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Thalamic disconnection as a bottleneck for brain-wide integration in dissociative PTSD

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Abstract

Traumatic experiences can lead to profound disruptions in identity and sensory perception, often manifesting as a sense of estrangement from one's own body. These dissociative symptoms are now alarmingly observed in over half of individuals with post-traumatic stress disorder (PTSD), defining a dissociative subtype (PTSD+DS). While neurophysiological changes across numerous hierarchical brain levels have been identified, the precise mechanisms driving this fractured experience of reality remain unclear. In particular, the role of the thalamus, a central hub for brain-body integration, is thought to be critical but has not been fully characterized in this context. Using the largest connectivity analysis including PTSD+DS, this retrospective study shows that dissociation is defined by a unique shift towards inefficient communication with insufficient thalamo-cortical connectivity. This is revealed through two nearly disjointed but hyperconnected network of brain regions – one exclusively containing higher-level cortical regions with diminished thalamic integration, alongside another with enhanced thalamic-brainstem/cerebellar coupling. Finally, novel analyses localized dissociation-specific shifts in cortico-thalamic synchrony to visual and sensorimotor regions, potentially explaining poor integration of perceptual and bodily information in PTSD+DS. With the ever-increasing prevalence of PTSD+DS, especially in a world with increasing wars, these findings suggest supplementing front-line psychotherapies with adjunctive interventions promoting better bottom-up sensorimotor processing.

Keywords: post-traumatic stress disorder (PTSD), fMRI, resting-state (rs-fMRI), functional connectivity, dissociation, dissociative subtype of PTSD, thalamus, thalamo-cortical

1. Background

Dissociation is emerging as a distinct transdiagnostic psychopathological process, characterized by disruptions in the normally well-integrated functions of consciousness, memory, identity, and perception of self and the environment[1,2]. Although dissociative phenomena occur across multiple psychiatric disorders, they are more strongly linked to trauma-related conditions[3–6]. Within post-traumatic stress disorder (PTSD), dissociative symptoms define a distinct subtype (PTSD+DS) affecting approximately 15–30% of those with PTSD[7,8], with recent provocative estimates approaching 50%[8] in the general population and almost 60% in specialized trauma-exposed populations like war veterans[8–10]. PTSD+DS is characterized by experiences of feeling disconnected or estranged from one's body, thoughts, or emotions (depersonalization) and/or perceiving one's surroundings as foggy, surreal, or visually distorted (derealization)[1,11,12]. Importantly, PTSD+DS is not simply a more severe form of PTSD but reflects a qualitatively distinct clinical and neurobiological phenotype[5,7,8,11–13].

Early neurobiological models of PTSD+DS focused on cortico-limbic mechanisms. These models proposed that excessive engagement of prefrontal control regions suppresses subcortical and limbic threat and arousal systems, resulting in emotional numbing and detachment[7,14–18]. Parallel evidence from temporal lobe epilepsy and stimulation studies supported a temporo-limbic model[19,20], implicating temporal association cortices in depersonalization and derealization[13]. While these frameworks captured key aspects of dissociative phenomenology, they relied on predominantly region-centric findings and did not account for the widespread, systems-level abnormalities increasingly observed in neuroimaging studies[21–23].

Recent work has shifted the field toward a network-based understanding of dissociation. PTSD+DS has been associated with large-scale alterations of the brain's intrinsic connectivity networks, including increased functional segregation of the default mode network (DMN) and abnormal coupling with salience and executive control networks[21–27]. In parallel, dissociation-specific patterns of midbrain[28–34], brainstem[35–38], and cerebellar[39–43] connectivity have been revealed in PTSD+DS. These findings suggest that dissociation reflects a disruption in hierarchical brain communication[44,45], rather than dysfunction within isolated circuits, implicating failures in the integration of sensory, interoceptive, and self-referential signals across multiple levels of the neuroaxis.

Within this hierarchical framework, the thalamus has emerged as a structure of particular relevance[46–49]. Beyond its classical role as a sensory relay, the thalamus plays a central role in regulating cortical excitability, coordinating inter-network communication, orchestrating functional brain network morphology, and maintaining oscillatory synchrony[50–52]. In PTSD, converging evidence indicates

thalamic dysfunction, including reduced activation[49,53,54], altered connectivity with major cortical hubs[55–58], and disruptions in thalamically-mediated alpha oscillations that support sensory gating and contextual processing[59–63]. These observations have led to the proposal that dissociative symptoms may reflect thalamocortical deafferentation[46,64,65]—a failure of thalamic coordination that decouples or disrupts cortical processing from ascending sensory and interoceptive signals. Similar thalamocortical disturbances documented in mild traumatic brain injury (mTBI)[66,67] provides support for this idea given mTBI's comorbidity with PTSD and shared symptoms of sensory disturbances, dissociation, and altered embodiment[68–74].

Despite these converging lines of evidence, thalamic integration across cortical, subcortical, brainstem, and cerebellar systems has not been systematically examined in trauma-related dissociation. In a recent whole-brain functional connectivity study, our group showed markedly increased functional connectivity across nearly every region of the brain in PTSD+DS as compared to healthy control subjects, consistent with a disruption of small-world network architecture [44] (a finding also observed in mTBI[75]). However, in keeping with majority of the field, the thalamus was modeled as single region, precluding assessment of thalamic nucleus-specific contributions to this reorganization.

To address this gap, we conducted the largest ROI-to-ROI resting-state functional connectivity analysis of PTSD to date, focusing on dissociation-related alterations in thalamocortical integration with brain regions spanning numerous hierarchical levels. Integrating whole brain ROI-to-ROI connectivity, graph-theoretic, and multivariate brain-behavior analyses on thalamo-cortical synchrony, we tested whether dissociative symptoms are associated with a distinct pattern of thalamic disintegration that differentiates PTSD+DS from PTSD and healthy individuals. We hypothesized that the PTSD+DS will be characterized by reduced thalamocortical integration, expressed as increased functional connectivity within cortical systems and within subcortical–brainstem systems, alongside diminished connectivity between these hierarchical levels. We further hypothesized finding subcortical and thalamic ROIs with inefficient hub-like properties in PTSD+DS. Finally, we hypothesized the emergence of a distinct dissociation-linked dimension that would co-align with synchrony across sensory, motor, and attention-based regions of thalamic and cortical regions.

Table 1: Participant Demographics and Clinical Scores. Mean scores ± standard deviation reported for age, CAPS IV total, CTQ total, and MDI depersonalization+derealization.

Measure	Controls	PTSD	PTSD + DS

Number (*N*)	82	121	66
Sex (*N*)	58 Females; 24 Males	64 Females; 57 Males	51 Females; 15 Males
Age (years)	35.8 ± 12.2	42.6 ± 11.6	42.1 ± 12.4
Ethnicity (*N*)	65 Caucasian; 8 Asian; 2 African; 3 Hispanic; 4 Unknown	106 Caucasian; 2 Mixed; 1 Aboriginal; 1 African; 3 Asian; 1 Hispanic; 7 Unknown	55 Caucasian; 2 Asian; 2 Mixed; 1 African; 1 Aboriginal; 1 Hispanic; 4 Unknown
Highest Level of Education (years)	16.1 ± 1.8	14.3 ± 2.2	14.2 ± 2.1
Employment Status (*N*)	52 Full-time work; 8 Part-time work; 14 Full-time school; 2 Part-time school; 2 Unemployed; 4 Unknown;	36 Full-time work; 19 Part-time work; 8 Full-time school; 0 Part-time school; 53 Unemployed; 5 Unknown	19 Full-time work; 16 Part-time work; 1 Full-time school; 2 Part-time school; 26 Unemployed; 2 Unknown
CAPS-IV Total	3.1 ± 6.9	65.4 ± 15.3	70.4 ± 22.5
CTQ Total	32.2 ± 8.5	55.7 ± 23.3	67.3 ± 18.9
MDI Depersonalization + Derealization	11.0 ± 2.0	15.3 ± 5.4	25.5 ± 9.3

Abbreviations: CAPS: Clinician-Administered PTSD Scale (Normalized to CAPS-IV); CTQ: Childhood Trauma Questionnaire; MDI: Multiscale Dissociation Inventory; N: Number of participants.

2. Results

ROI – ROI Connectivity

The contrast between those with PTSD and healthy controls (PTSD > Controls) showed significant connectivity differences between cortical ROIs, while connectivity differences with thalamic ROIs did not reach statistical significance. This pattern was characterized by hyperconnectivity between frontal midline structures (paracingulate gyrus [PaCiG], ventromedial prefrontal cortex [vmPFC]) and associative temporal regions (inferior/medial temporal gyrus [I/MTG]). Additionally, hypoconnectivity emerged between frontal midline structures (vmPFC, anteromedial prefrontal cortex [amPFC]) and lateral frontal cortices (superior/middle frontal gyrus [S/MFG]) (Figure 1A).

A markedly different pattern emerged between PTSD+DS and healthy controls (PTSD+DS > Controls). Here, connectivity differences were widespread and encompassed both cortical and thalamic regions. The majority of the statistically significant connectivity differences reflected a pattern of hyperconnectivity in PTSD+DS, when compared to healthy controls. Notably, these connectivity changes segregated into two largely disjointed hyperconnected clusters:

(1) a cortical-only cluster, and
(2) a subcortical cluster involving thalamic, cerebellar, midbrain/brainstem, and select cortical regions (e.g., ITG, temporal fusiform cortex [TFus]).

The anatomical separation of these clusters is illustrated in Figure 1B (green arrow in lower panel), with a visible gap in altered connectivity between the cortical and thalamic/subcortical regions (upper panel). Only a small number of hypoconnectivity effects were observed, primarily involving secondary motor areas (supplementary motor area [SMA]) and the salience-related opercular regions.

Graph Theoretic Analyses

To examine how these connectivity alterations affect overall network properties, graph theoretic analyses were performed on these hyperconnected networks. These analyses uncovered nodes (ROIs) with abnormally high average path length, indicating an inefficient connectivity pattern with other nodes within the network.

In the PTSD > Controls contrast, only left cerebellum lobule VIII emerged as significantly altered. On the contrary, the PTSD+DS > Controls contrast uncovered a broader set of inefficient nodes, additionally including cerebellar (vermis 10), brainstem (locus coeruleus), thalamic (left inferior Pulvinar [PuI]) and cortical (supplementary motor area [SMA], anterior temporal fusiform cortex [aTFusC]) regions (Figure 2). These findings indicate more extensive hierarchical disruption in the dissociative subtype.

Joint Brain-Behavior Analyses

To evaluate the behavioral and clinical relevance of these thalamo-cortical connectivity changes, we identified 24 significant thalamo-cortical factors reflecting robust patterns of functional synchrony between thalamic nuclei and brain-wide cortical nodes (Figure 3). These factors were jointly aligned with behavioral, clinical, and demographic measures, yielding latent brain-behavior dimensions (patterns of thalamo-cortical synchrony aligned with specific behavioral dimensions).

The primary brain-behavior dimension ($r = 0.55$, $p = 0.02$) aligned positively with derealization severity (MDI-Derealization) and emotion dysregulation (DERS total) and aligned negatively with severity of childhood trauma (CTQ), depersonalization (MDI-Depersonalization), and depressive symptoms (BDI). Collectively, this primary dimension was indicative of a dissociative symptom dimension. The secondary brain-behavior dimension ($r = 0.47$, $p = 0.37$) predominantly reflected PTSD symptom severity (CAPS). Notably, the axes of these two dimensions were largely orthogonal, indicating distinct underlying brain-behavior relationships (Figure 4).

Spatially, the primary dissociation-related brain-behavior dimension co-aligned with the medial pulvinar (PuM) and ventral posteromedial thalamus (VPM) in the positive direction, while aligning with the lateral pulvinar (PuL), inferior pulvinar (PuI), and the ventral anterior/lateral thalamus (VA/VL) nuclei in the negative direction. Cortically, this dimension mapped onto somato-motor regions (pre-central gyrus), precuneus, and higher-order visual association regions (cuneal cortex, temporal-fusiform gyrus) in the positive direction, and onto primary visual regions (supra-calcarine cortex), socio-emotional regions (temporal pole), sensory salience regions (parietal operculum, posterior insula), and DMN hubs (posterior cingulate cortex [PCC]) in the negative direction (Figure 5).

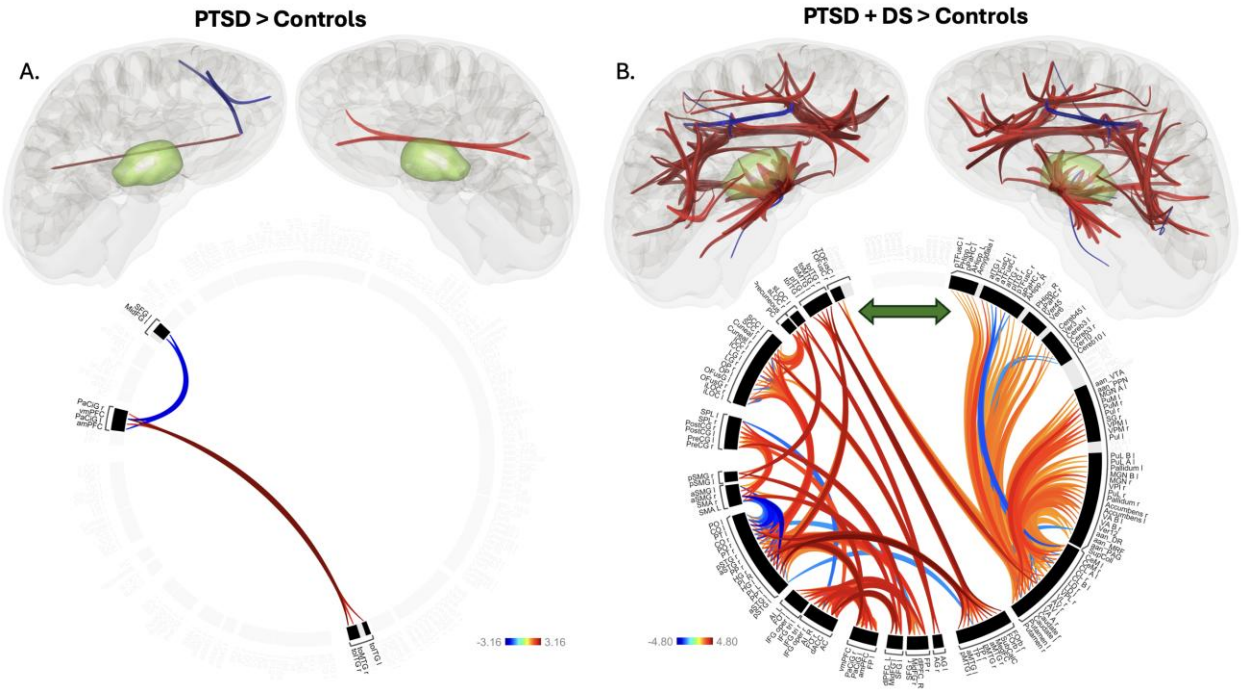


Figure 1 – Prominently disjointed functional connectivity changes (shown by the green arrow) within cortical ROIs, and thalamic/brain-stem ROIs in PTSD+DS, as compared to controls (shown on the right, B. PTSD + DS > Controls).

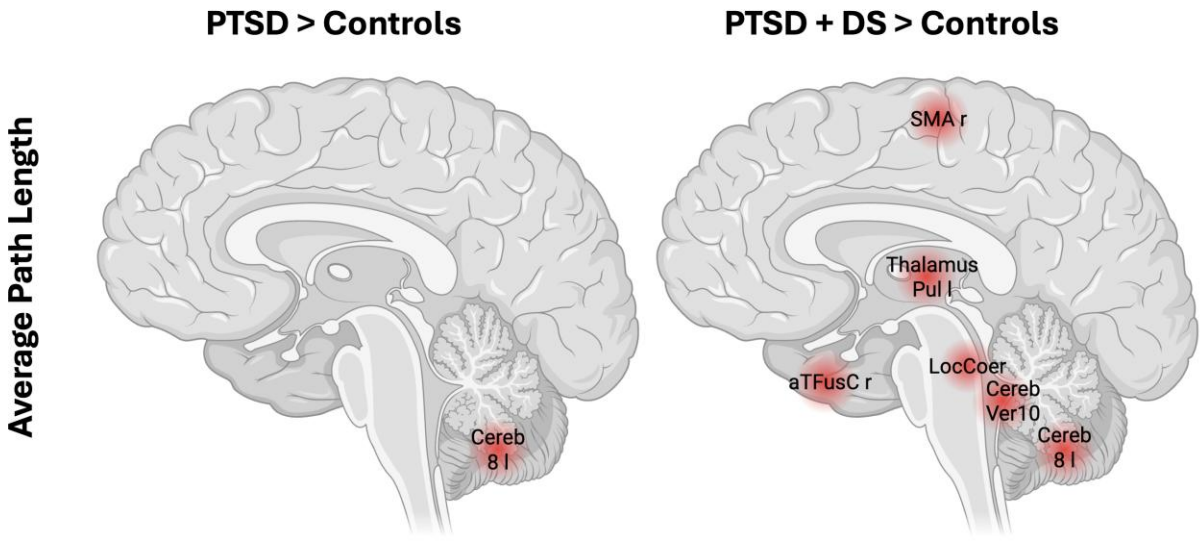


Figure 2 - Nodes with longer average path length in those with PTSD (left) and PTSD + DS (right), as compared to healthy controls. These represent regions with potentially inefficient functional connectivity within the entire graph of ROIs shown in Figure 1. Abbreviations: SMA – Supplementary Motor Area, Pul – Inferior Pulvinar, LocCoer – Locus Coereleus, Cereb – Cerebellum, Ver – Vermis, aTFusC – Anterior Temporal Fusiform Cortex, l – left, r – right.

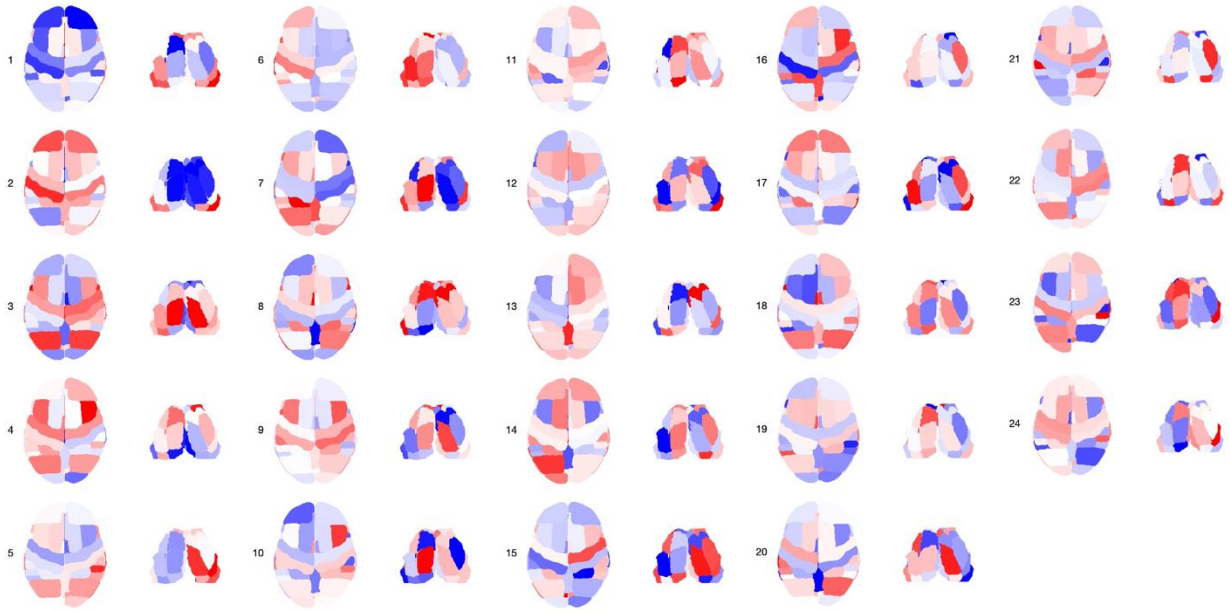


Figure 3 - Joint thalamo-cortical factor contributions. Each factor consists of a cortical ROI contributions (left) and thalamic ROI contributions (right). Positive contributions are shown in red and negative contributions are shown in blue. The factors were identified using regularized canonical correlation analysis (RCCA) and tested for significance using bootstrapping. Only significant factors are shown.

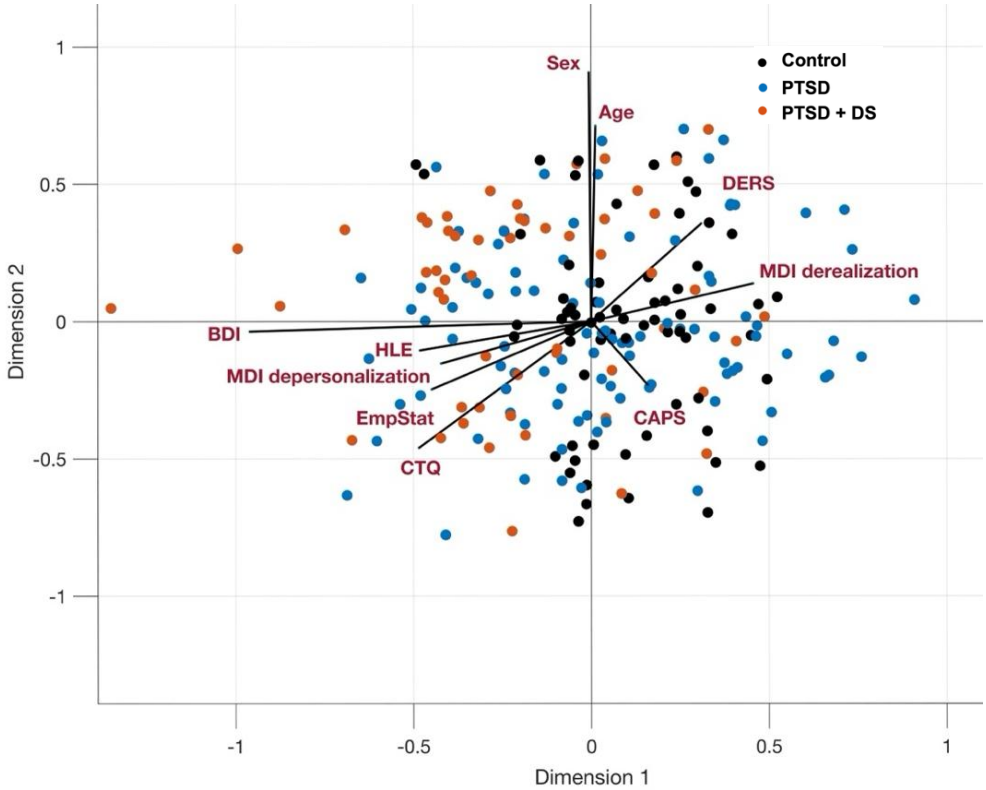


Figure 4 – Top two brain-behavior dimensions plotted alongside all participants. Participants in the healthy control group are shown in black, those in the PTSD group are shown in blue and those in the PTSD + DS group are shown in orange. Abbreviations: MDI – Multiscale Dissociation Inventory, DERS – Difficulties in Emotion Regulation Scale, CAPS – Clinician Administered PTSD Scale, CTQ – Childhood Trauma Questionnaire, BDI – Beck Depression Inventory, HLE – Highest Level of Education, EmpStat – Employment Status.

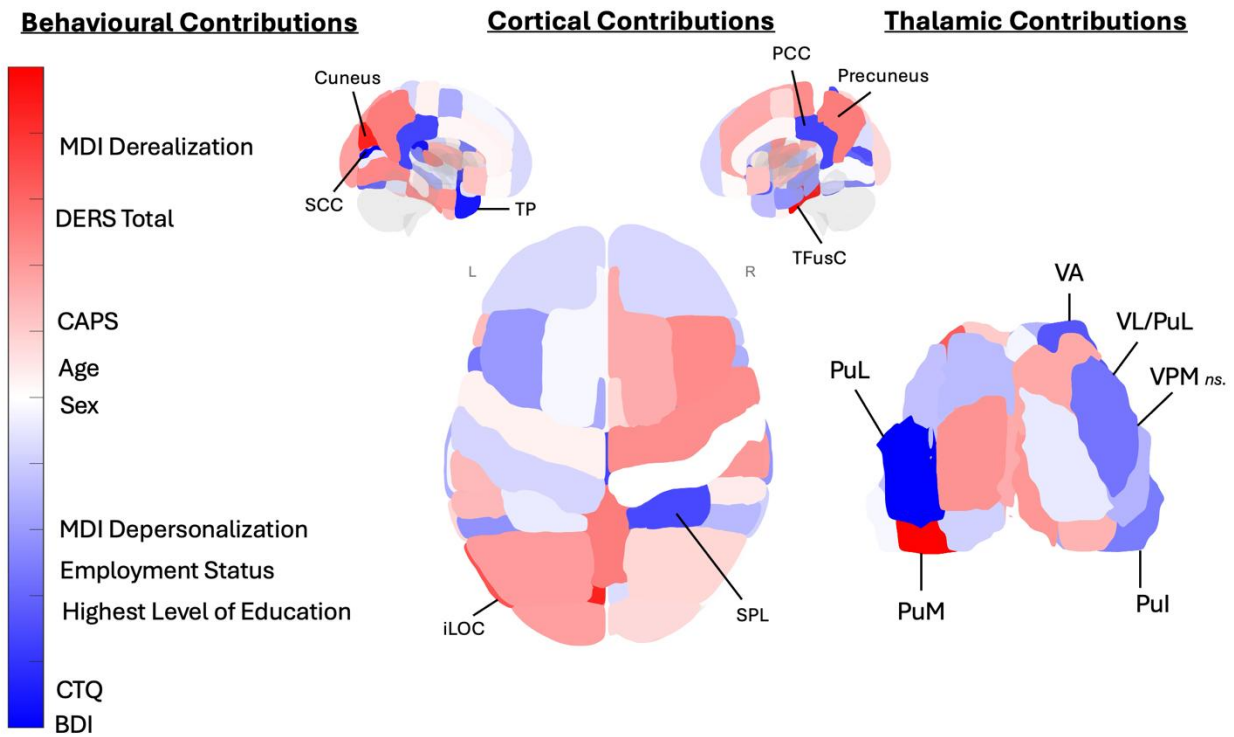


Figure 5 - Primary brain-behavior dimension aligned with dissociative measures, showing contributions of the behavioral measures (left panel), cortical ROIs (middle), and the thalamic ROIs (right). Red represents positive alignment with this dimension and blue represents a negative alignment with this dimension. Abbreviations: MDI – Multiscale Dissociation Inventory, DERS – Difficulties in Emotion Regulation Scale, CAPS – Clinician Administered PTSD Scale, CTQ – Childhood Trauma Questionnaire, BDI – Beck Depression Inventory, SCC – Supra-Calcarine Cortex, TP – Temporal Pole, PCC – Posterior Cingulate Cortex, TFusC – Temporal Fusiform Cortex, iLOC – Inferior Lateral Occipital Cortex, SPL – Superior Parietal Lobule, PuL – Lateral Pulvinar, PuM – Medial Pulvinar, PuI – Inferior Pulvinar, VA – Ventral Anterior Nucleus, VL – Ventral Lateral Nucleus, VPM – Ventral Postero-Medial Nucleus, ns. – not seen in image.

3. Discussion

Convergent evidence from numerous lines of inquiry points toward critical connectivity changes between brain regions spanning many hierarchical brain levels in those with PTSD+DS. Evidence not only suggests hyperconnected cortical ICNs and disorganized inter-ICN connectivity between salience, interoceptive, executive and sensorimotor brain networks[21,40,76–78], but also altered involvement of bottom-up circuits[79], and brainstem/midbrain regions[37]. Previous work by Shaw et al. (2023) further demonstrated that such shifts towards hyperconnectivity are not confined to specific large-scale networks but rather represent a global shift in functional connectivity patterns across the brain at rest[44], and during trauma memory recall[40]. These findings have often been interpreted as patterns of widespread cortical overdrive that inhibit hierarchically lower brain regions under the corticolimbic model of dissociation[7,13,80], and more recently within the predictive processing/coding framework that suggests an accumulating mismatch (*i.e.* prediction error) between top-down cortical predictions of the world and bottom-up subcortical sensory input[81–83]. Despite these efforts, the mechanisms underlying such large-scale shifts in connectivity have remained elusive. The current study closes this gap by

uncovering dissociation-specific reorganization of large-scale connectivity centered around the thalamus that could unite these findings into a cohesive framework to better understand dissociative pathophysiology. This is particularly relevant given the alarming rise in PTSD+DS prevalence in general populations[8] and war veterans[8–10], projected to rise with the increased frequency of wars.

Thalamo-cortical deafferentation in dissociation

The results of this study collectively point towards a marked failure of thalamo-cortical integration during rest in those with PTSD+DS. Rather than staying strongly integrated across multiple levels of the neuroaxis, the thalamic nuclei were instead more strongly aligned with lower-level structures, including subcortical, brainstem, and cerebellar regions. This shift effectively bifurcated the overarching pattern of hyperconnectivity into two nearly disjointed hyperconnected clusters. One cluster exclusively comprised of hyperconnected regions within the cerebral cortex, consistent with the findings of Shaw et al. (2023). Meanwhile, the other cluster predominantly contained hyperconnected thalamo-brainstem and thalamo-cerebellar loops.

Contextualized within current literature, our findings further support the idea that dissociative symptoms may be rooted in thalamo-cortical deafferentation[37] by showing that hyperconnected cortical hubs may operate largely in isolation, lacking commensurate integration with thalamic relays. Such thalamo-cortical deafferentation would disrupt the thalamus's essential role in contextualizing sensory, motor, and emotional information, contributing to decontextualized salience processing, depersonalization, emotional blunting, breakdown in sensorimotor coordination, and altered interoception that is characteristic of dissociation. This often clinically presents as people feeling disconnected from their body, the world and their current reality, resulting in an "autopilot"-like state frequently associated with a loss of volitional control, agency and purpose.

Furthermore, the few hypoconnected nodes observed in those with PTSD+DS included insular/opercular regions, consistent with previously observed shifts away from the emotionally contextualized anterior insula and towards more sensory posterior insular processing in dissociation[17,84,85]. These shifts could further exacerbate the decontextualized processing of sensory information potentially arising from thalamo-cortical deafferentation in PTSD+DS.

Thalamic integration with runaway lower-level loops in dissociation

The second hyperconnected network observed in this study, comprising of thalamic nuclei, brainstem, and cerebellar regions, suggests a parallel subcortical system operating unmodulated by cortical input in those with PTSD+DS. These findings support a large body of evidence showing dissociation-linked disruptions in lower-level nodes of the innate alarm system (IAS)[86], such as increased ventromedial

PAG activation at rest[79] and hyperconnectivity within cerebellar and brainstem regions during traumatic memory recall[40]. The cortically decoupled thalamus may allow unregulated “runaway” signalling from lower-level sensorimotor and interoceptive pathways that fail to adequately integrate with higher-level conscious processing, in-turn impeding adequate updating of prediction errors based on current sensory experiences[81–83], potentially driving poor emotional and sensorimotor contextualization[17].

Graph-theoretic analysis further supports this interpretation, revealing inefficient hub properties within subcortical nodes of the IAS, such as the locus coeruleus (LC) and the thalamic pulvinar (Pu), both central to the brain’s arousal and attentional orienting systems (see Figure 2). Efficient thalamic hubs, and that of the pulvinar in particular, are essential for maintaining the modular structure of functional brain networks[50], long-range cortical-cortical connections[87], adequate prediction errors based on current sensory information[88], and alpha oscillatory activity essential for attentional control[59,61,89]. The inefficient hub-like behavior of the pulvinar in PTSD+DS is consistent with a failure to coordinate sensory gain[90], breakdown of regular network structure[24,44], dysregulated prediction errors[81–83], and shifts in oscillatory alpha synchrony[91,92]. This also helps explain the observed therapeutic potential of modulating alpha rhythms to restore long-range network coherence and emotional contextualization in those with PTSD[93,94]. Furthermore, the LC’s inefficient integration (high average path length) in PTSD+DS is particularly notable given its central role in regulating arousal, salience processes, and attentional gating through widespread noradrenergic innervation across the cortex[95–97] and the thalamus[98]. LC disruptions, as that observed in PTSD[99], could therefore interrupt overall cortical integration of arousal that may struggle to adequately adapt to situational needs, as is often seen in dissociative symptomatology.

Interestingly, temporal regions were the only cortical bridge between the two hyperconnected clusters, a finding in accordance with temporolimbic models of dissociation and clinical observations of dissociative experiences in temporal-lobe epilepsy[100].

Together, these findings integrate prior neurobiological models of dissociation, positioning the thalamus as a critical hub whose decoupling from the cortex reorganizes communication across multiple levels of the neuroaxis.

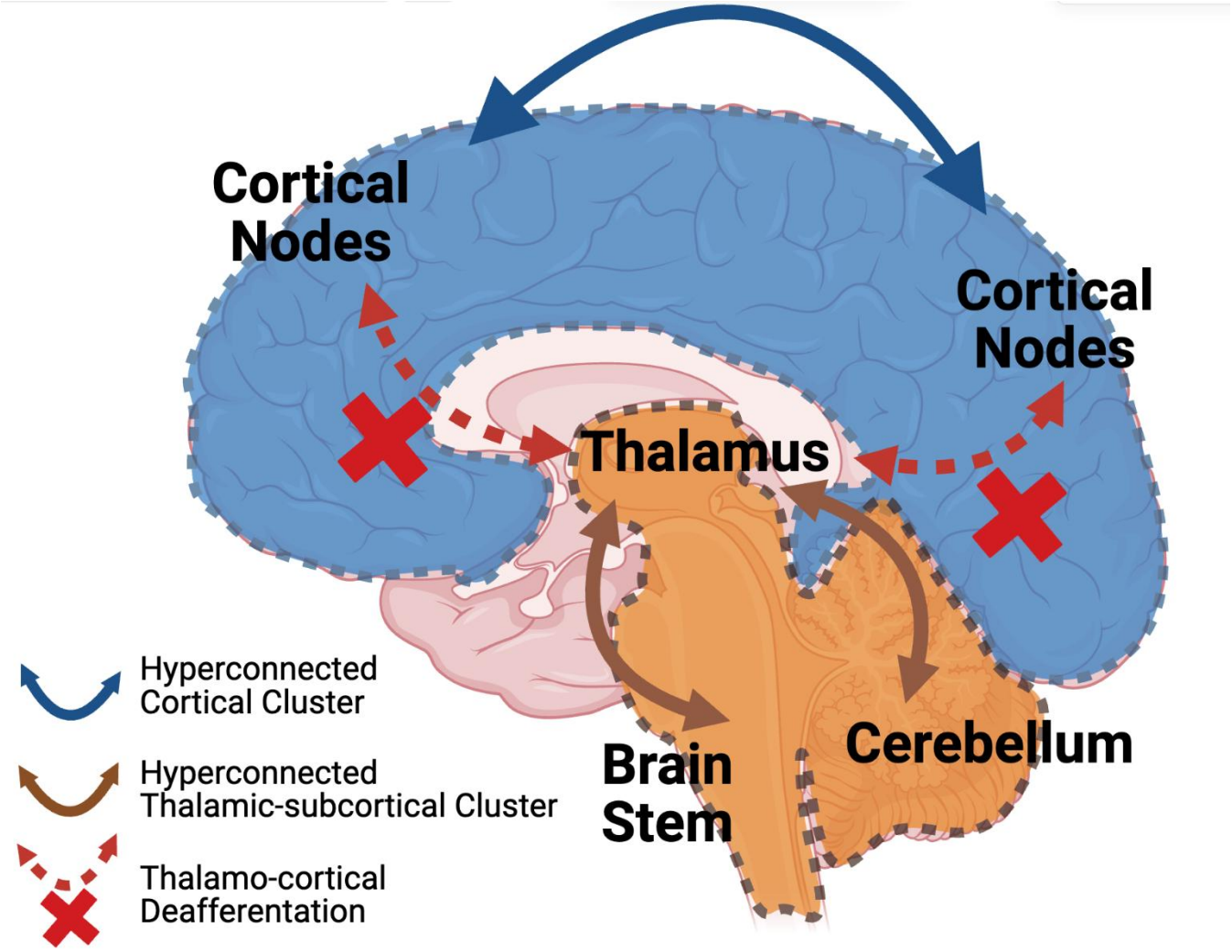


Figure 6 - Illustration of the two disjointed hyperconnected clusters, showing prominent thalamo-cortical deafferentation where the hyperconnected clusters do not show commensurate connectivity between thalamic and most cortical nodes.

Thalamic pulvinar-centered mechanism links visual sensory processing to dissociation

The thalamo-cortical patterns associated with the dissociative symptom profile identified in this study (Figure 4) provide key insights into the sensory integration disturbances characteristic of PTSD+DS.

The thalamic nuclei most strongly aligned with dissociative symptomatology were the medial, lateral, and inferior pulvinar sub-nuclei (abbreviated as PuM, PuL and PuI, respectively). While these are all closely associated with sensory integration and bottom-up attentional processes, they regulate complementary but distinct attentional faculties based on their downstream connections. The medial pulvinar (PuM) is a central hub for multisensory integration, interoceptive processing, and attentional orienting[88,101], owing to widespread projections to limbic, salience, and DMN regions (including anterior and posterior cingulate)[102–104]. On the other hand, the lateral (PuL) and inferior pulvinar (PuI), are deeply involved in visual attention processes[104,105] through reciprocal connections across multiple levels

of the visual cortex[104,106], including higher-order visual association regions located in the medial temporal lobe[107].

Hence, the dissociation dimension (Figure 5) showing co-alignment of PuM, PuI, and PuL with cortical visual association regions (cuneal cortex, temporal-fusiform gyrus), social and sense-of-self processing regions (temporal pole, posterior cingulate), and spatial orienting regions (precuneus, SPL) may suggest that visuospatial and self-referential interoceptive inputs may be amplified yet poorly integrated with salience information in PTSD+DS. These thalamo-cortical patterns further elucidate previously observed shifts in pulvinar-cortical associations contributing to the "blunted" attentional profile observed in those with the dissociative subtype[58]. These also explain clinical reports of heightened but detached visual processing of one's own body and environment in derealization/depersonalization[13] states, consistent with the breakdown of body-space representations maintained in the dissociation-aligned precuneus and the posterior parietal cortex (in the SPL)[108].

Additionally, these pulvinar nuclei all receive convergent input from the superior colliculus[104,109], forming retinotectal pathways that support the orienting response to threat-related stimuli that is often disrupted in PTSD[102,106,110]. The co-alignment of these pathways with symptoms of dissociation helps explain why bottom-up, sensorimotor-focused therapies such as Deep Brain Reorienting (DBR), which target early orienting and tectal-pulvinar circuitry, show promise in individuals with dissociative symptoms[77,93,111–113].

Ventral thalamic nuclei link somatomotor processing to dissociation

Beyond the pulvinar, the ventral posteromedial nucleus (VPM), a relay for somatosensory input from the face and intraoral regions, also showed co-alignment with dissociative symptoms and the precentral gyrus. Breakdown of such circuitry supporting mind-body integration could contribute to the sensation of "numbness" or the "unreal" quality of bodily experiences in depersonalization[114]. Given VPM's critical role in mapping the body schema, its co-alignment with primary somatomotor regions could represent a compensatory mechanism for disrupted interoceptive processing that paradoxically amplifies somatomotor signals failing to integrate properly with higher-order bodily self-awareness, ultimately resulting in decontextualized representation of sensorimotor information from the body and face. The increased hub-like changes in the locus coeruleus within the PTSD+DS might also further exacerbate the relay of decontextualized sensorimotor information to the cortex through its noradrenergic-driven modulation of thalamocortical gain and signal-to-noise ratios in the VPM[115].

Similarly, the ventral anterior/lateral nuclei (VA/VL), that co-aligned with the dissociation dimension, serves as the primary thalamic relay for cerebellar and globus pallidus output to motor cortices, and was accompanied by cortical regions responsible for socio-emotional processing (temporal pole),

sensory salience (parietal-operculum, posterior insula), and sense-of-self processing (posterior cingulate). Collectively, the alignment of these ventral thalamic nuclei (VPM and VA/VL) with the dissociation dimension could reflect the disruption of coordinated voluntary sensorimotor action with interoceptive feedback, potentially contributing to the subjective sense of being an "observer" of one's own actions characteristic of dissociation.

Taken altogether, these results suggest that dissociation involves a breakdown in thalamic-mediated coordination of visuospatial, somatosensory, and interoceptive signals, producing amplified yet poorly integrated perceptual and bodily information. The result may be a fragmented sense of embodiment and self-other boundaries—core features of dissociative phenomenology.

Dissociation is distinct from hyperarousal-driven CAPS symptomatology

The orthogonality of the dissociation dimension to CAPS severity is particularly noteworthy, suggesting that dissociative symptoms reflect a neurobiologically distinct phenotype, not simply a more severe form of PTSD. The greater loading of childhood trauma (CTQ) alongside the dissociation dimension rather than the CAPS severity dimension aligns with evidence that early adversity disrupts thalamo-cortical development[116] and oscillatory patterns[91], affecting downstream arousal-based developmental processes. Considering the thalamo-cortical patterns associated with this dimension, these results suggest that as dissociation intensifies, the brain may shift from thalamically-mediated integration toward alternative, less efficient pathways and subcortical “runaway” loops, resulting in greater disconnect between one’s subjective experience and the external reality.

Future work is needed to further characterize the neurobiological underpinnings of specific mental states that are currently collectively referred to as dissociation. These include transdiagnostic symptoms of depersonalization, derealization, dissociative amnesia, identity dissociation, and somatic manifestations of dissociation. Such understanding will be critical for personalized treatment approaches that optimize recovery from traumatic stress and dissociation, especially in a world with increasingly traumatic global stressors such as wars.

4. Conclusion

In conclusion, the current study uncovers two nearly disjointed hyperconnected networks in PTSD+DS – one exclusively cortical with diminished cortico-thalamic integration, alongside another with enhanced thalamic-brainstem/cerebellar coupling. This architectural pattern provides direct empirical support for the thalamocortical deafferentation hypothesis of dissociation, extending it beyond a simple disconnection to a functional reorganization of hierarchical brain communication that is likely adaptive in

the context of chronic or developmental trauma. The resultant dampening or disengagement from sensory input in the present moment may serve as a protective mechanism, particularly when opportunities for escape or active coping are limited like those experienced during wars. The cortical-only cluster, enriched in midline frontal and associative temporal regions, may represent an "island" of hyperconnected self-referential processing that operates without normal thalamic gating and sensory context, explaining the paradoxical combination of intense self-focused rumination alongside emotional numbing and decontextualized sensorimotor processing. Finally, the dissociation-specific involvement of sensorimotor and visual thalamic nuclei (pulvinar subdivisions and VPM), coupled with the identification of LC and pulvinar as inefficient network hubs, illuminates how thalamic gating failures might produce the fragmented self-awareness that defines dissociative symptoms. Collectively, our findings highlight that PTSD+DS might not simply be a variant of PTSD with quantitatively more severe symptoms[117], but rather a qualitatively distinct neurocircuitry phenotype potentially impacting a sizeable global population, where current front-line psychotherapies could benefit[118] from adjunctive bottom-up interventions like Deep Brain Reorienting (DBR).

5. Detailed Methods

Participant Information

This study included data from 269 participants (healthy controls *N* = 82; PTSD *N* = 121; PTSD+DS *N* = 66) recruited from the London, Ontario, Canada community through referrals from healthcare workers and community advertisements over a 12-year period (2009-2022). All study participants provided written informed consent in accordance with the protocol approved by the Research Ethics Board at Western University (HSREB #120706) in London, Ontario, Canada.

Inclusion Criteria

A primary diagnosis of PTSD, confirmed via the Clinician-Administered PTSD Scale (CAPS), was required for inclusion in either PTSD group. To ensure the use of the most current diagnostic standards, 123 participants were assessed using CAPS-IV, while the remaining 146 were assessed using the updated CAPS-5 once it was available. To ensure compatibility with prior data, the CAPS-5 total scores were normalized to the CAPS-IV scale, following established procedures[77,93].

Inclusion into the dissociative PTSD subtype (PTSD+DS) group further required specific symptom thresholds in accordance with standard procedure[77,119,120], including participants with a CAPS-IV score of >= 2 for both frequency and intensity of depersonalization or derealization, or a symptom severity score of >= 2 for depersonalization or derealization within the CAPS-5.

Finally, inclusion in the control group required participants to have no lifetime history of psychiatric diagnoses.

Exclusion Criteria

Comorbid alcohol or substance abuse/dependency not in sustained full remission, and a diagnosis of schizophrenia or bipolar disorder were exclusion criteria for participants in either of the PTSD groups (PTSD and PTSD+DS). Participants were excluded from the control group if they had any lifetime Axis-I psychiatric disorders, as determined by the CAPS and the Structured Clinical Interview for DSM Disorders (SCID). General exclusion criteria for all groups included pregnancy, failure to meet MRI safety standards, or a history of head injury involving loss of consciousness.

Clinical Questionnaires

Beyond the CAPS, the study collected a comprehensive battery of behavioral, clinical, and demographic data, including the Childhood Trauma Questionnaire (CTQ)[121], Beck Depression Inventory (BDI)[122], depersonalization and derealization subscales of the Multiscale Dissociation Inventory (MDI)[123], Difficulties in Emotion Regulation Scale (DERS)[124], age, biological sex, employment status (EmpStat), and the highest level of education (HLE).

Imaging and preprocessing protocol

A 3T Siemens Trio MRI scanner (Siemens Medical Solutions) equipped with a 32-channel head coil was used for all MRI scans. The scanning session for each participant consisted of a high-resolution, axial three-dimensional Magnetization-Prepared Rapid Acquisition Gradient Echo (MPRAGE) scan (Inversion Time[TI] = 900ms, Repetition Time[TR] = 2000ms, Echo Time[TE] = 4.2ms, Flip Angle[FA] = 9°, 192×256×256, slice thickness=1 mm), followed by a six-minute functional MRI (fMRI) scan utilizing a two-dimensional Gradient Echo (GRE) Echo-Planar Imaging (EPI) sequence (TR/TE = 3,000/20ms, FA=90°, 120×128×128×62, slice thickness=2 mm) during which the participants were instructed to allow their minds to wander freely without focusing on any specific thought. All measurements reported in this study represents a unique participant, with no repeated measures within participants.

All data preprocessing and subsequent analyses were conducted using SPM12 and the CONN toolbox (version 22a), consisting of realignment and unwarping, motion correction using 12-degrees-of-freedom (DOF), frequency-domain phase-shift slice timing correction to account for interleaved acquisition, outlier scrubbing using ART, simultaneous segmentation and normalization to the MNI152 atlas space, spatial smoothing using a 3.5mm Gaussian kernel, and finally, band-pass filtering within the 0.008–0.09 Hz frequency range. The preprocessing parameter choices, like that of the 3.5mm Gaussian kernel for

spatial smoothing, were specifically selected to maintain consistency with previously established preprocessing pipelines used to assess thalamo-cortical associations[125].

ROI-to-ROI analysis

A large-scale ROI-to-ROI analysis was performed utilizing a total of 178 regions, integrating 101 cortical and subcortical ROIs from the Harvard–Oxford atlas with 26 cerebellar ROIs from the Automatic Anatomical Labeling (AAL) atlas, 30 thalamic ROIs from the Kumar thalamic atlas[125], 9 ROIs from the Harvard Ascending Arousal Network (AAN)[126], and 12 previously investigated custom ROIs[127–129] spanning the anterior/posterior insula, anterior/posterior hippocampus, medial prefrontal cortex and the superior colliculus. Out of the 106 standard ROIs available in the Harvard-Oxford atlas, 2 insular ROIs, 2 hippocampal ROIs, and 1 brainstem ROI were excluded to avoid duplication with the more detailed ROIs of these regions. This specific set was selected for its comprehensive whole-brain coverage spanning cortical and subcortical nodes, its prevalence in existing literature, its seamless integration with the CONN toolbox, and a functionally-derived parcellation of the thalamus that is ideally suited to capture thalamo-cortical synchrony. Functional connectivity was determined by calculating pairwise bivariate correlation coefficients between the preprocessed BOLD time series of each ROI pair. These coefficients then underwent Fisher transformation to normalize the distribution for inter-subject comparisons. Between-group analyses of variance (ANOVA) were performed to evaluate the following two-sided contrasts: PTSD > Controls, PTSD + DS > Controls. reported contrasts are two-sided, with reverse effects denoted by negative F-statistics and T-statistics. To account for multiple comparisons, results were corrected at the cluster level using a false discovery rate threshold of p-FDR < 0.05, after hierarchical clustering. Comprehensive statistical data—including effect size estimates (η^2 for the F-statistic and Cohen's d_z for the T-statistic) and both uncorrected and FDR-corrected p-values—are provided in Supplementary Table 1. The η^2 and d_z were computed using the following formula,[130]

$$\eta 2 = \frac{F \times df_{effect}}{F \times df_{effect} + df_{error}}$$

$$d_z = \frac{T}{\sqrt{n}}$$

where F and T represent the F-statistic and T-statistic values, respectively, df_{effect} was the degrees of freedom of the effect, df_{error} was the degrees of freedom of the error, and n was the number of participants.

Graph-theoretic analysis

Next, graph-theoretic analysis were performed to better understand the impact of the ROI-to-ROI connectivity changes on the efficiency of information flow within the brain. A graph adjacency matrix was estimated using the ROI-to-ROI connectivity matrix, thresholded using a cost-level edge-defining threshold of 0.15 and a two-sided false discovery rate corrected threshold of 0.05 (p-FDR < 0.05). The resultant graph was used to estimate the average path length of each ROI and its deviations from healthy patterns through the PTSD > Controls and PTSD + DS > Controls contrasts.

Joint Brain-Behavior Analyses

Finally, thalamo-cortical shifts that align with specific behavioral dimensions were assessed using a novel two-step brain-behaviour analysis. First, regularized canonical correlation analysis (RCCA) was performed between the denoised time series of the thalamic and cortical ROIs to identify robust patterns of thalamic and cortical coactivation. To ensure robustness and stability of these thalamo-cortical factors, only the factors that survived a p-value threshold of 0.05 were deemed statistically significant, where the p-value was estimated using 1000-fold permutation testing with a randomized subgroup of participants selected for each fold. Next, the weights of the statistically significant thalamo-cortical factors identified in step 1 were back-projected for each participant to identify their thalamic and cortical timecourses for each thalamo-cortical factor. These were used to estimate the thalamo-cortical synchrony for each factor, for each participant, by computing the Pearson's correlation coefficient between their thalamic and cortical time courses. Finally, these estimates of synchrony for each thalamo-cortical factor were used in an RCCA alongside each participants' clinical, behavioral and demographic information. A similar 1000-fold permutation testing-derived p-value threshold of 0.05 was used to identify statistically significant brain-behavior dimensions with specific behavioral profiles and its' associated patterns of thalamo-cortical synchrony. The reduction in overall model dimension due to this two-step process, the use of 1000-fold permutations to derive p-values, and the use of L2-regularization within RCCA worked together to find the brain-behavior dimensions most stably found across all participants, mitigating risks of multicollinearity and model weight instability[131]. Finally, the publicly available and validated version of RCCA was utilized in this study (available at https://github.com/mlnl/cca_pls_toolkit) to ensure algorithmic accuracy and improve replicability of these findings in other datasets. Participants with missing behavioural, demographic, and clinical variables were excluded from this analysis.

6. Data Availability Statement

The data supporting the results in this study are available within the manuscript and the accompanying supplementary information. The data use agreement governing the dataset used in this study restricts public sharing, and hence the dataset is not publicly available.

7. Code Availability Statement

Analyses used standard SPM12, CONN (version 22a) analysis pipelines and algorithms (e.g. hierarchical clustering algorithm), and the publicly available implementation of regularized CCA (RCCA) accessible at https://github.com/mlnl/cca_pls_toolkit, as described in the detailed methods section. No further custom code or algorithm was used in this study.

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Author Contributions Statement

S.B. Shaw: Conceptualization, Methodology, Data collection & curation, Data Analysis, Writing. **B. Terpou:** Writing. **B. Kearney:** Writing. **M. Densmore:** Data curation, Methodology. **J. Théberge**: Methodology. **P. Frewen**: Methodology. **M. McKinnon**: Funding Acquisition. **R. Lanius**: Conceptualization, Supervision, Methodology, Funding Acquisition, Data Analysis Writing.

Conflict of Interests Statement

S.B. Shaw, B. Terpou, B. Kearney, M. Densmore, J. Théberge, P. Frewen, M. McKinnon, and R. Lanius do not have any conflicts of interest to disclose.

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