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Spatiotemporal Psychopathology – An integrated brain-mind approach and catatonia

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ABSTRACT

Catatonia is featured by complex symptoms combining motor, affective and behavioral phenomena as well as by its syndrome character with trans-diagnostic occurrence. It paradigmatically shows the limits of current forms of psychopathology like affective and cognitive approaches with respect to both clinical symptoms and brain mechanisms. We therefore suggest Spatiotemporal Psychopathology (STPP) which, as recently introduced, is here developed further following the latest findings in both clinical psychiatry and neuroscience. STPP is characterized by two core features: (i) an experience-based approach that accounts for symptoms primarily in terms of first-person experience of time-space as distinct from third-person observation of specific functions and related behavior; (ii) an integrated brain-mind approach where the brain's neural topography and dynamic, e.g., inner time and space, are shared by the mind's mental topography and dynamic, e.g., time-space experience, as their "common currency". We demonstrate how these two features can well account for both symptom complexity and trans-diagnostic nature of catatonia. In conclusion, catatonia can serve as paradigmatic example for the need to develop a more comprehensive psychopathological approach in psychiatry. This is provided by STPP that allows integrating subjective experience, clinical symptoms and the brain's neural activity in terms of their inner space-time, e.g., topography and dynamic.

1. Introduction

One key challenge in current psychiatry concerns our understanding of the psychopathological symptoms, that is, how they can be characterized and connected to abnormalities in the brain? Psychopathology concerns the empirical and theoretical framework in which subjective experience, clinical symptoms, and behavior, in psychiatric patients can be described, categorized, and classified (see Parnas et al., 2008, 2013; Stanghellini, 2009; Stanghellini and Ballerini, 2011; Stanghellini and Broome, 2014; Stanghellini, 2019) for discussing the notion of psychopathology). Catatonia, a psychomotor syndrome, paradigmatically exemplifies the difficulties any psychopathology encounters, because it is characterized by complex symptoms and occurrence across different diagnostic categories. Patients with catatonia exhibit motor, affective, and behavioral symptoms (Hirjak et al., 2019a,b, 2022a,b; Northoff et al., 1996; Bush et al., 1997; Mittal et al., 2017). Further, catatonia can occur in different psychiatric disorders like uni- and bipolar affective disorders, schizophrenia spectrum disorders, autism and others (Hirjak et al., 2020a,b; Hefter et al., 2019).

The diagnosis and treatment of catatonia in daily clinical routine raises a number of questions: How can we account for its symptom complexity and trans-diagnostic occurrence? How can current neuroimaging findings be integrated into the classification of catatonia, because currently, there is no single psychiatric disorder in which neuroimaging (particularly structural or functional magnetic resonance imaging [MRI]) is used for classification or diagnosis? In this paper, we make the case that catatonia shows the limits of current psychopathological approaches that focus mostly on affective and cognitive symptoms including their extension to specific regions and networks in the brain (Halligan and David, 2001; David and Halligan, 2000). In contrast to historical nosological concepts of mental illness, the observable behavior of patients (their psycho- and sensorimotor functions) has become almost irrelevant in the current classification systems ICD-10, DSM-5 and ICD-11. This means that many observable clinical signs such as gait, stance, facial expressions (mimic), gestures, daily activity, speech, prosody, involuntary movements, and fine motor skills currently

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receive little attention from clinical colleagues and have no diagnostic relevance. Also, the diagnostic criteria for catatonia according to ICD-11 and DSM-5 include fewer than 10 catatonic symptoms and do not take into account the subjective experience of these patients. At the same time, catatonia requires an integrated brain-mind model that also includes behavior and extends beyond current experience-based approaches, as phenomenological psychopathology (Parnas et al., 2008, 2013; Fuchs, 2013; Stanghellini, 2009; Stanghellini et al., 2021; Messas et al., 2018; Stanghellini and Broome, 2014). Specifically, one needs to intimately connect neural and mental levels, e.g., brain and experience in a non-reductive way (Northoff et al., 2020a,b), with observable behavior in order to account for the psychomotor nature of catatonia beyond its motor manifestations (Hirjak et al., 2019b, 2020a,b, 2022b; Northoff et al., 2021a,b).

The goal of the current paper is two-fold. First, we aim to provide an updated overview of Spatiotemporal Psychopathology (STPP) (Northoff, 2016a,b, 2018, 2020; Fingelkurts and Fingelkurts, 2019) that focuses specifically on the connection of brain's neural activity in terms of their inner time-space, e.g., topography and dynamic, subjective experience and clinical symptoms/behavior. We hypothesize that STPP will allow a deeper understanding of psychiatric disorders in general and pave the way for new, more effective, treatment strategies comprising psychotherapeutic psychopharmacology and brain stimulation techniques. Secondly, we apply such spatiotemporal approach to catatonia showing that it can well account for both symptom complexity and transdiagnostic nature. In particular, we hypothesize that motor, affective, and behavioral catatonic symptoms might be best explained by aberrant time-space experience and that this dysfunction is also reflected at the first-person experience of self, body and world. Further, we hypothesize that motor, affective, and behavioral catatonic symptoms might be best explained by aberrant time-space experience and that this dysfunction is also reflected at the neural level in the corresponding topography of brain networks and their dynamic.

2. Spatiotemporal Psychopathology and symptoms: experience of space and time

2.1. Psychopathological symptoms – function- vs experienced-based approaches

Current affective and cognitive forms of psychopathology (Panksepp, 2004; Halligan and David, 2001; David and Halligan, 2000) view the psychopathological symptoms in terms of specific functions. Affect-related symptoms in uni- and bipolar (mood) disorders (depression and mania) are associated with emotional functions; cognitive symptoms in schizophrenia and mood disorders are supposedly mediated by particular cognitive functions including working memory, attention, planning abilities, cognitive control and domain-general cognition; sensory-perceptual and motor symptoms as in schizophrenia, mood disorders and catatonia are associated with the respective sensory and motor functions. Deficits in these various functions are of transdiagnostic nature and supposed to lead to the transnosological psychopathological symptoms – one can thus speak of a function-based approach (Fig. 1a).

This is different in phenomenological psychopathology. As in its name, phenomenological psychopathology (Stanghellini et al., 2019; Parnas et al., 2013; Northoff, 2019) focuses on the first-person experience of the psychopathological symptoms as distinguished from their third-person observation. This implies a shift from third-person perspective on function and behavior to first-person perspective of experience: the subjects themselves are supposed to describe their experiences of for instance auditory-verbal hallucinations (AVH) as distinguished from the third-person observation or description of hallucination-related behavior. This said, the first-person experience of the patient her/himself is taken here as main measure or reference of psychopathological symptoms rather than the third-person observation and description/classification by the psychiatrist.

How does such first-person experience-based approach stand in relation to the function-based approach? Ideally, one would say that

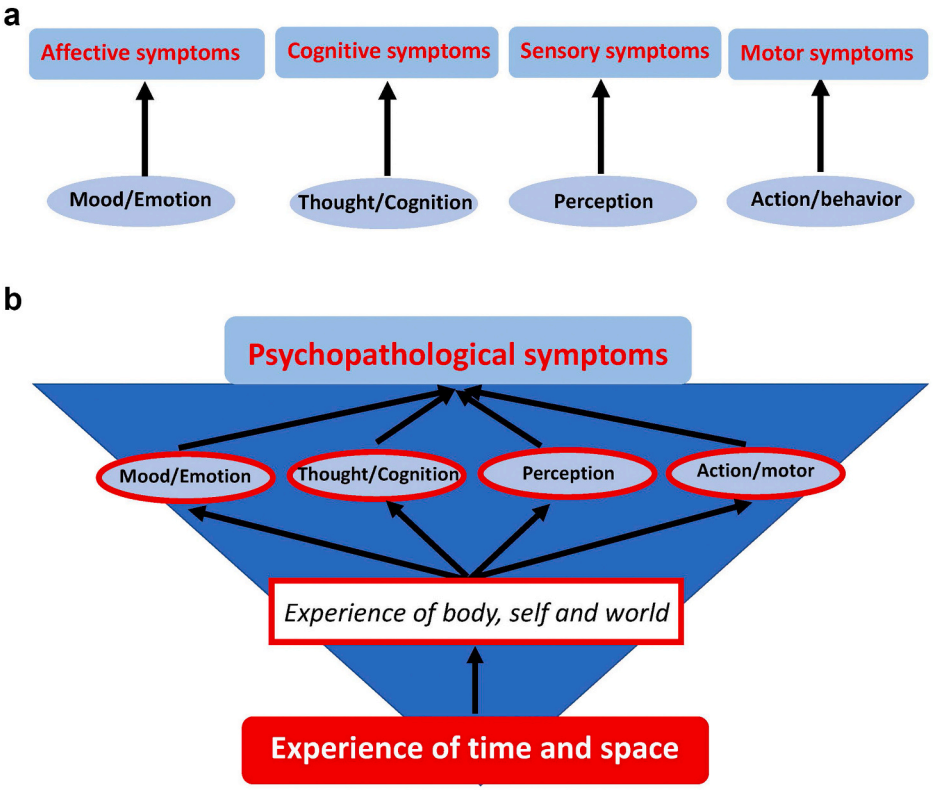

Fig. 1. a. Function-based approach to psychopathological symptoms. This figure illustrates the background assumption of current psychopathology that the different functional domains (mood, cognition, etc.) are related directly, exclusively and sufficiently to the different psychopathological symptoms in psychiatric disorders.
b. Experienced-based approach with four-layer hierarchy of psychopathological symptoms. This figure illustrates that experience of time-space as well as of self, body, and world provides the background layer within which the different functions/domains (perception, mood, cognition etc.) are embedded which, in turn, relates to the different psychopathological symptoms. The psychopathological symptoms are here understood to result from the interaction of experience and functions/domains rather than being directly, exclusively, and sufficiently related to the functions/domains themselves as in the current approach (Fig. 1a).

different forms of self or first-person experiences are related to distinct functions. That is not the case, though. For instance, the same function-based symptoms like AVH can be experienced in different ways: one patient may feel threatened by the intrusive voices and be admitted to inpatient psychiatry while another with the same kind of AVH may not report major changes in her/his experience going unnoticed and non-treated for 30 years (as it happened to one of my patients). From a patients' perspective, the voices can say good or bad things. The contents of the voices are often embedded in the patient's life story and are therefore of a subjective and very personal nature. It is similar with AVH-associated behavior. This said, the level of suffering and the way the patients deal with AVH can also be quite different. Conversely, different symptoms like delusions of persecution, thought disorders, catatonic phenomena and depressive thoughts/feelings may go along with the same experience, namely the first-person experience of extreme uncertainty, anxiety or even fear (Shorter and Fink, 2018).

Together, these examples demonstrate that experience and function may dissociate from each other: the same first-person experience may accompany different functions while conversely the same function could go along with different first-person experiences. This suggests double dissociation of experience and function. Both can thus not be equated and translated one-to-one into each other. Hence, experience and function refer to distinct aspects or layers of psychopathological symptoms. Therefore, phenomenological psychopathology cannot be identified with cognitive or affective psychopathology.

2.2. First-person experience – structure and holistic

How can we further characterize the first-person experience of psychopathological symptoms? To address that question, we briefly need to go back to function-based approaches. Function-based approaches focus on the content of psychopathological symptoms as well as on valence of thoughts, behaviors and experiences. Contents concern for instance the negative affect or thoughts (e.g., negative view of oneself, others and/or the future) in depression or, the content of the AVH, that is, what the voices the patient hears are talking about. Yet another example are delusions which often reflect technical, social and socio-economic contents. This said, there is a strong focus on contents in the function-based approaches. This goes along with the isolation of single contents like the ones of the different functions like emotion, cognition, behavior etc., - there is a focus on single isolated contents which supposedly correspond to the distinct symptoms. Furthermore, to better understand psychiatric disorders, it is also important to examine the valence of thoughts, behaviors and experiences as well as their neurobiological underpinnings. All three elements are interconnected, but always play a different role for a patient and his/her behavior.

In contrast, experience-based approaches neither focus on specific contents or valence of thoughts, behaviors and experiences nor consider them to be isolated. Rather than on contents, the focus is here on the structure, form or organization of patient's own first-person experience. This shifts the focus from specific affective, cognitive, sensory, or motor contents to the overall organization of our first-person experience within which the different contents are integrated and embedded. Often, personal history and development also play a decisive role. Rather than on specific contents, phenomenological psychopathology therefore focuses more on body, self, world, time and space as these are considered key elements for organizing and structuring the human experience (Fuchs, 2013; Parnas et al., 2013; Stanghellini et al., 2019; Northoff, 2019).

Finally, the function-based approach isolates and reduces the psychopathological symptoms in an atomistic way to single separable functions associated with circumscribed disturbance of brain regions and networks. This is different in the experience-based approach which, due to the integration of body, self, world, time and space in experience implies a more holistic approach. The different co-occurring psychopathological symptoms are consequently considered distinct parts of a whole; the whole by itself refers to an underlying abnormal organization of the structure or form of self-/first-person experience (Stanghellini et al., 2019; Parnas et al., 2013).

2.3. Space and time as foundation – four-layer hierarchy of psychopathological symptoms

The more holistic experience-based approach raises the question for the relation among the different co-occurring psychopathological symptoms: what binds or glues them together the different contents by providing their intimate link that makes possible their co-occurrence (Northoff et al., 2021b)? Phenomenological psychopathology focuses on the first-person experience of body, self, world, time and space: they provide the "glue" and thereby organize and structure the different contents of our self-experience. The co-occurrence of different symptoms with their respective contents is thus traced to the way the structure or organization of our first-person experience of body, self, world and time and space is altered in psychiatric disorders (Parnas et al., 2013; Stanghellini et al., 2019).

Usually, body, self, world and time and space are considered in a more or less similar and analogous way without any hierarchy among them (Stanghellini et al., 2019; Fuchs, 2013). That is different in STPP, though. STPP introduces a certain hierarchy in the structure or organization of our experience: it considers the experience of time-space to be most basic and fundamental while the experience of body, self, and world rests and is based on that. STPP therefore extends phenomenological psychopathology by introducing a layered hierarchy into first-person experience itself.

The focus on space-time as most basic foundation for the first-person experience of body, self and world is supported by various studies on the importance of time-space experience for the experience of body, self and world. For instance, the experience of abnormal slowness in depression shapes the experience of the body as being heavy and sluggish showing abnormal embodied temporality and anomalous vital rhythms (Stanghellini et al., 2017a, 2021). Analogously, time (and space) experience of fragmentation and abnormal anticipation dominates and shapes the experience of the self, body and world in schizophrenia as many historical (Eugène Minkowski and Wolfgang Blankenburg) and contemporary (Stanghellini et al., 2017a,b, 2020; Arantes-Gonçalves et al., 2022; Fuchs, 2007, 2013; Klar and Northoff, 2021) authors have described.

Together, this (and other more neuroscientific reasons; Northoff et al., 2020a,b) provides the ground for STPP to consider space-time experience as more basic and fundamental than the first-person experience of self, body and world. Specifically, space and time are considered constitutive for organizing and structuring and thereby relating the different psychopathological symptoms. This is supposed to be manifest in an abnormal first-person experience of self, body and world which, in turn, modulates the affective, motor, cognitive and sensory functions in an abnormal way yielding the psychopathological symptoms. STPP thus proposes a four-layer hierarchy from the constitution of space-time over the first-person experience of self, body and environment to the various functions and from there to psychopathological symptoms (Fig. 1b).

Considering such four-layer hierarchy, STPP is neither contradictory to experience-based approaches nor incompatible with function-based approaches. It extends and specifies experience-based approaches by introducing a hierarchical structure of experience with differentiation of its constitution through space-time and manifestation in first-person experience of body, self and world. At the same time, STPP provides a more holistic and thereby more comprehensive framework for function-based approaches as the various functions are now considered within the broader framework of the four-layer hierarchy of space-time, self-world-body, and functions, and symptoms (Northoff, 2016a,b). More precisely, STPP aims to integrate both approaches (phenomenological psychopathology and function-based approach) and also plausibly relate them to aberrant neurobiological processes, i.e.; alterations of respective brain dynamics and topography. Put in a nutshell, STPP provides an umbrella

framework for (i) integrating and reconciling phenomenological with function-based affective/cognitive psychopathology; and (ii) linking them with modern neuroscientific approaches in order to better understand the pathomechanisms of mental illness.

2.4. Catatonia – experience-based topography of its symptom complexity

Catatonia is a psychomotor syndrome that includes affective, motor and behavioral symptoms. Catatonia is an interesting disorder because it can manifest with different symptoms that simultaneously affect three psychopathological domains (motor, affective and behavioral). How is such co-occurrence of different symptoms and their respective functions possible? The function-based approach would consider catatonia in terms of isolated functions – this is for instance most prevalent in the current motor view of catatonia (Walther et al., 2019; Mittal et al., 2017). Catatonia is here considered a motor disorder that can be traced to dysfunction of the motor brain networks (Walther et al., 2019). That neglects the co-occurrence of the strong affective symptoms and especially the bizarre behavioral changes which both cannot be reduced to mere motor functions (Hirjak et al., 2020a, 2022a,b; Northoff et al., 2021a,b) (for overview of different catatonia concepts see Table 1).

Accordingly, the function-based approach with its focus on isolated functions comes to its limits in the case of catatonia which requires a more holistic and structure-based framework like STPP. This leads us back to the first-person experience of catatonia. Rather than just observing, assessing and classifying the various motor, affective and cognitive-behavioral symptoms in third-person perspective, one may want to consider the catatonic patient's first-person perspective: how do they experience the individual very heterogeneous symptoms? How does it feel not to move for hours if not days? How does it feel to constantly repeat sentences and bizarre behaviors (echolalia and echopraxia)? Or, how do patients with catatonia experience their extreme anxiety (fear) and negativism (despite life-threatening constellations of eating and drinking refusal)? Last but not least, what is it like to experience several symptoms from three different functional domains at the same time? Two earlier studies of ours collected the first-person experience of post-acute catatonic patients using a self-assessment-scale especially for catatonia developed by the authors (Northoff et al., 1996, 1998; An update of this self-rated questionnaire is already in preparation.). In the first study, Northoff et al. (1996) retrospectively examined 24 patients with catatonia according to Rosebush et al. (1990) and Lohr and Wisniewski (1987) criteria. The authors found that catatonia patients experience their intense emotional (anxiety) and cognitive (ambivalence) alterations rather than altered movements. Further, patients reported extreme ambiguity that they were unable to decide what and when to do (Northoff et al., 1996). Overall, this study points out the co-occurrence and co-constitution of affective, cognitive, and motor changes in the patients' first-person experience: abnormal experience of affective or cognitive changes like overflooding or ambiguity leads to and generates the bizarre motor and behavioral alterations with the latter being the manifestation of the former. The later study (Northoff et al., 1998) compared 22 akinetic catatonia patients with 22 major depressive, 22 paranoid schizophrenic, 22 residual schizophrenic, and 22 akinetic Parkinson's disease (PD) patients. Unlike in PD patients, catatonia patients did not report the first-person experience of altered movements even when in an acute state of posturing and akinesia. Instead, they reported strong overflooding emotions which, either positive like joy or negative like anxiety, could no longer control anymore – they felt overwhelmed and overflooded by emotions. Hence, the same symptom, e.g., akinesia, posturing, or catalepsy can be associated with different first-person experiences – this supports the prime importance of experience over function as one hallmark of STPP. That underlines the prime importance of a holistic more topographic approach to psychopathological symptoms that focuses on the relationships among the

Table 1
Different concepts to approach catatonia.

	STPP	Psychomotor theory	Motor theory
Key idea and message	Spatial (topography) and temporal (dynamic) features of the brain's neural activity are considered constitutive for organizing and structuring different catatonia symptoms	"Catatonia is a psychomotor syndrome."	"Catatonia is a motor syndrome."
Key brain regions and frequencies	Whole-brain topographic approach focusing on the relative relationship among different regions/networks rather than considering single regions or networks. All frequencies are considered with the pattern of changes from time point to time point, e.g., dynamics.	Higher-order frontoparietal networks involving OFC, PFC, SMA and M1 slower and faster frequency ranges	Cortical and subcortical motor regions involving SMA, M1, basal ganglia, and cerebellum faster frequency related to motor function
Key neurotransmitter systems	All transmitter systems are considered in their relative balances like between dopamine and serotonin rather than searching for the transmitter systems in isolation independent of each other	Mainly gamma-aminobutyric acid (GABA)-ergic, glutamatergic and serotonergic transmission	Mainly dopaminergic transmission
Applied neuroimaging methods and measures	Both fMRI and EEG/MEG. Dynamic measures like power law exponent (PLE), intrinsic neural timescales, sample entropy and complexity; Topographic measures like the global signal and core-periphery	Structural (VBM; TBSS; tractometry (along tract statistics using TractSeg); graph analytics (CCO and BC)) and functional MRI; multivariate data fusion techniques for multimodal MRI	Structural and functional MRI
Applied clinical assessments	Space and time experience in psychosis scale (STEP) Scale for subjective experience of catatonia	Northoff Catatonia Rating Scale (NCRS)	Bush-Francis Catatonia Rating Scale (BFCRS)
Requirements for investigators	Psychiatric, neuroscientific and engineering/physics background	Psychiatric and neuroscientific background	Psychiatric and neuroscientific background
Pros and cons	PROS: direct connection of neuronal (brain) and phenomenal (experience) and symptom (behavior) levels	PROS: Captures the whole symptom-experience-behavior spectrum of catatonia	PROS: Fewer methodological difficulties because of the focus on purely motor functioning
	CONS: Novel methodological tools for analysis of both neuronal and phenomenal/mental and behavioral activity are required and developed extending beyond the current more cognitive-based tools and measures	CONS: Methodological challenge to capture all three (heterogenous) symptom domains of catatonia with neuroimaging	CONS: Catatonia is reduced to purely motor dysfunction

Abbreviations: Orbitofrontal cortex = OFC; Prefrontal cortex = PFC, Supplementary motor area = SMA; Primary motor cortex = M1; voxel-based morphometry = VBM; tract-based spatial statistics = TBSS, clustering coefficient = CCO; local betweenness centrality = BC.

different functions rather than their isolation as in the function-based approaches (see also Northoff et al., 2021b).

One may finally raise the question for time-space experience in catatonia. Are the abnormal experiences of ones' catatonic symptoms related to abnormal time-space experiences? One could for instance imagine that the extreme emotion overflooding or ambiguity can be traced to an experience of time fragmentation or extreme standstill which subsequently generates posturing and akinesia. That remains to be explored in the future, though. Finally, one may argue that such experience-based approach does not yield proper diagnostic separation. That was not the case though in our earlier study (Northoff et al., 1996, 1998) where we were able to distinguish the first-person experience of catatonia in schizophrenia or affective disorders patients from those schizophrenia and affective disorders patients that did not suffer from catatonia – this suggests some diagnostic specificity of the experience-based holistic topographic approach of STPP. However, subjective experience of patients as a diagnostic criterion does not occur in current classification systems ICD-10, DSM-5 and ICD-11. In the case of catatonia, it would be more than appropriate because it could facilitate the differential diagnostic differentiation from other neuropsychiatric syndromes (delirium, serotonergic syndrome, etc.) (Hirjak et al., 2019b).

3. Spatiotemporal Psychopathology and the brain: integrated brain-mind approach

3.1. Extension of function-based approaches to the brain – gap between brain and symptoms

Affective and cognitive forms of psychopathology (Panksepp, 2004; Halligan and David, 2001; David and Halligan, 2000) link symptoms to specific functions which, in turn, relate to their specific neural correlates in the brain. For instance, working memory is traced to the dorsolateral prefrontal cortex while auditory perception is associated with the auditory cortex. Alterations in these regions are then associated with the respective symptoms like cognitive changes in thought disorders and/or AVH in schizophrenia (Hugdahl et al., 2022).

The isolation of different symptoms in terms of their functions finds its continuation on the neural side in the isolation of different regions or networks that supposedly provide their neural correlate (Poeppel, 2020). Analogous to the different symptoms and their functions, the brain itself is here considered in a module-based way: the different regions and networks are considered to mediate different functions (or modules) and consequently the symptoms (Menon, 2011; Xi et al., 2021). As different symptoms co-occur, interactions between the different regions and networks are added to the picture as for instance

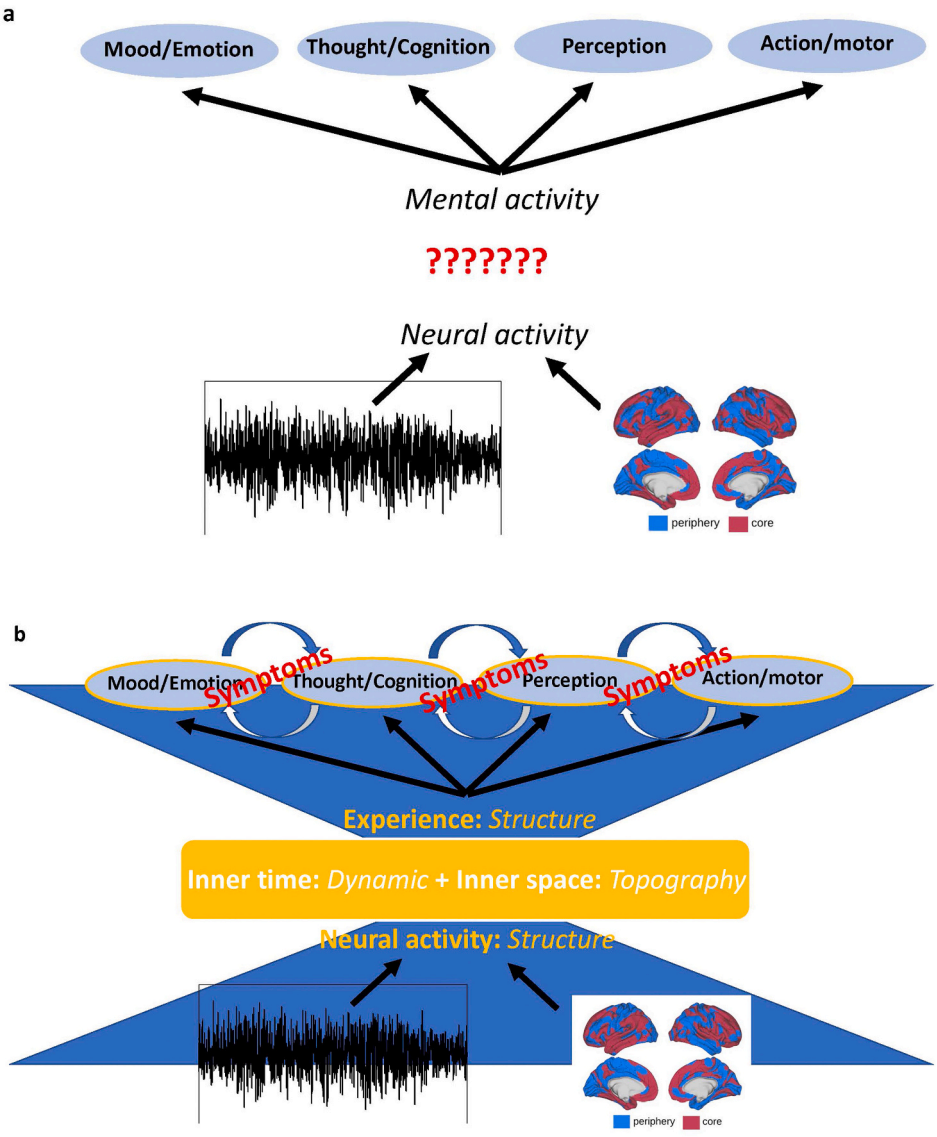

Fig. 2. a. Gap between neural and mental activity in current function-based approaches to psychopathology. This figure illustrates the current gap between the brain's neural activity (illustrated below by its temporal (lower left) and spatial (lower right) features on the one hand and the mental activity (upper part) including its abnormalities as in the various psychopathological symptoms. The gap is indicated by the red question marks symbolizing the current lack of knowledge about the connection of neural and mental activity.
b. This figure shows that the temporal, e.g., dynamic, and spatial, e.g., topography, structure is shared by both neural activity (lower part) and experience (upper part) as their "common currency" (Northoff, 2021). The degree to which that topographic and dynamic structure is altered will, in turn, shape the kind of psychopathological symptoms including their co-occurrence across different functions/domains (indicated by the blue/white arrows among the symptoms in the upper part) (Northoff, 2022). Lower right: the brain shows the distinction of the transmodal core (regions of the default mode network etc.) and unimodal periphery (visual and auditory etc. cortex). The core-periphery topography is for instance abnormal in distinct ways in depression (Scalabrini et al., 2020), schizophrenia (Yang et al., 2017), and bipolar disorder (Zhang et al., 2019). Lower left: The timeseries on the left illustrates the fluctuations of raw time series data in fMRI (and similarly also in EEG) whose speed pattern are for instance too slow in depression (Northoff, 2018; Lu et al., 2022).

prototypically manifest in the triple network hypothesis of schizophrenia (Menon, 2011; Xi et al., 2021). For instance, there is also a relationship of sensorimotor integration abilities, brain structure and function, and AVH symptom expression (Wolf et al., 2021).

Despite all its success in cognitive neuroscience (Poeppel, 2020), this model of brain leaves open the intimate connection of symptoms to the neural changes: why and how can changes in neural activity yield and generate the kind of abnormal experiences and subsequently the symptoms themselves? Philosophically speaking, we are still confronted with a gap between brain and symptoms, something which, in the healthy domain of brain and consciousness, has been described as explanatory gap or hard problem (Northoff and Zilio, 2022). The function-based approach thus lacks a proper model of how the brain's neural activity is connected to the abnormal mental activity of symptoms; that is, the brain-symptom connection remains opaque (Fig. 2a). We require an integrated brain-mind model to render more transparent the brain-symptom connection. Such a model could also pacify the critics of modern neuroscience and neurobiological research by accounting for the mental, e.g., experience, in a non-reductive way.

3.2. Integrated brain-mind model – topography and dynamic as "common currency" of brain and experience

How can we draw closer and tighter connection of neural and mental activity? One way is to search for features that are shared and are thus common to both. What do neuronal and mental features share? For that we need to go back to the brain itself and most notably its spontaneous activity. While the brain's task-related activity is characterized by specific functions (like affective or cognitive), the spontaneous activity, as measured in resting state without any specific task or stimuli, is determined by its spatial and temporal features (Northoff et al., 2022): the spontaneous activity constructs its own inner time and space in its neural activity as distinguished from the outer space and time of the world (Kant, 1781/1998; Northoff, 2012; Northoff et al., 2020a,b).

The brain's inner time and space is for instance manifest in its spatial topography, that is, the organization of the different brain regions as part of an overall organization across the brain as whole (Northoff et al., 2022). At the same time, the brain is featured by different frequencies in its neural fluctuations which amount to a dynamic with different timescales (Wolff et al., 2022). The brain's inner time and space can thus be characterized by the topography and dynamic of its spontaneous neural activity.

How can the brain's topography and dynamic provide an intimate connection to mental features? We recall that symptoms are experienced in terms of time and space and that this experience, in turn, yields the symptoms when stepping up the ladder of the four-layer hierarchy. This raises the question where and how the experience of abnormal time and space originates. We suppose that it may come from and, in part, be based on the abnormal constitution of the brain's inner time and space, namely its topography and dynamic (Fig. 2b). The brain's abnormal topography and dynamic in both its spontaneous and task-related activity on the neural level should thus manifest on the mental level in the first-person experience of abnormal time-space – time-space are shared by neural and mental levels as their "common currency" (Northoff et al., 2020a,b). This is indeed supported by various mental features including self (Northoff et al., 2020a), consciousness (Northoff and Zilio, 2022) and mind-wandering (Hua et al., 2022). The assumption of time-space providing the "common currency" of brain and mind carries major implications for the relationship of brain and symptoms. If neural and mental levels are connected through their shared time-space, abnormal changes in the brain's topography and/or dynamic should lead to corresponding mental changes with abnormal first-person experiences of time-space which are key in generating psychopathological symptoms across a variety of psychiatric disorders, e.g., transnosologically.

3.3. Brain-symptom connection I – abnormal slowness of motor, cognitive and affective function in depression

Speed of experience may provide one prototypical example of a "common currency" between brain and symptoms. Depressed patients experience abnormal mental slowness of their inner time which, in turn, is manifest in the abnormal slowness of their mood, social behavior, psychomotor activity and cognition (Fuchs, 2013). Decreased speed in inner time perception and the various symptoms is related to decreased speed on the neuronal level, that is, neural activity shows decreased variability as index of neuronal speed in their spontaneous activity (Northoff et al., 2018). Abnormally slow speed is thus shared by both brain and symptoms in depression providing their "common currency" (Northoff, 2011; Northoff et al., 2018, 2020a,b).

How does the abnormally slow time speed in depression yield the extreme affective changes. Based on Spatiotemporal Neuroscience (Northoff et al., 2020a,b), STPP assumes that changes in the brain's inner spatiotemporal topography and dynamic provide an abnormal spatiotemporal envelop (or framing) for cognitive, sensory, motor, and affective functions in depression: the affective functions are simply processed too slow which, in turn, shapes and changes the affective content towards an extremely sad and depressive content ("if, due to abnormal slowness, one experiences no change at all, the affect becomes sad and hopeless"; Northoff et al., 2018). The same occurs in the case of motor functions where one can observe abnormally slow activity in motor cortex yielding psychomotor retardation (Lu et al., 2022).

Together, one can observe altered organization of the whole brain's topography and dynamic in depression. The decreased slowness of the motor cortex is the result of an overall topographic and dynamic reorganization of the brain in depression: the topographic focus of the whole brain's activity is shifted towards the slower transmodal default-mode network (DMN) at the expense of the unimodal sensory and motor regions (Scalabrini et al., 2020; Lu et al., 2022). Such topographic-dynamic re-organization towards the DMN and slower inner time, in turn, is manifest in more or less corresponding first-person experiences of an abnormally slow time and restricted space in depression.

Yet another example of abnormal mental slowness in depression are thoughts. The speed of the changes of internally- and externally-oriented thoughts, e.g., thought dynamic is much slower with lower power in acute depressed subjects than those in healthy subjects (Rostami et al., 2022). The abnormally slow and powerless thought dynamic, in turn, shapes the thought content and structure as manifest in rumination, e.g., brooding in the depressed subjects (Rostami et al., 2022). Accordingly, the abnormally slow dynamic in both brain and experience provides an abnormal spatiotemporal envelop which slows down motor, cognitive and affective functions and consecutively results in the depressive symptoms.

3.4. Brain-symptom connection II – neuro-mental topography and dynamic of catatonia

Catatonia is a syndrome that can occur in the context of different psychiatric (and non-psychiatric) disorders most notably mood disorders (depression and mania) and schizophrenia (Hirjak et al., 2022a; Hirjak et al., 2019b; Northoff et al., 2004). How is that possible? One approach can be made from the topographic side. A recent overview demonstrates whole-brain topography of different psychomotor mechanisms including both cortico-cortical and subcortical-cortical which all lead to motor cortex changes: depression, mania and schizophrenia may show different cortico-cortical and subcortical-cortical changes which all lead to motor cortex changes as their final common functional pathway (Northoff et al., 2021a,b,c; Hirjak et al., 2022b; Northoff, 2002). Assuming that neural topography transforms into mental topography, one would assume certain similarities in the experiences of space in those depressed, manic and schizophrenic subjects (Stanghellini et al., 2017a,b, 2020, 2021) that develop different catatonic symptoms.

Yet another approach to the question for the syndrome nature of catatonia comes from the dynamic side. Both depressed and schizophrenic patients show abnormal time experience with standstill of time albeit in distinct ways: subjects with depression complain about slowness of time while schizophrenia subjects report time fragmentation (Stanghellini et al., 2016, 2017a,b; Arantes-Gonçalves et al., 2022). Both slowness and fragmentation can, though, in extreme degrees, lead to an experience of standstill of time where nothing at all changes and moves anymore (Northoff et al., 1996, 1998); that, in turn, may provide the temporal envelope for the motor functions which thereby come to a complete standstill – this, as we suppose, is manifest catatonic akinesia, mutism and posturing. On the other hand, there can also be an acceleration of the experience of time and space, as we know it from manic patients. In a manic state, patients talk very fast, are impatient, impulsive, cannot sit still and sleep, and feel great. This can also be the case in hyperkinetic catatonia, as one pole of periodic catatonia. This said, in the context of bipolar disorders and schizophrenia (Russo et al., 2020), there can be fluctuations in psychomotor activity; these are similar to catatonic states. From a clinical perspective, the temporal slowing or acceleration and first-person experience of spatial restriction or expansion in patients with catatonia can be well understood: in the context of akinesia, posturing, mutism and catalepsy, time passes very slowly, patients are restricted in their radius of action (Fig. 3). Vice versa, frequent and sometimes short-term changes in psychomotor functioning such as agitation, impulsivity, aggression, hyperkinesia, as we know it from patients with periodic catatonia, are a transdiagnostic phenomenon, which may also occur in rapid-cycling bipolar disorders and schizophrenia (Fig. 3). A previous fMRI study by Russo et al. was able to show a functional reconfiguration of the spatiotemporal structure of intrinsic brain activity to occur in bipolar disorders, depending on the state in which the patients are (Russo et al., 2020).

Although MRI studies to better understand the temporal-spatial abnormalities in catatonia are still rare, a recent study by Sambataro et al. (2021) showed that catatonia patients exhibit reduced network dynamic when compared to non-catatonic patients: they show lower resting-state network changes and longer dwell times in a state characterized by high within-network correlation of the sensorimotor, visual, and default-mode network. Hence, when showing akinesia, mutism and posturing, catatonia patients remain literally static without any dynamic changes and time standing still when they dwell abnormally long in one and the same state on both neural and mental-behavioral levels (Fig. 3). Standstill of both time and space may thus be shared as the "common currency" of both neural and mental activity in akinetic catatonia. However, future studies are warranted that combine neural, behavioral, and first-person experiential data of catatonia. The authors think that psychiatry can benefit from multimodal studies that translate the previously known pathomechanisms of catatonia (GABAergic dysfunction) into structural and functional magnetic resonance imaging (Hirjak et al., 2019a, 2021; Wasserthal et al., 2020). This can be done either by multimodal PET studies (CAVE: due the radiation and ethical reasons a longitudinal examination is not possible) or the recently developed JuSpace toolbox (Dukart et al., 2021) for cross-modal correlations between MRI-based modalities with nuclear imaging derived estimates. The authors also believe that modern neuroimaging in combination with clinical, instrumental and ambulatory assessments, taking into account artificial intelligence approaches, will help to compensate the ethical and subjective/clinical challenges in studies on catatonia. While we fully concur that currently imaging does not provide any biomarker for clinical diagnosis, the introduction of the spatiotemporal approach aims to remedy exactly that: due to the fact the STPP establishes the so far missing intimate connection of neural and symptom levels (through their shared time-space structure), we aim to provide diagnosis-specific spatiotemporal biomarkers for different mental disorders. Due to novel methods of analysis with time-space measure of topography and dynamic (see also Table 1), we can better capture inter-individual differences even on the neural level of imaging; these, in turn, can then be linked to corresponding changes on the phenomenal and behavioral level which again can be analysed with the same measures as the neural level (see for instance Rostami et al., 2022 who demonstrates abnormal power spectrum of thought dynamic in depression). For instance, depression is featured by abnormal slowness in both neural and mental activity (Rostami et al., 2022; Northoff et al., 2018) while schizophrenia exhibit temporal imprecision and irregularity in both brain (Wolff et al., 2022; Northoff et al., 2021a,b,c) and experience (Arantes-Gonçalves et al., 2022) (STEP scale). Although in the early stages due to these and various other results, we propose that STPP holds the promise to fill this gap in the use of brain imaging for clinical diagnostic.

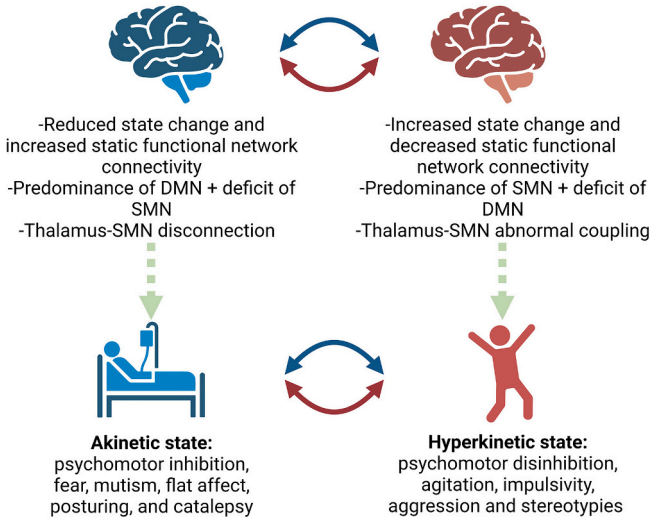

Fig. 3. Akinetic and hyperkinetic catatonic states and their neuronal correlates according to recent neuroimaging evidence.

4. Conclusion

Catatonia is a psychomotor syndrome featured by symptom complexity and trans-diagnostic occurrence. This sheds a paradigmatic light on the kind of psychopathology required to properly explain and account for it. Unlike the current forms of affective and cognitive psychopathology, catatonia may require what we recently introduced as STPP. STPP can be characterized by two background assumptions, (i) an experience- rather than function-based approach; and (ii) an integrated brain-mind model with time-space providing their "common currency". This provides, for the first time, direct and intimate connection of brain and symptoms. That sheds a novel light on both symptom complexity and trans-diagnostic occurrence of catatonia which can be seen as paradigmatic example for the need of a more comprehensive psychopathology. STPP provides such approach by integrating brain, first-person experience and psychopathological symptoms covering motor, sensory, affective and cognitive-behavioral domains in a unified model.

CRediT authorship contribution statement

GN: original idea and design of the study. GN: first draft of the manuscript. GN and DH: discussion of the topic, writing and manuscript revision.

Declaration of competing interest

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

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Fig. 3 was created by BioRender.com.

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