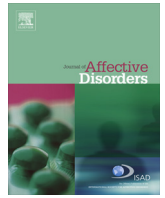




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## Review

## Spatiotemporal Psychopathology II: How does a psychopathology of the brain's resting state look like? Spatiotemporal approach and the history of psychopathology

Georg Northoff<sup>a,b,c,d,e,\*</sup><sup>a</sup> University of Ottawa Institute of Mental Health Research, Ottawa, Canada<sup>b</sup> Center for Cognition and Brain Disorders, Hangzhou Normal University, Hangzhou, China<sup>c</sup> Center for Brain and Consciousness, Taipei Medical University (TMU), Taipei, Taiwan<sup>d</sup> College for Humanities and Medicine, Taipei Medical University (TMU), Taipei, Taiwan<sup>e</sup> ITAB, University of Chieti, Italy

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## ABSTRACT

Psychopathology as the investigation and classification of experience, behavior and symptoms in psychiatric patients is an old discipline that ranges back to the end of the 19th century. Since then different approaches to psychopathology have been suggested. Recent investigations showing abnormalities in the brain on different levels raise the question how the gap between brain and psyche, between neural abnormalities and alteration in experience and behavior can be bridged. Historical approaches like descriptive (Jaspers) and structural (Minkoswki) psychopathology as well as the more current phenomenological psychopathology (Paarnas, Fuchs, Sass, Stanghellini) remain on the side of the psyche giving detailed description of the phenomenal level of experience while leaving open the link to the brain. In contrast, the recently introduced Research Domain Classification (RDoC) aims at explicitly linking brain and psyche by starting from so-called 'neuro-behavioral constructs'. How does Spatiotemporal Psychopathology, as demonstrated in the first paper on depression, stand in relation to these approaches? In a nutshell, Spatiotemporal Psychopathology aims to bridge the gap between brain and psyche. Specifically, as demonstrated in depression in the first paper, the focus is on the spatiotemporal features of the brain's intrinsic activity and how they are transformed into corresponding spatiotemporal features in experience on the phenomenal level and behavioral changes, which can well account for the symptoms in these patients. This second paper focuses on some of the theoretical background assumptions in Spatiotemporal Psychopathology by directly comparing it to descriptive, structural, and phenomenological psychopathology as well as to RDoC.

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\* Correspondence to: Royal Ottawa Healthcare Group, University of Ottawa Institute of Mental Health Research, 1145 Carling Avenue, Room 6467, Ottawa, ON, Canada K1Z 7K4. Tel.: +1 613 722 6521x6801; fax: +1 613 798 2982.

E-mail address: [georg.northoff@theroyal.ca](mailto:georg.northoff@theroyal.ca)

URL: <http://www.georgnorthoff.com>

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## 1. Introduction

Psychiatric disorders have always been around as their descriptions can be traced to ancient Egypt and Greece. However, as clinical (and later scientific) discipline psychiatry was not established before the mid/end of 19th century and beginning of 20th century. At that time there was no brain scanning yet available so that diagnosis had to rely on description and observation. The need to categorize and classify the various psychic symptoms led to the development of a separate discipline, namely psychopathology. Roughly, psychopathology concerns the empirical and theoretical framework in which symptoms, behavior, and experiences in psychiatric patients can be described, categorized, and classified (see Parnas et al., 2008, 2013; Stanghellini et al., 2009; Stanghellini and Ballerini, 2010; Stanghellini and Broome, 2014 for discussing the notion of psychopathology).

What are the criteria according to which psychopathology classifies and categorizes psychiatric symptoms and disorders? Presupposing rough classification, past and current approaches put the focus on either subjective criteria as related to subjective experience by the patients themselves (see Parnas et al., 2008; Stanghellini et al., 2009a,b,c, Stanghellini and Ballerini, 2010) or objective criteria as manifest in the objectively observable behavior of the patients (see for instance DSM V). Especially the latter approach, the focus on objective criteria as in behavior has been linked to neural changes in the brain as for instance in cognitive (Halligan and David, 2001; Frith, 1992) and affective (Panksepp, 2004) approaches to psychopathology. In contrast, the exact relation of phenomenological approaches (Parnas et al., 2008, 2013), that rely more on subjective-experiential criteria, to neural changes in the brain remain somewhat unclear.

The spatiotemporal approach, in contrast, seems to consider all three criteria, neural, phenomenal, and behavioral. As we have seen in the first paper, the spatiotemporal approach has its starting point in the brain itself and, more specifically, in the brain's intrinsic activity and its spatiotemporal structure. This is the neural side of things. At the same time the spatiotemporal approach also considers subjective experience and aims to link it directly to the spatiotemporal structure of the brain's intrinsic activity requiring what I previously described as 'neuro-phenomenal approach' (see below and Northoff (2014c)). We have seen in the first paper that the spatial structure of the brain's intrinsic activity may for instance be accessible in subjective experience of the balance between self and environment-focus. The same holds, analogously, for the temporal structure of the brain's intrinsic activity that could be accessed in subjective experience of time flow. Finally, the spatiotemporal approach also considered objectively observable behavioral symptoms as related to the brain's extrinsic activity and its various functions, cognitive, affective, sensorimotor and social.

Taken together, the spatiotemporal approach conceives three different levels, neural, phenomenal, and behavioral. Most importantly, the spatiotemporal approach claims that the three levels do not just

merely extrinsically stand side-by-side without any intrinsic connection. Instead, the spatiotemporal approach assumes that all three levels, neural, phenomenal, and behavioral are intrinsically linked (and glued together if one wants to say so) by their spatiotemporal features that provide a grid underlying (or inherent in) all three levels. The first paper focused on demonstrating the utility of such spatiotemporal approach for a particular psychiatric disorder, depression, which can also be applied to other disorders like schizophrenia (Northoff, 2015a, b,c,d).

The aim in the present paper consists in describing and outlining the main features of such spatiotemporal approach to psychopathology. This will be done by comparing Spatiotemporal Psychopathology to past and present approaches in current psychopathology, descriptive psychopathology as can be traced to the German psychiatrist Jaspers (1997), structural psychopathology as originated by the French psychiatrist Minkowski (1930/1993, 1927, 1933), and the most recent introduction of the RDoC criteria by Cuthbert and Insel (2013).

## 2. Descriptive psychopathology

### 2.1. Subjective experience and quantification

What is descriptive psychopathology? A recent textbook defines descriptive psychopathology as "the precise description of and categorization of abnormal experiences as recounted by the patient and observed in its behavior" (Oyeboode, 2008, p. 4). This already points out one hallmark of descriptive psychopathology namely the inclusion of both objective behavior and subjective experience in describing and classifying psychiatric symptoms. Historically, descriptive psychopathology can be traced to the German psychiatrist Jaspers (1997) and his seminal work "General Psychopathology" that appeared in German in 1927. He explicitly urged for the need to recount and consider the patients' subjective experiences of his own self, body, time, space, and the world (see below for details) thus going way beyond the merely objective observation of behavioral alterations as manifest in psychiatric symptoms.

Why did Jaspers put such strong emphasis on subjective experience? Phenomenology is a philosophical movement that, in a nutshell, emphasized consciousness as starting point to explore and analyse the world (including traditional philosophical concepts as in metaphysics and epistemology) (Husserl, 1980, 1982, 1989). In order to access consciousness (and subsequently the world), we need to consider our subjective experience that lays bare the structure of consciousness (and subsequently of the world itself). Based on the phenomenological movement that started at the beginning of 20th century, Jaspers argued for the relevance of subjective experience in describing (and understanding) the psychiatric patients' symptoms: we have to describe the patients' subjective experience and hence their consciousness in general including how they subjectively

experience their symptoms in order to get an insight into psychiatric disorders. Jaspers (1997) consequently described the patients' subjective experiences and classified and categorized psychiatric disorders accordingly. Though extending Jaspers in some important aspects (see below), this approach finds its continuation in our days in what is called currently 'phenomenological psychopathology' (Parnas et al., 2008, 2013; Kendler and Parnas, 2008; Fuchs, 2013; Stanghellini, 2009a,b,c, Stanghellini and Ballerini, 2010) or 'phenomenological psychiatry' (Broome et al., 2013).

How can we include the patients' subjective experience in a systematic way? Importantly, the subjective experience of psychiatric patients has to be merely described while withholding any kind of judgement or explanation (as for instance in psychoanalysis as an explanatory (rather than descriptive) psychopathology; see Northoff, 2011a,b). Let us listen to Jaspers himself: "It gives a concrete description of the psychic states that the patients actually experience. It reviews the interrelations of these, delineates them as sharply as possible and creates a suitable terminology. Since we never perceive the psychic experience of the other in any direct fashion, there has to be an act of empathy. Our chief help in all this comes from the patients' own self-descriptions. We confine ourselves solely to the things that are present to the patients' consciousness. Conventional theories, psychological constructions, interpretations and evaluations must be let aside." (Jaspers 1997, pp. 55–56).

The emphasis on merely describing (rather than explaining) patients' subjective experience raises several methodological or epistemological issues like the issue of generalization, the inference from individual cases to groups or categories of patients, and how empathy can be realized and implemented (see Parnas et al., 2008, 2013; Kendler and Parnas, 2008; Stanghellini, 2009a,b,c for discussing these issues). One major issue is the quest for objective quantification and reliability of the subjective experiences as reported by single subjects. In order to obtain features of subjective experience that are reliable, one cannot just rely on single subjects and their merely qualitative reports but needs to investigate the subjective experiences of several subjects in a quantitative way. Though it needs to develop further, recent studies indeed demonstrate semi-quantitative analyses of qualitative interviews for subjective experiences of body (Stanghellini et al., 2014) and time (Stanghellini et al., 2015) as well as quantitative analyses of subjective experience of time flow (with for instance visual analog scales; see Thoennes and Oberfeld, 2015; Bschor et al., 2004; Mahlberg et al., 2008) (see first paper). These studies clearly demonstrate that objective quantification of subjective experience is indeed possible without losing their core features.

Spatiotemporal Psychopathology stands well in the tradition of General Psychopathology in that it aims for including subjective experience. Importantly, it aims to include subjective experience not merely in a qualitative way, i.e., in terms of single case reports, as it is often the case in phenomenological psychopathology. Instead, Spatiotemporal Psychopathology aims for quantification of the features of subjective experience. Why? This is important for obtaining objectivity and reliability which makes possible the inference from the single to case to a general cohort of various cases.

However, the need for quantification of subjective measures goes beyond pointing to a methodological cornerstone of Spatiotemporal Psychopathology. Spatiotemporal Psychopathology claims for direct linkage between subjective-experiential and objective-neuronal measures. Such linkage can be tested for by correlation analysis which is possible only by including quantified measures on both sides. As for instance demonstrated in Fig. 3 in the first paper, I suppose that the subjective experience of time flow is directly related to the degree of the balance between infraslow/slow and fast oscillations in the brain's intrinsic activity: the more the neural balance tilts towards the infraslow/slow oscillations, the slower and decelerated the subjective experience

of time flow. Such correlation holds obviously across different subjects and can be calculated only if we have quantified measures of the subjective experiential features of time flow.

In addition for correlating it with spatiotemporal measures of the brain's intrinsic activity, subjective experience also needs to be quantified in order to correlate it with the objective behavioral measures as related to the psychopathological symptoms. I for instance postulated that the degree of subjective experience of time flow is related to the degree of social withdrawal and psychomotor retardation: the stronger the subjective experience of slowness and deceleration of time flow, the stronger the degree of social withdrawal and psychomotor retardation. Taken together, the quantification of subjective experiential features is a central methodological tool for Spatiotemporal Psychopathology in that it makes possible their direct linkage, i.e., correlation, with both neural and behavioral data.

## 2.2. Form versus content

A central feature of descriptive psychopathology is the strong emphasis on the form or structure of experience rather than exclusively focusing on the contents themselves. Jaspers was more interested in the form than the contents of consciousness; he determined the form of consciousness by the way a given content is presented to consciousness as well as by the content's relationship to the subject of experience (Jaspers, 1997).

How though can we specify the form of experience as distinguished from its contents? Any content in our experiences is set against the ongoing time and the pre-existing space as they ground and base our consciousness. Moreover, contents are set against and related to the subject of experience, the self, its body, and its moods. This pertains to what is often described as the holism of consciousness that is made possible by its particular form including space, time, self, environment, and body within which the content must be integrated in order to be subjectively experienced.

Such holism of consciousness is well reflected in the following quote by Parnas et al. (2013): "Jaspers argues that consciousness is neither static nor atomic in nature; it exists rather as a kind of ever-changing streaming of flow, manifest in not separable fragments but as mutually interdependent or interpenetrating unity: "phenomena do not originate in discrete fashion... There is always a total state of consciousness which makes it possible for individual phenomena to arise.". Recognition of this crucial holism is bound up with phenomenology's distinctive emphasis on the form (structure) rather than the contents of our awareness – i.e., on how things appear or on how they show up against a particular framework involving intentional mode, time or space; or a pervasive mood – and sense of self and reality." (Parnas et al., 2013, p. 271).

Spatiotemporal Psychopathology takes this emphasis on the form rather than the contents very seriously and extends its application from experience to the brain. Specifically, Spatiotemporal Psychopathology conceives the brain and its neural activity in terms of form rather than aiming to decipher the neural correlates of specific contents as related to affective, cognitive, social, or sensorimotor functions. The focus on form entails a shift from the brain's extrinsic or stimulus-induced or task-evoked activity, as related to contents, to the brain's intrinsic activity.

The emphasis on the form of the brain's neural activity is at odds with most current approaches in present-day neuroscience. Current neuroscience focuses mainly on the neural processing of particular contents (as related to the applied stimuli or tasks) and how they are related to spatial and temporal changes in the brain's neural activity, its extrinsic or stimulus-induced/task-evoked activity. This content-based view of the brain, an extrinsic view, is most often presupposed in for instance behavioral, affective, and

cognitive neuroscience as well as in current affective and cognitive neuropsychiatry (Northoff, 2014a).

Spatiotemporal Psychopathology takes the extrinsic view of the brain with its focus on the brain's extrinsic activity, i.e., stimulus-induced or task-evoked activity, only as one half of the brain, namely the upper half of the brain that is visible on the surface. This raises the question for the lower half of the brain. This, as based on recent resting state findings, can be found in the brain's intrinsic activity whose exact features and purpose remain unclear these days (see first paper and Northoff, 2014a). By invoking the old philosophical distinction between form and content, as it can be traced among other philosophers to Kant, and applying it to the brain (Northoff, 2012, 2014a,b), Spatiotemporal Psychopathology extends the application of the notion of form from experience to the brain and its intrinsic activity. The characterization of the brain's intrinsic activity in terms of form (or structure) rather than contents makes possible its characterization by space and time and hence spatiotemporal structure.

Unlike current cognitive and affective forms of psychopathology and neuropsychiatry, Spatiotemporal Psychopathology takes its starting point not from the brain's extrinsic or stimulus-induced/task-evoked activity and their related contents. Instead, it takes the brain's intrinsic activity and its spatiotemporal structure as starting point and conceives the extrinsic activity as mere modulation of the former. This entails a (conceptual) shift from contents to form in characterizing the brain's intrinsic activity. And it is the abnormalities in the form of the brain's intrinsic activity, its spatiotemporal structure, that, so Spatiotemporal Psychopathology, can be directly linked to the subjective experience in psychiatric patients (which in turn can be linked to the contents and their objectively observable behavioral symptoms). Hence, consideration of the brain in terms of its form, i.e., the spatiotemporal structure of its intrinsic activity, is a central hallmark feature of Spatiotemporal Psychopathology without which it would remain impossible.

Since the brain's intrinsic activity can be characterized by a particular and highly individualized spatiotemporal structure, I suppose that any contents (whether cognitive, affective, sensorimotor or social) and their underlying extrinsic activity must first and foremost be integrated within the brain's intrinsic activity and its spatiotemporal structure (or form). The degree and the way the contents and their extrinsic activity are integrated into the brain's intrinsic activity determine how they appear to us in our consciousness and hence how we experience them. This is exemplified by my assumption that I suppose the temporal form (or structure) of the brain's intrinsic activity, the temporal balance between infraslow/slow and fast oscillations to be directly related to the subjective experience of temporal flow.

Spatiotemporal Psychopathology determines form as spatiotemporal (see below or details of the concept spatiotemporal) (and uses it synonymously with the concept of structure). Most important, Spatiotemporal Psychopathology supposes direct correspondence in spatiotemporal form or structure between neural and phenomenal levels, i.e., between brain and experience. For instance the temporal balance between infraslow/slow and fast oscillations in the brain's intrinsic activity is supposed to correspond to the temporal balance between slowness/deceleration and fastness/acceleration of time flow in subjective experience.

### 2.3. Different levels of experience

Spatiotemporal Psychopathology aims to directly link brain and experience and thus their respective neural and phenomenal level. However, only the phenomenal level can be accessed in

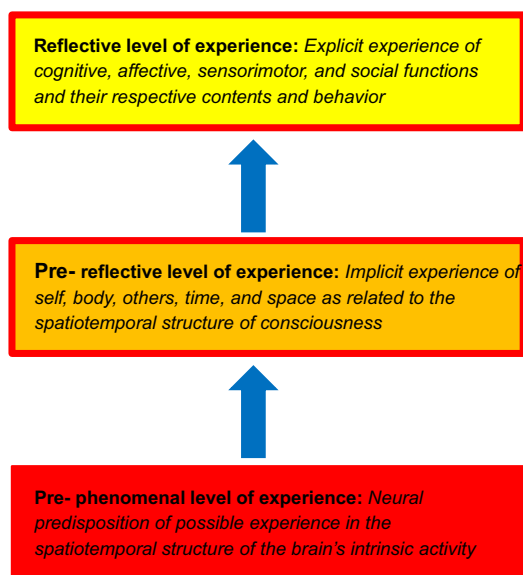
experience while the neural level, our own brain, remains closed to use in experience, i.e., consciousness. We can for instance not experience our infraslow/slow oscillations in consciousness as such, there are no neural features in our experience that can only be characterized by phenomenal features (entailing what I described as 'autoepistemic limitation'; Northoff 2004a,b,c, 2011a,b). Despite the non-accessibility of neural features (as neural) in experience, Spatiotemporal Psychopathology nevertheless claims for direct spatiotemporal correspondence between neural and phenomenal features with the former translating into the latter. How can methodologically access such neuro-phenomenal correspondence in which only one side, the phenomenal side, can be accessed in our subjective experience? For that to be possible Spatiotemporal Psychopathology proposes to go beyond the current concepts of experience from a reflective over a pre-reflective to a pre-phenomenal level (see Northoff, 2014b for more conceptual details).

Jaspers emphasized the reflective level of consciousness that can be directly accessed mostly in form of linguistic or verbal utterances. The pre-reflective dimension targets deeper layers in our experience or consciousness that are not directly accessible to reflection as for instance pre-verbal and pre-linguistic experiences of body, self, time and space entailing what is often described as pre-reflective self-consciousness (Fuchs, 2008, 2013; Parnas et al., 2008, 2013; Zahavi, 2005). Current day phenomenological psychopathology emphasizes especially the pre-reflective level of experience (Parnas et al., 2008, 2013; Stanghellini 2009a,b,c, 2010; Fuchs, 2008, 2013) and does therefore extend Jaspers' descriptive psychopathology from the reflective to the pre-reflective level of experience.

However, Spatiotemporal Psychopathology requires something even more radical. By focusing on the intrinsic activity and its spatiotemporal structure, Spatiotemporal Psychopathology goes not only beyond the reflective level of experience to its pre-reflective levels but rather goes beyond experience or consciousness itself (independent of whether it is accessed reflectively or pre-reflectively) to the brain. Hence Spatiotemporal Psychopathology remains outside the realm of experience, i.e., consciousness, and can therefore no longer be considered phenomenological but spatiotemporal.

At the same time though, Spatiotemporal Psychopathology assumes direct correspondence between neural and phenomenal level, between brain and experience. How is that possible? This raises the question how the intrinsic activity's spatiotemporal structure can correspond to and be transformed into the spatiotemporal structure of subjective experience. If so, the former, the intrinsic activity's spatiotemporal structure must be pre-phenomenal rather than non-phenomenal (Northoff, 2014b). Unlike current-day neuroscience that conceives the brain in a non-phenomenal way, Spatiotemporal Psychopathology focuses on the pre-phenomenal features of the brain and finds them in the spatiotemporal structure of its intrinsic activity: due to its pre-phenomenal nature, the intrinsic activity's neural features, i.e. its spatiotemporal structure predisposes its own transformation into corresponding phenomenal features in subjective experience.

How can we now determine the pre-phenomenal level? While the pre-reflective level is still experienced but not accessible to cognitive reflection, the pre-phenomenal level goes one step or level even deeper since it cannot be experienced as such and is no longer directly accessible in experience, i.e., phenomenal. However, as indicated by the prefix 'pre-', the 'pre-phenomenal' level includes the seeds or predispositions for subsequent (reflective and pre-reflective) phenomenal or subjective experience, the neural predispositions of consciousness as I describe them (Northoff, 2013a,b,c, 2014b) (see Fig. 1).



**Fig. 1.** Different levels of experience in Spatiotemporal Psychopathology. The figure shows the different levels of experience as suggested in Spatiotemporal Psychopathology. Descriptive psychopathology as originating in Jaspers focuses on the reflective level of experience. This has been complemented by the pre-reflective level of experience in current phenomenological psychopathology. Spatiotemporal Psychopathology extends the pre-reflective level to the pre-phenomenal level. By itself the pre-phenomenal level can no longer be experienced as such but, rather than being non-phenomenal, nevertheless predisposes pre-reflective experience and its spatiotemporal structure in consciousness.

How can we illustrate the distinction between reflective phenomenal, pre-reflective phenomenal, and pre-phenomenal levels of experience? Take the example of time and cognition in depression. The depressed patient may describe his cognitions as slow and decelerated which is the way he experiences them in his consciousness in a reflective-phenomenal way. The pre-reflective phenomenal access may now trace back the reflective level to the experience of time itself and its manifestation in self and body with both being pre-reflectively experienced as slow and staggering.

Finally, the pre-phenomenal level may trace the pre-reflective experience of manifestations of the slowed and decelerated time, self and body to the pre-phenomenal level of a disturbed balance between temporal continuity and temporal flow (see the first paper): the disturbed balance between temporal continuity and flow in the brain's intrinsic activity cannot be directly experienced as such but nevertheless predisposes the subjective experience of slowness and deceleration on both pre-reflective and reflective phenomenal levels.

Taken together, Spatiotemporal Psychopathology stands well in the tradition of past and current Descriptive Psychopathology. The emphasis on the importance of subjective experience in addition to mere objective behavioral observation is taken up and extended from reflective and pre-reflective levels to a pre-phenomenal level where neural activity is predisposed to be transformed into phenomenal experience. This goes along with a specification of the concept of form as it is supposed in descriptive psychopathology. The concept of form is determined primarily in spatiotemporal terms (rather than in terms of self, body, and others) on the level of pre-reflective experience which makes possible to extend it to the neural level (where only time and space can be found as such but no self, body or other). At the neural level the brain's intrinsic activity (rather than its extrinsic activity) is determined by a particular spatiotemporal structure (or form) which, as I assume, predisposes its own direct translation (or transformation) into corresponding spatiotemporal features, i.e., form, on pre-

reflective and reflective levels of subjective experience, i.e., consciousness.

### 3. Structural psychopathology

#### 3.1. Meaning, coherence and unity

How can we make sense of the different objectively observable symptoms and the related subjective experiences? While Jaspers' descriptive psychopathology and current day successors in phenomenological psychopathology refrain from explanatory frameworks, structural psychopathology raises the question for the overall meaning and the unity underlying the various symptoms and experiences. One most prominent early author in this direction was the French Psychiatrist E. Minkowski in his seminal works about depression (Minkowski, 1930/1993) and schizophrenia (Minkowski, 1927, p. 33; Urfer, 2001).

What exactly though does the concept of meaning refer to? Stanghellini and Ballerini (2010), determines the search for meaning in the following way: "Structural psychopathology goes beyond the description of isolated symptoms and the use of some of those symptoms to establish a diagnosis. It aims to understand to meaning of a given world of experiences and actions grasping the underlying characteristic modification that keeps the symptoms meaningfully interconnected." (Stanghellini and Ballerini, 2010, p. 320).

How though can we determine such meaningful coherence and unity in further detail? This is the moment where the concept of form or structure comes in again. Imagine a melody. The composer composed the melody in such way that no single tone in the melody can be exchanged and replaced by another one without changing the melody as a whole. The single tone is interconnected with and inter-dependent on the other single tones and vice versa. The melody can therefore not be conceived as mere collection or addition of single tones. Instead, the melody can be characterized by a particular form or structure which makes its single elements, the tones as the contents, interconnected and inter-dependent.

The same now, analogously, holds in the case of psychiatric symptoms and experiences. The single symptoms and experiences including their respective contents are inter-connected and inter-dependent on the basis of an underlying form or structure. Most importantly, Spatiotemporal Psychopathology claims that the brain itself, its intrinsic activity, can be determined and characterized by a form or structure. This means that a single neural activity in for instance one particular cell, region or network is inter-dependent and inter-connected with the absent or present neural activities in other cells, regions, or networks with the latter in part determining and constituting the former. This is often described as context-dependence of neural activity in current day neuroscience (see Northoff and Mushiak, 2015).

Spatiotemporal Psychopathology now characterizes such context-dependence of neural activity in terms of form or structure tracing it back to the brain's intrinsic activity and its spatiotemporal structure. This entails that the spatiotemporal structure gives the brain's intrinsic activity a meaningful whole, coherence and unity: the single neural activity in a particular cell, region, or network can only be understood in the context of the neural activity of the other cells, regions, and networks. In short, the brain's intrinsic activity and its spatiotemporal structure can be characterized by a meaningful whole, coherence, and unity.

Why does Spatiotemporal Psychopathology so much emphasize the meaningful wholeness, coherence and unity of the brain's intrinsic activity and its spatiotemporal structure? The main claim is that neural and phenomenal activity, brain and experience, are supposed to correspond with regard to their spatiotemporal structure. If so one would assume that the meaningful whole,

the coherence and the unity of the intrinsic activity's spatiotemporal structure is transferred to the phenomenal level and the subjective experience such that the latter can also be characterized by a meaningful whole, coherence and unity. This is exactly what Spatiotemporal Psychopathology assumes which links it to structural psychopathology which aims to determine the meaningful whole, coherence, and unity in experience.

How can we provide an example or such meaningful whole, coherence and unity? Subjective experience in depression can be characterized by spatial dysbalance between self- and environment-focus with increased self- and decreased environment-focus (see first paper). Based on the neural data, I now postulated that the phenomenal dysbalance between self- and environment-focus and their respective internal and external mental contents may be related to the spatial dysbalance between DMN and CEN in the brain's intrinsic activity. In the same way the meaningful whole, coherence, or unity of experience is spatially shifted abnormally towards the self at the expense of the environment, the meaningful whole, coherence and unity of the intrinsic activity is correspondingly shifted in its spatial structure as manifest in the spatial dysbalance between DMN and CEN.

### 3.2. Time and space

What though does this meaningful whole, unity, and coherence, i.e., its form or structure consist in? Minkowski assumes that space and time first and foremost constitute the form of structure that links different symptoms and experiences into one meaningful whole, coherence and unity. Importantly though space and time are here not conceived in a merely objective way as we measure and observe them from the outside as in science presupposing what can be described as "objective time". Instead, time and space are conceived here in a subjective way, as they are experienced in consciousness, which is often denoted by the concepts of "lived time and space" (see Minkowski, 1933).

What is the difference between objective and lived time? Objective time concerns the way we observe time as for instance in terms of single discrete points in time and space that seem to remain segregated and independent of each other. There is no inter-dependence and -connectedness between the different single discrete points in time and space and hence no meaningful whole, coherence and unity. Lived time, in contrast, refers to the way we subjectively experience time that is rather continuous and like a flow with linkages and inter-dependences between different points in time (see for instance Northoff, 2014b,d). Time in this sense, lived time, is consequently shows a meaningful whole, unity, and coherence.

Due to its objective nature, objective time is often considered to be real while lived time remains only subjective and therefore not real. However, taken the stance of subjective experience or consciousness, lived time is as real (in experience) as objective time (seems to be real in the world). To mark this difference, one may want to characterize lived time as virtual since it cannot be observed as directly as objective time while at the same time nevertheless being real (for at least subjective experience or consciousness).

Spatiotemporal Psychopathology aligns itself with structural psychopathology in that it conceives space and time as the basic constituents of the meaningful whole, coherence, or unity underlying the different psychiatric symptoms and experiences. Space and time in a virtual sense constitute the form or structure of subjective experience, i.e., consciousness as manifest in lived space and time which surfaces in the temporal and spatial structure underlying subsequent contents as related to cognitive, affective, social, and sensorimotor functions. The meaningful whole, unity and coherence of psychiatric symptoms is consequently traced to

the temporal and spatial structure into which cognitive, affective, social, and sensorimotor functions and their respective contents are integrated and organized.

One of the central tenets of Spatiotemporal Psychopathology is to specify the form or structure underlying lived time and space. An example of such meaningful whole, coherence and unity in time and space is for instance the temporal balance between temporal continuity, the sameness, and temporal flow, the change. And particular event, i.e., stimulus or task, must be integrated into the ongoing temporal balance between temporal continuity and flow. This, as Spatiotemporal Psychopathology claims, holds on the neural level with regard to the integration of extrinsic activity into the spatiotemporal structure of intrinsic activity.

The same now holds on the phenomenal level where specific contents as related to cognitive, affective, sensorimotor and social functions need to be integrated into the ongoing spatiotemporal structure of experience, i.e., consciousness. Having stated the role of the meaningful whole, coherence and unity in analogous ways on both neural and phenomenal level, it is now easy to see how the former, the neural level and its spatiotemporal structure with its meaningful whole, coherence and unity translates and transforms into the meaningful whole, coherence and unity of experience on the phenomena level.

### 3.3. "Trouble generateur"

Minkowski (1930/1993) spoke of a generative disorder, the "trouble generateur" in psychiatric disorders that refers to a deeper underlying symptom, "a kernel underlying the manifest symptoms in all their variety that keeps them meaningfully interconnected or united" (Urfer, 2001, p. 281). What though exactly is the trouble generator? At first glance and taken an objective scientific stance, one would assume the 'trouble generateur' to be the cause like a biochemical or genetic anomaly. That though is not the case. Minkowski rather associates the 'trouble generateur' with the way the person or subject is situated within the world which in turn determines how it subjectively experiences that very same world including its time and space in her own consciousness. The 'trouble generateur' is an "expression of a profound and characteristic modification of the human personality in its entirety" (Minkowski, 1927, p. 12) and reflects "the way in which personality is situated, in normal as well as in pathological terms, in relation to lived time and lived space." (Minkowski 1930/1993, p. 2).

Minkowski associates the 'trouble generateur' in psychiatric disorders with the personality, subject or self which by itself may be altered including how it relates to time and space. This entails that psychiatric disorders can be conceived as disorders of the self which, given the different kinds of changes in the self in basically all psychiatric disorders, carries some truth (see also Northoff, 2014c). This also the reason why current-day successors like Stanghellini and Ballerini (2010), considers not only time and space as reference for subjective experience but also self, body, and others (see Stanghellini et al., 2014, 2015).

Spatiotemporal Psychopathology shares with structural psychopathology the strong focus on time and space, i.e. lived time and space. However, rather than linking space and time to the self and body as subjectively experienced, Spatiotemporal Psychopathology traces lived space and time back to the brain's intrinsic activity and its virtual spatiotemporal structure. Besides the extension from consciousness and the phenomenal level to the brain and its pre-phenomenal level, this also entails more or less reversal in the relationship between time/space and self/body. When assuming self and body as 'trouble generateur', structural psychopathology (and its current successors) seems to presuppose self and body as primary while lived time and space are secondary as being tied and linked to the former.

Spatiotemporal Psychopathology, in contrast, reverses their relationship: instead of lived time and space being based on self and body, time and space (in their virtual manifestation in the brain's intrinsic activity) are conceived as primary upon and within which self, body and others are constructed (see for instance Northoff, 2014b). Self and body as subjectively experienced (and thus in their lived rather than objective versions) on the phenomenal level can then be regarded as more detailed spatiotemporal specifications and elaborations of the basic spatiotemporal structure of the brain's intrinsic activity.

Why does Spatiotemporal Psychopathology suggest such reversal in the relationship between time/space and self/body? First and foremost there is indeed empirical evidence for possible subjective experience of time and space, i.e., inner time and space consciousness, without the experience of the own self or body. This is, for instance the case in schizophrenic patients who still experience time and space while no longer experiencing their own self. That suggests that the experience of time and space can dissociate from the experience of self and body: even if the latter disintegrates, the former nevertheless remain intact (though in an altered, i.e., fragmented way). Secondly, time and space in their virtual gestalt can be linked directly to the brain and its different spatiotemporal forms of neural activity while there is no such direct neuro-phenomenal link between brain and self/body.

In sum, Spatiotemporal Psychopathology considers alterations in virtual time and space of the brain's intrinsic activity as 'trouble generateur' rather than 'locating' the latter in the self, subject, body, or self-world relation. Taken in this sense Spatiotemporal Psychopathology extends structural psychopathology from the reflective/pre-reflective phenomenal level of consciousness and the subject of consciousness to the pre-phenomenal level of the brain's intrinsic activity.

Importantly though, just as Minkowski's concept of 'trouble generateur', the alterations in virtual time and space of the brain's intrinsic activity cannot be considered an ethiological concept that refers to underlying causes either. Instead, the alterations in virtual time and space of the brain's intrinsic activity in particular and spatiotemporal psychopathology in general aim to reveal pathogenetic concepts that, revolving around space and time and their respective forms, reveal direct neuro-phenomenally corresponding spatiotemporal features. These spatiotemporal concepts aim contributing to better understand the genesis, the pathogenetic processes that are implicated in transforming the brain's abnormal intrinsic activity into abnormalities in both subjective experience and objectively observable behavior.

### 3.4. Different levels of symptoms

The concept of 'trouble generateur' entails a deeper level of abnormalities that underlies the psychiatric symptoms as they can be observed on the surface, the behavior. In addition to the surface level of the objectively observable behavior, structural psychopathology assumes a deeper level. The assumption of such deeper level underlying the surface symptoms has resonated much in the history of psychiatry and has resurfaced several times in different concepts. These include Bleuler's 'primary symptoms, Jaspers' 'psychic processes (Jaspers, 1997), and, more recently, Huber's "basic symptoms" in schizophrenia (Huber, 2002; Ebisch et al., 2013).

Most recently, Kendler distinguished between 'surface symptoms' and 'deeper symptoms' when raising the following question: "to what extent should we continue our focus in our nosology on "surface" symptoms and signs picked or their reliability rather than trying to develop potentially more informative or "deeper" symptoms that might emerge from careful phenomenological analysis?" (Kendler, 2008, pp. 7–8) (see Fig. 2a).

Spatiotemporal Psychopathology aligns well with the distinction between "deeper" and "surface" symptoms linking both with

distinct forms of neural activity. Surface symptoms are supposed to be related different functions, cognitive, affective, social, and sensorimotor which neurally can be accounted for by stimulus-induced or task-evoked activity, i.e., extrinsic activity. The "deeper" symptoms in contrast concern concepts like increased self-focus, decreased environment-focus, increased past-focus, and decreased future-focus. I assume that they are related to the brain's intrinsic activity, and more specifically the resting state's spatiotemporal structure. Accordingly, "deeper" symptoms are supposed to be primarily spatiotemporal symptoms which, due to the fact that extrinsic activity is based on intrinsic activity, is carried forth to the various functions and their respective "surface" symptoms.

In addition to surface and deeper levels, Spatiotemporal Psychopathology assumes a yet even deeper level, the deepest level, as I say. The deepest level consists in the brain's intrinsic activity and its spatiotemporal structure which is assumed to be manifest in both deeper and surface levels as in subjective experience and objectively observable behavior. Though tentatively at this point in time, Spatiotemporal Psychopathology assumes that the resting state's spatiotemporal organization or form accounts for what Minkowski (and others) were searching for, "a kernel underlying the manifest symptoms in all their variety that keeps them meaningfully interconnected or united", while at the same time extending it to the brain (see Fig. 2b and c).

How can we characterize the three levels, surface, deeper, deepest, in further detail? The surface level can be characterized by the different functions, cognitive, affective, sensorimotor, and social, and their respective contents. This is manifest in the objectively observable abnormalities in behavior as in various psychiatric symptoms like hallucinations, catatonia, delusions, psychomotor retardation and agitation, thought disorder, sadness, guilt, joy, happiness, social withdrawal, etc. Hence, neurally the surface symptoms are most likely related to abnormalities in extrinsic activity reflecting their neural correlates (i.e., the sufficient neural conditions) (Northoff, 2013a,b,c, 2014b).

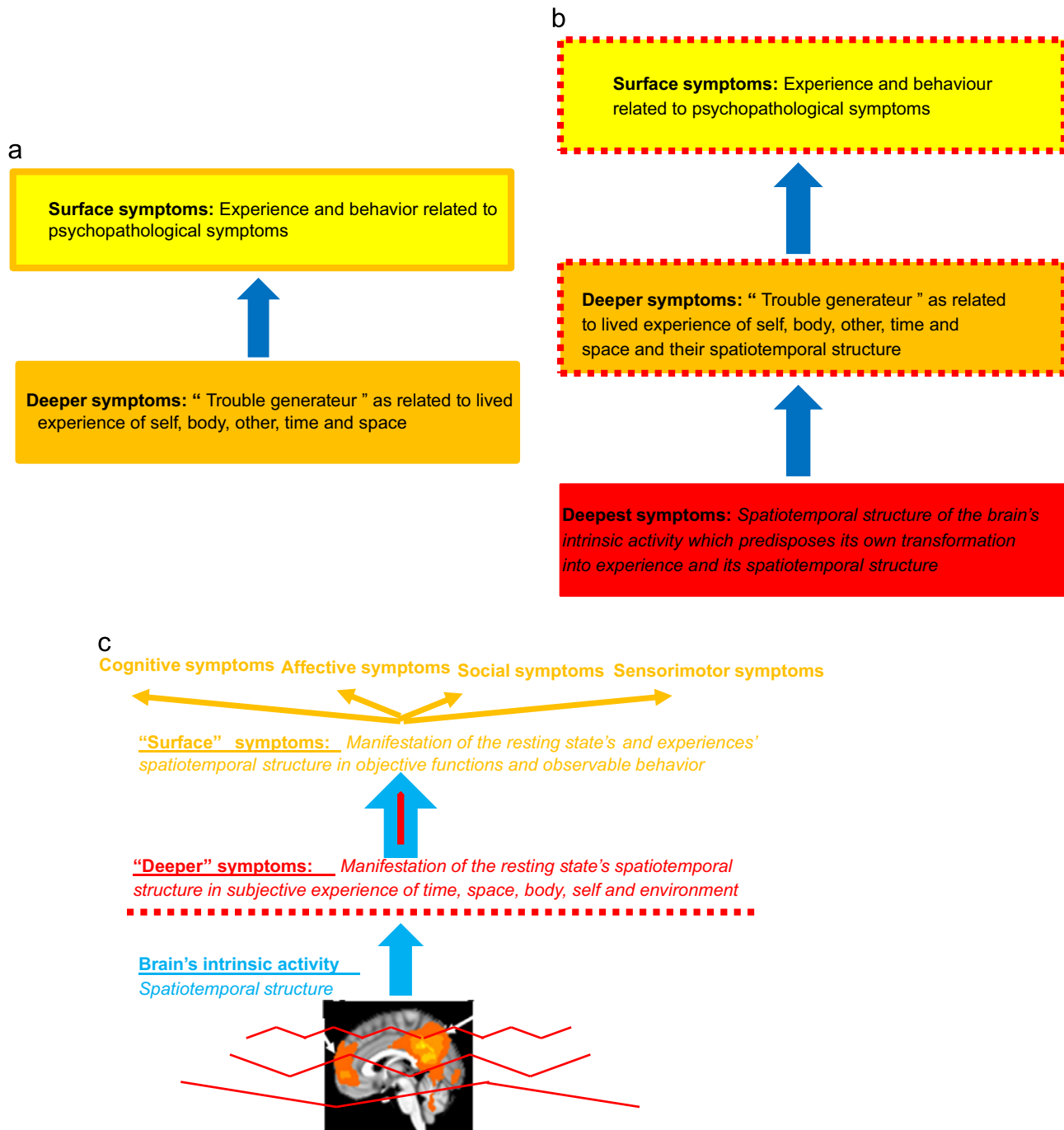
The deeper level concerns the subjective experience of self, time, space, body, and others. This is reflected in the abnormalities in inner time consciousness in both schizophrenia and depression, ego-disturbances in schizophrenia, abnormal shift between self- and environment-focus in mania and depression, and the abnormal balance between past- and future focus in bipolar disorder. Phenomenally, one may associate the deeper level with the pre-reflective phenomenal level of experience while neurally the deeper level may correspond (more or less) to the spatiotemporal structure of the brain's intrinsic activity.

Finally, the deepest level extends beyond the phenomenal realm of experience and consciousness to the pre-phenomenal realm of the brain's intrinsic activity and how it relates to the world. This is the level that can no longer be directly experienced as such neither on the reflective nor the pre-reflective level of experience. This though does not mean that the deepest level does not bear any relationship to experience. Spatiotemporal Psychopathology assumes that the deepest level predisposes experience, it provides the necessary conditions of possible experience and must therefore be conceived as pre-phenomenal (rather than non-phenomenal) and refers to the neural predispositions (rather than neural correlates) of abnormal psychiatric experiences and behavior.

## 4. Operational psychopathology

### 4.1. DSM and the neglect of phenomenology

Building on the early European psychopathologists like Kraepelin and the observation of discrepancies in diagnostic classification in UK and USA, a unitary diagnostic system, DSM, was developed in



**Fig. 2.** Different levels of symptoms in structural psychopathology (a) and Spatiotemporal Psychopathology (b, c). The figure shows the different levels of psychopathological symptoms as suggested in Structural (a) and Spatiotemporal (b, c) Psychopathology. Structural psychopathology assumes surface and deeper symptoms with the latter being related to what they call 'trouble generateur'. Spatiotemporal Psychopathology, in contrast, extends the two-level account of psychopathological symptoms to a three-level account including surface, deeper and deepest symptoms. The deepest psychopathological symptoms are related to the spatiotemporal structure of the brain's intrinsic activity and how that in turn stands in relation to the social, cultural, biographical and ecological context of the respective subject (see in text). Hence, the deepest psychopathological symptoms may biographical and thus hermeneutic psychopathological symptoms as distinguished from the behavioral–cognitive surface symptoms and deeper phenomenal symptoms.

USA (and complemented by ICD in Europe). The emphasis was here on reliability of diagnostic categories that is, the degree to which different psychiatrists (in eventually different countries) come to the same diagnosis. In contrast, the validity of diagnostic categories, the degree to which the criteria do indeed mirror the phenomenon the question, is rather problematic and considered to be a major problem in DSM (see Andreasen, 2007). Moreover, as Andreasen (2007) points out dramatically in the title of her paper, the

introduction of DSM has led to the neglect of subjective experience and phenomenology altogether at the expense of objective observable behavioral and reliable symptoms.

The neglect of subjective experience and phenomenology is one point of criticism on DSM in particular and current operational diagnostic systems in general. Spatiotemporal Psychopathological shares that criticism since it regards subjective experience as essential methodological tool to access deeper symptoms like



increased self-focus and decreased environment-focus in depression (see first paper) or alterations in inner time consciousness in both depression and schizophrenia (see Northoff, 2014). The deeper symptoms themselves can be accessed best directly in subjective experience while they are indirectly manifest in the surface symptoms, e.g., the various functions and their respective contents.

Most importantly, subjective experience and phenomenology also provide an access door to the deepest symptoms, the pre-phenomenal changes in the brain's intrinsic activity and its spatiotemporal structure. Specifically, subjective experience of time and space can guide neuroscientific investigation how the changes in the brain's temporal structure like its temporal balance between infraslow/slow and fast oscillations must look like (in order to account for corresponding spatiotemporal abnormalities in subjective experience of time, i.e., inner time consciousness). This indicates a double methodological role of subjective experience. First, subjective experience is a methodological tool that provides direct access to pre-reflective layers of experience like self, body, time, and space that by themselves are not directly manifest in objective behavioral symptoms. Secondly, subjective experience and its spatiotemporal structure can serve as methodological template that can serve to orient and guide neuroscientific investigation as recently suggested by Stoyanov et al. (2012a, b) and developed in the gestalt of a nenurophenomenal approach (Northoff, 2014b,c,d).

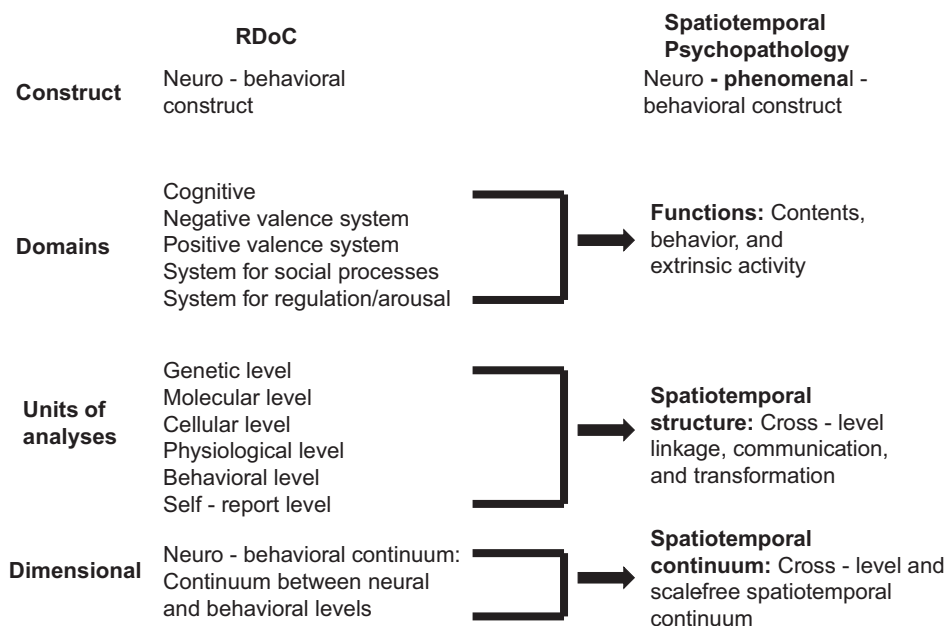
In sum, one can speak of a double neglect of subjective experience and phenomenology in current operational psychopathology like DSM. This concerns the access of subjective experience to deeper symptoms like self, body, time, and space, as well as the use of its spatiotemporal features for exploring the deepest level, the pre-phenomenal level of the brain and the spatiotemporal structure of its intrinsic activity. Accordingly, to neglect subjective experience as methodological tool is to preclude access to self, body, and time/space as well as to disregard a potentially important source of information where and how to look in the brain.

#### 4.2. RDoC – neurobehavioral versus neuro-phenomenal-behavioral constructs

In addition to disregarding subjective experience and phenomenology, DSM has been criticized for neglecting the brain itself and its different levels ranging from genes over molecules and biochemical to regions and circuits. This neglect has led to the development of a novel classification, the Research Domain Criteria (RDoC) (Cuthbert and Insel, 2013 for an overview). RDoC can be characterized by three different main features namely constructs, domains, and unit of analyses which shall be discussed in the following (see Fig. 3).

Instead of categories of symptoms, as in DSM, RDoC aims to start with a particular construct, a neuro-behavioral construct. This already points out the duality of brain and behavior, of neural and behavioral abnormalities. A behavioral anomaly that shows no clear correspondence to a specific neural alteration as for instance a particular neural network cannot be considered a proper starting point in RDoC. Neither can a purely neuronal abnormality without any corresponding behavioral change serve as starting point. The focus is on the duality and integration between neural and behavioral levels: "Fifth, and critically important, the system is intended to provide a structure that places equal weight on behavioral functions and upon neural circuits and their constituent elements – that is, to be an integrative model rather than one based primarily on either behavior or neuroscience." (Cuthbert and Insel, 2013, p. 6).

The neurobehavioral construct must fulfill two criteria. First there must be empirical and quantified evidence for the behavioral construct itself, an abnormality for which mere observation of single cases is not sufficient. Secondly, there must be equally strong evidence that the behavioral construct in question maps onto a biological system like a particular neural circuit or function. One example of such neurobehavioral construct, as they say, are hallucinations which as behaviorally well validated construct can be mapped onto a neural circuit encompassing auditory and prefrontal cortex (see Ford et al., 2014).



**Fig. 3.** Comparison between RDoC and Spatiotemporal Psychopathology. The figure shows the comparison between RDoC and Spatiotemporal Psychopathology. The comparison focuses on the three central features of RDoC, construct, domains and unit of analyses. Additionally I included the feature of dimension. There is strong overlap or similarity between RDoC and Spatiotemporal Psychopathology with the difference that the latter starts with neuro-phenomenal-behavioral constructs, associates the different domains with different functions and extrinsic activity, and links the different unit of analyses by the spatiotemporal dimension which entails a cross-level scale-free spatiotemporal continuum.

How does Spatiotemporal Psychopathology stand in relation to neuro-behavioral constructs as starting point? Spatiotemporal Psychopathology agrees with the inclusion of both behavior and brain. However, based on descriptive psychopathology, Spatiotemporal Psychopathology extends the duality of behavior and brain to a triadic structure that includes experience, i.e. the phenomenal level. Behavior reflects the surface level while the brain mirrors the deepest level. That though leaves open their link and, more specifically, how neural activity is and can be transformed into behavioral activity. This, as Spatiotemporal Psychopathology claims, requires considering experience as intermediate between brain and behavior analogous to the way that the deeper level mediates between deepest and surface levels. Rather restricting itself to brain and behavior as RDoC does, Spatiotemporal Psychopathology includes all three, brain, experience, and behavior. The concept of neuro-behavioral constructs may consequently be extended to what I describe as neuro-phenomenal-behavioral construct.

One such neuro-phenomenal-behavioral construct consists for instance in the triadic link between ruminations (surface level of behavior), increased self-focus (deeper level of experience), and spatiotemporal structure of the brain's intrinsic activity with the spatial dysbalance between DMN and CEN in depression (see the first paper). Analogously, there is a triadic link between psychomotor retardation (surface level of behavior), slowing and deceleration of subjective time flow, and temporal dysbalance between infraslow/slow and fast oscillations (see the first paper). Such neuro-phenomenal-behavioral constructs can also be observed in other disorders like schizophrenia where one can find in the triadic linkage between thought blockades (surface level of behavior), temporal fragmentation in inner time consciousness (deeper level), and decreased or disrupted cross-frequency phase-phase/power coupling (deepest level) in schizophrenia (see Northhoff, 2015a,b,c,d, 2014d).

Together, these examples make it clear that Spatiotemporal Psychopathology considers subjective experience as integral part leading to neuro-phenomenal-behavioral constructs. If in contrast, one only presuppose neuro-behavioral constructs, as RDoC does, one neglects the phenomenal level of subjective experience without which one will remain unable to understand how neural abnormalities (deepest level) transform into behavioral symptoms (surface level).

#### 4.3. RDoC – domains and behavior

In addition to constructs, RDoC assumes five different domains according to which the respective neuro-behavioral construct needs to be classified. These domains include cognitive systems, negative valence system, positive valence system, system for social processes, and system for arousal/regulatory function.

Let us give examples. Hallucinations for instance show often voices with negative content pertaining to the negative valence system. At the same time, many hallucinations are verbal and based on past experiences thus implicating memory and language and other cognitive systems. The own internal thoughts can be misperceived as external voices entailing the system for social processes and one can also hear several voices that converse with each other (see Ford et al., 2014 for an overview in Table 1).

The same can also be done for ruminations in depression. Ruminations concern thoughts and implicate cognitive functions like attention, executive function, and reasoning. They are often coupled to negative emotions like guilt and shame thus recruiting negative valence system. Mania, in contrast, can be characterized by positive thoughts thus recruiting the positive valence system. Coming back to depression, ruminations and the increased self-focus go along with decreased environment-focus that is

behaviorally manifest in social withdrawal and psychomotor retardation. This implicates the system for social processes. Finally, depressed patients with ruminations often show extremely high degrees of arousal and upregulation of their vegetative functions mirroring the involvement of the system for arousal/regulatory functions.

How do the five domains in RDoC stand in relation to Spatiotemporal Psychopathology? The five domains essentially reflect what I refer to as the various functions of the brain, cognitive, affective, vegetative, social, and sensorimotor including their respective contents. The consideration of one and the same behavioral construct in different domains or functions is an interesting move in RDoC. It more or less parallels (though is not identical) the analogous assumption in Spatiotemporal Psychopathology that one symptom on the deeper level like the increased self-focus is manifest in the different functions on the surface level and respective behavioral alterations.

However, there is an important difference to consider. RDoC assumes that a behavioral construct is manifest in different functions while Spatiotemporal Psychopathology presumes a neuro-phenomenal construct (like the increased self-focus) to be manifest on the surface level of the different functions. Behavior is considered a starting point in RDoC and then specified in terms of the different functions and their neural correlates as the former's manifestation. Spatiotemporal Psychopathology, in contrast, considers a neuro-phenomenal (rather than a behavioral or neuro-behavioral) construct as starting point and proceeds from there to the various functions which are then manifest in behavior. Hence, rather than being a starting point as in RDoC, behavior is here the end point.

#### 4.4. RDoC – units of analyses

Complementing constructs and domains, RDoC suggests different units of analyses. The units of analyses range from genes and molecules over cells and circuits to physiology, behavior, and self-report. One and the same neuro-behavioral construct and its manifestation in the different domains can be investigated and analysed on different levels, the unit of analyses.

How can we exemplify the units of analyses? Let us give the example of the increased self-focus in depression for which we recently developed a cross-level model (Northhoff and Sibille, 2014a,b). Let me summarize the main points of such cross-level model for the increased self-focus. On the genetic level, genes encoding for a specific type of GABA-ergic interneurons, Somatostatin (SST)- and Parvalbumin (PV) GABA-ergic interneurons seem to be deficient in PACC-VMPFC while in DLPFC only SST-related genes are deficient. This leads to alterations in GABA-A receptors (and potentially in GABA-B receptors too) which remain to be explored. Postmortem studies observed deficits in SST interneurons and PV interneurons in PACC-VMPFC in depression while in DLPFC only SST (but not PV) interneurons are decreased.

On the level of regions and circuits this may lead to resting state hyperactivity in PACC-VMPFC and concomitant hypoactivity in DLPFC which on the network level translates into hyperactivity in DMN and hypoactivity in CEN. Behaviorally, as discussed in the first paper, this dysbalance between DMN and CEN is manifest in ruminations as related to an increased self-focus and social withdrawal mirroring a decreased environment-focus. Finally, on the level of self-report the increased self-focus and ruminations can be tested and investigated with subjective scales like the various Beck scales, ruminations scales, and self-scales like the self-consciousness scale (see Table 1 and 2 in Ford et al. (2014) for auditory perception construct and acute threat construct on different levels of analyses).

How are the different units of analyses related to Spatiotemporal Psychopathology? Spatiotemporal Psychopathology fully concurs with RDoC in investigating one and the same phenomenon on different levels or units of analyses. There is thus inclusion and smooth transition from genes over molecules and cells, regions and networks to subjective experience and ultimately behavior. This is well shared between Spatiotemporal Psychopathology and RDoC and distinguishes the former from both DSM and the historical forms of psychopathology (see above) that do not include such multi- and cross-level approach.

However, as indicated in its name, Spatiotemporal Psychopathology emphasizes the spatiotemporal dimension which distinguishes it from RDoC. Why does Spatiotemporal Psychopathology focus so much on space and time and is even described as spatiotemporal? Let us start again with RDoC and see what it leaves out. RDoC emphasizes the different domains and the different units of analyses. What remains unclear though is how the different units of analyses as well as the different domains among each other are related to each other. Recurring to structural psychopathology (in though a slightly different way), Spatiotemporal Psychopathology raises the following question: what is the meaningful whole that provides unity and coherence between the different units of analyses as well as between the different domains? Hence the question that structural psychopathology raised within the phenomenal context of lived experience (see above) is now posed within the broader context of the different levels ranging from genes over the brain to experience and behavior.

Spatiotemporal Psychopathology argues that space and time provide the underlying form or structure that allows for the different units of analyses as well as the different domains to be one meaningful whole, coherent and unity. Space and time are assumed to make possible direct interaction between the different units of analyses such that changes on one level can directly translate into corresponding spatiotemporal changes in the respective other ones; this is possible even if the different levels operate on different spatiotemporal scales thus presupposing scale-free spatiotemporal interaction between the different levels.

Analogously to the different units of analyses, changes in the different domains, i.e., functions, may correspond to each other since they are structured by one and the same underlying form, space and time as they can be traced back to the intrinsic activity's spatiotemporal structure. I demonstrated how changes in the temporal structure of the brain's intrinsic activity in specific regions and networks translate into corresponding temporal changes on the level of subjective experience of self and environment in depression. That in turn is supposed to surface in the various domains or functions and their respectively associated behavior. Future studies may want to investigate whether and if so how the spatiotemporal structure of genes translates into the spatiotemporal structure of molecules, cells and regions. That though is a scenario for the future.

#### 4.5. RDoC – dimensional and ecological approach

One of the main hallmark features of RDoC is the presupposition of a dimensional approach. Psychiatric symptoms are conceived as extremes on a continuum ranging from the normal to the abnormal. For instance, the dysbalance between increased self-focus and decreased environment-focus is an extreme on a continuum of different possible constellations between both foci. Healthy subjects range in the middle of that continuum with balance between self- and environment-focus. Manic patients, in contrast, can be located at the extreme end opposite to depression; they show the opposite balance with increased environment-focus and decreased self-focus.

Such dimensional approach is not novel and unique to RDoC. Previous alternative approaches like cognitive (Halligan and David,

2001, Frith, 1992) and affective (Panksepp 2004) psychopathology also presuppose such dimensional approach. Spatiotemporal Psychopathology fully endorses such dimensional approach and stands therefore in line with these approaches (though differing in other aspects). Hence, just like RDoC and these cognitive and affective approaches, Spatiotemporal Psychopathology will aim to investigate heterogeneous samples of subjects that best possibly cover the full spectrum of the spatiotemporal continuum curve.

Most importantly, Spatiotemporal Psychopathology relates space and time and their respective balances like the one between temporal continuity and temporal flow (see first paper) to a continuum on the neural level like the one between infraslow/slow and fast oscillations. This entails a focus on various forms of spatiotemporal continua and how they are related to the continua of spatial and temporal measures of the brain's intrinsic activity. Most interestingly, the point on such spatiotemporal continuum curve where a "normal" spatiotemporal feature (that does not lead to any psychopathological symptoms with abnormalities in behavior and experience) transforms into an "abnormal" one (with behavioral and experiential abnormalities and psychopathological symptoms) is of high interest. This point, the border between the "normal" and the "pathological" may be signified by "points of non-linearity beyond which overt psychopathology is more likely or more severe, and thus contribute to an understanding of the precise factors that demarcate the continuity from normal range functioning to various degrees of impairment." (Ford et al., 2014, p. 301).

One recent criticism on RDoC is that it neglects the social dimension of behavior and reduces it to mere neural constructs (Walter, 2013). The brain including its intrinsic activity cannot be conceived in merely neural terms but is always already embedded and situated within an ecological or environmental context. In addition to such embeddedness there is embodiment meaning that the brain operates in close conjunction with the body and is embodied. Moreover, subjective experience and mental features like self or free will are extended in that they operate across the boundaries between body and world and extend into the respective ecological environment. Finally, there is active interaction between brain/body and environment on the basis of action entailing enactment.

Walter (2013) now argues that RDoC neglects the 4 E's (embodiment, embeddedness, enactment, extension) of the mind as they have been discussed in philosophy of mind. Applied to Spatiotemporal Psychopathology, this means that we need to conceive the brain's intrinsic activity and its spatiotemporal structure not only in merely neural terms but also in social, cultural and ecological contexts entailing context-dependence (see above as well as Northoff and Mushiaké, 2015).

There is indeed strong support for that the intrinsic activity is strongly impacted by early life events and its respective social, cultural, and ecological environment (Han and Northoff, 2008; Han et al., 2013; Northoff, 2014b). The brain's intrinsic activity and its spatiotemporal structure can therefore not be considered in purely neural terms but in neuro-social, neuro-cultural and neuro-ecological terms. Subsuming all three, Spatiotemporal Psychopathology presupposes an inherently social, cultural, and ecological context when using the concepts of brain, experience, and behavior. The consideration of such context-dependence on all three levels, neural, phenomenal, and behavioral, opens the door for considering neurodevelopmental disorders like schizophrenia as well as for investigating neuro-social, neuro-cultural, and neuro-ecological differences in psychiatric symptoms.

## 5. Conclusion

Following the demonstration of how the brain's intrinsic activity and its spatiotemporal structure are related to

psychological symptoms in depression (see first paper), I here outlined some of the main features of what I call Spatiotemporal Psychopathology. The central hallmark features of Spatiotemporal Psychopathology are the consideration of subjective experience and its relation to both behavior and brain. As such Spatiotemporal Psychopathology extends both historical traditions and current forms of psychopathology like descriptive, phenomenological, and structural, and hermeneutic ones that emphasize the need to consider subjective experience.

At the same time Spatiotemporal Psychopathology aims to directly link subjective experience to the brain's intrinsic activity and its spatiotemporal structure. This goes beyond past and present psychopathological approaches in that it for the first time provides direct linkage between neural and phenomenal levels as reflected in what I recently described as 'neuro-phenomenal approach' (see Northoff 2014b,c,d). Such neuro-phenomenal linkage is supposed to be possible by the spatiotemporal structure of form which is assumed to be carried over and transformed from the neural level of the brain's intrinsic activity to the phenomenal level of subjective experience. Hence, Spatiotemporal Psychopathology extends descriptive, phenomenal and structural approaches to psychopathology to the brain by providing direct link between brain and experience.

The link to the brain and its intrinsic activity puts Spatiotemporal Psychopathology in the vicinity of brain-based approaches to psychopathology like cognitive and affective psychopathology and RDoC. The difference though is the focus of Spatiotemporal Psychopathology on the spatiotemporal dimension which is assumed to underlie all three, neural, phenomenal, and behavioral levels: only when considering the dimensions of space and time we can understand how neural changes can be transformed into phenomenal and ultimately behavioral ones. Hence Spatiotemporal Psychopathology can be assumed to take an intermediate position between experience- and brain-based approaches to psychopathology.

Despite its overlaps with past and present approaches, the concept of Spatiotemporal Psychopathology is a novel one. It requires much elaboration in the future in both theoretical and empirical aspects. Theoretically, methodological and epistemological questions about the access to the intrinsic activity's spatiotemporal structure and its link with phenomenal features in subjective experience need to be addressed. While empirically, we need more specific hypotheses and subsequent experimental-empirical testing of neuro-phenomenal-behavioral constructs as they characterize and occur in different disorders. The first paper highlighted some neuro-phenomenal-behavioral constructs that may be relevant in depression (and mania). Others need to be developed for other psychiatric disorders and specifically for those where major resting state abnormalities can be found consistently.

How can we validate such spatiotemporal approach to psychopathology? One way is to test whether it may lead to novel forms of symptom classification and categorization, a spatiotemporal one rather than one based on behavior (RDoC), cognition (Halligan and David, 2001) or affect/emotions (Panksepp, 2004). That may go along with the development of novel therapeutic approaches like spatiotemporal approaches to established therapies like psychotherapy and stimulation therapies using TMS, deep brain stimulation, or otherwise. Those therapies may be guided and based on the individuals' spatiotemporal features in intrinsic activity, subjective experience, and behavior. If the spatiotemporally-based and guided forms of therapy are more successful than the ones that are not based on and guided by the individuals' spatiotemporal features, the spatiotemporal approach may be validated and may henceforth be assumed to at least partially the real working and mechanisms of the brain including its neuro-phenomenal-behavioral transformations and linkages. Put slightly different, Spatiotemporal Psychopathology needs to stand the test of time in neuroscience, phenomenology and psychiatry in order to be validated.

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## Conflict of interest

I declare no conflict of interest.

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