:291–296.

62. Bortolato B, Miskowiak KW, Köhler CA, Vieta E, Carvalho AF (2015): Cognitive dysfunction in bipolar disorder and schizophrenia: A systematic review of meta-analyses. Neuropsychiatr Dis Treat 11:3111–3125.

63. Hawang WJ, Lee TY, Shin WG, Kim M, Kim J, Lee J, Kwon JS (2019): Global and specific profiles of executive functioning in prodromal and early psychosis. Front Psychiatry 10:356.

64. Sheffield JM, Karcher NR, Barch DM (2018): Cognitive deficits in psychotic disorders: A lifespan perspective. Neuropsych Rev 28:509–533.

65. Bang M, Kim KR, Song YY, Baek S, Lee E, An SK (2015): Neurocognitive impairments in individuals at ultra-high risk for psychosis: Who will really convert? Aust N Z J Psychiatry 49:462–470.

66. Huang AS, Rogers BP, Woodward ND (2019): Disrupted modulation of thalamus activation and thalamocortical connectivity during dual task performance in schizophrenia. Schizophr Res 210:270–277.

67. Ramsay IS, Nienow TM, MacDonald AW 3rd (2017): Increases in intrinsic thalamocortical connectivity and overall cognition following cognitive remediation in chronic schizophrenia. Biol Psychiatry Cogn Neurosci Neuroimaging 2:355–362.

68. Giraldos-Chica M, Rogers BP, Damon SM, Landman BA, Woodward ND (2018): Prefrontal-thalamic anatomical connectivity and executive cognitive function in schizophrenia. Biol Psychiatry 83:509–517.

69. Wang J, Jiang Y, Tang Y, Xia M, Curtin A, Li J, et al. (2020): Altered functional connectivity of the thalamus induced by modified electroconvulsive therapy for schizophrenia. Schizophr Res 218:209–218.

70. Anticevic A, Haut K, Murray JD, Repovs G, Yang GJ, Diedel C, et al. (2015): Association of thalamic dysconnectivity and conversion to psychosis in youth and young adults at elevated clinical risk. JAMA Psychiatry 72:882–891.

71. Cho KI, Kim M, Yoon YB, Lee J, Lee TY, Kwon JS (2019): Disturbed thalamocortical connectivity in unaffected relatives of schizophrenia patients with a high genetic loading. Aust N Z J Psychiatry 53:889–895.

72. Yao B, Negrer SFW, Kahn RS, Thakkar KN (2020): Altered thalamocortical structural connectivity in persons with schizophrenia and healthy siblings. Neuroimage Clin 28:102370.

73. Antonucci LA, Taurisano P, Fazio L, Gelao B, Romano R, Quarto T, et al. (2016): Association of familial risk for schizophrenia with thalamic and medial prefrontal functional connectivity during attentional control. Schizophr Res 173:23–29.

74. Xi C, Liu ZN, Yang J, Zhang W, Deng MJ, Pan YZ, et al. (2020): Schizophrenia patients and their healthy siblings share decreased prefronto-thalamic connectivity but not increased sensorimotor-thalamic connectivity in unaffected relatives of schizophrenia patients. Brain Imaging Behav 14:133–147.

75. Zhu F, Liu Y, Liu F, Yang R, Li H, Chen J, et al. (2019): Functional asymmetry of thalamocortical networks in subjects at ultra-high risk.
for psychosis and first-episode schizophrenia. Eur Neuropsychopharmacol 29:519–528.
76. Antonucci LA, Di Carlo P, Passiatore R, Papalino M, Monda A, Amoroso N, et al. (2019): Thalamic connectivity measured with fMRI is associated with a polygenic index predicting thalamo-prefrontal gene co-expression. Brain Struct Funct 224:1331–1344.
77. Karimi B, Silwal P, Booth S, Padmanabhan N, Dhume SH, Zhang D, et al. (2021): Schizophrenia-associated LRRTM1 regulates cognitive behavior through controlling synaptic function in the mediodorsal thalamus. Mol Psychiatry 26:6912–6925.
78. Elvsåshagen T, Shadrin A, Frei O, van der Meer D, Bahrami S, et al. (2020): Thalamic nuclei volumes in psychotic disorders and in youths with psychosis spectrum symptoms. Am J Psychiatry 177:1159–1167.
79. Romer AL, Knott AR, Houts R, Brigidi BD, Mof et al. (2011): Complementary distribution of glutamatergic cerebellar and thalamocortical neuron subtypes. Eur J Neurosci 35:1524–1532.
80. Huang AS, Rogers BP, Sheffield JM, Jabbrzikowski ME, Anticevic A, Blackford JU, et al. (2020): Thalamic nuclei volumes in psychotic disorders and in youths with psychosis spectrum symptoms. Am J Psychiatry 177:1159–1167.
81. McTeague LM, Rosenberg BM, Lopez JW, Carreon DM, Huemer J, Jiang Y, et al. (2020): Identification of common neural circuit disruptions in emotional processing across psychiatric disorders. Am J Psychiatry 177:411–421.
82. Di Carlo P, Pergola G, Antonucci LA, Bonvino A, Mancini M, Quarto T, et al. (2020): Multivariate patterns of gray matter volume in thalamic nuclei are associated with positive schizotypy in healthy individuals. Psychol Med 50:1501–1509.
83. Pergola G, Trizio S, Di Carlo P, Taurisano P, Mancini M, Amoroso N, et al. (2017): Grey matter volume patterns in thalamic nuclei are associated with familial risk for schizophrenia. Schizophr Res 180:13–20.
84. Kuramoto E, Ohno S, Furuta T, Unzai T, Tanaka YR, Hioki H, Kaneko T (2015): Ventral medial thalamic neurons send thalamocortical afferents more widely and more preferentially to layer 1 than neurons of the ventral anterior-ventral lateral complex in the rat. Cereb Cortex 25:221–235.
85. Kuramoto E, Furuta T, Nakamura KC, Unzai T, Hioki H, Kaneko T (2009): Two types of thalamocortical projections from the motor thalamic nuclei of the rat: A single neuron-tracing study using viral vectors [published correction appears in Cereb Cortex 2012; 22: 2703]. Cereb Cortex 19:2065–2077.
86. Clascá F, Rubio-Garrido P, Jabaudon D (2012): Unveiling the distribution of glutamatergic cerebellar and GABAergic basal ganglia afferents to the rat motor thalamic nuclei. Eur J Neurosci 33:95–109.
87. Sampaikumar V, Miller-Hansen A, Murray Sherman S, Kasthuri N (2021): An ultrastructural connectomic analysis of a higher-order thalamocortical circuit in the mouse. Eur J Neurosci 53:750–762.
88. Bodor AL, Giber K, Rovó Z, Ulbert I, Acsády L (2008): Structural correlates of efficient GABAergic transmission in the basal ganglia-thalamus pathway. J Neurosci 28:3090–3102.
89. Kuramoto E, Fujiyama F, Nakamura KC, Tanaka Y, Hioki H, Kaneko T (2011): Complementary distribution of glutamatergic cerebellar and GABAergic basal ganglia afferents to the rat motor thalamic nuclei. Eur J Neurosci 33:95–109.
90. Sampathkumar V, Miller-Hansen A, Murray Sherman S, Kasthuri N (2021): Thalamic Connectivity System in Psychiatric Disorders
91. Popa D, Spolidoro M, Provile RD, Guyon N, Belliveau L, Léna C (2013): Functional role of the cerebellum in gamma-band synchronization of the sensory and motor cortices. J Neurosci 33:6552–6556.
92. Lindeman S, Hong S, Kros L, Mejias JF, Romano V, Oostenveld R, et al. (2021): Cerebellar Purkinje cells can differentially modulate coherence between sensory and motor cortex depending on region and behavior. Proc Natl Acad Sci U S A 118:x20015292118.
93. Andreasen NC, O’Leary DS, Cizadlo T, Amit S, Rezai K, Ponto LL, et al. (1996): Schizophrenia and cognitive dysmetria: A positron-emission tomography study of dysfunctional prefrontal-thalamic-cerebellar circuitry. Proc Natl Acad Sci U S A 93:9885–9990.
94. Magnotta VA, Adix ML, Caprahan A, Lim K, Gollub R, Andreasen NC (2008): Investigating connectivity between the cerebellum and thalamus in schizophrenia using diffusion tensor tractography: A pilot study. Psychiatry Res 163:193–200.
95. Ke SE, Jung S, Sung G, Bang M, Lee SH (2021): Impaired cerebrocerebellar white matter connectivity and its associations with cognitive function in patients with schizophrenia. NPJ Schizophr 7:38.
96. Cau H, Agosta F, Filippi M (2015): A selective review of structural connectivity abnormalities of schizophrenic patients at different stages of the disease. Schizophr Res 161:19–26.
97. Deng Y, Hung KSY, Liu SSY, Chui WWH, Lee JCW, Wang Y, et al. (2019): Tractography-based classification in distinguishing patients with first-episode schizophrenia from healthy individuals. Prog Neuropsychopharmacol Biol Psychiatry 88:66–73.
98. Cao H, Chen OY, Chung Y, Forsyth JK, McEwen SC, Gee DG, et al. (2018): Cerebellum-thalamo-cortical hyperconnectivity as a state-independent functional neural signature for psychosis prediction and characterization. Nat Commun 9:3836.
99. Cao H, Ingvar M, Hultman CM, Cannon T (2019): Evidence for cerebro-thalamic-cortical hyperconnectivity as a heritable trait for schizophrenia. Transl Psychiatry 9:192.
100. Argyropoulos GD, Christidi F, Karavasilis E, Velonakis G, Antoniou A, Bede P, et al. (2021): Cerebro-cerebellar white matter connectivity in bipolar disorder and associated polarity subphenotypes. Prog Neuropsychopharmacol Biol Psychiatry 104:110034.
101. Batail JM, Colignon J, Soulas M, Robert G, Barillot C, Drapier D (2020): Structural abnormalities associated with poor outcome of a major depressive episode: The role of thalamus. Psychiatry Res Neuroimaging 305:111158.
102. Igelström KM, Webb TW, Graziano MSA (2017): Functional connectivity between the temporoparietal cortex and cerebellum in autism spectrum disorder. Cereb Cortex 27:2617–2627.
103. Du Y, Yao H, Wang S, Pearson GD, Calhoun VD (2020): Identifying commonality and specificity across psychosis sub-groups via classification based on features from dynamic connectivity analysis. Neuroimage Clin 27:102284.
104. Parker KL, Kim YC, Kelley RM, Nessler AJ, Chen KH, Muller-Ewald VA, et al. (2017): Delta-frequency stimulation of cerebellar deep brain stimulation for treatment of schizophrenia: A double-blind, randomized, sham-controlled clinical trial. Biol Psychiatry 82:64–72.
105. He H, Luo C, Luo Y, Duan M, Yi Q, Bisswal BB, Yao D (2019): Reduction in gray matter of cerebellum in schizophrenia and its influence on static and dynamic connectivity. Hum Brain Mapp 40:517–528.
106. Ji JL, Diehl C, Schleifer C, Tamminga CA, Kashavan MS, Sweeney JA, et al. (2019): Schizophrenia exhibits bi-directional brain-wide alterations in cortico-striato-cerebellar circuits. Cereb Cortex 29:4463–4487.