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# The brain's spontaneous activity and its psychopathological symptoms – "Spatiotemporal binding and integration"

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ABSTRACT

Neuroimaging provided much insight into the neural activity of the brain and its alterations in psychiatric disorders. However, despite extensive research, the exact neuronal mechanisms leading to the various psychopathological symptoms remain unclear, yet. In addition to task-evoked activity during affective, cognitive, or other challenges, the brain's spontaneous or resting state activity has come increasingly into the focus. Basically all psychiatric disorders show abnormal resting state activity with the relation to psychopathological symptoms remaining unclear though. I here suggest to conceive the brain's spontaneous activity in spatiotemporal terms that is, by various mechanisms that are based on its spatial, i.e., functional connectivity, and temporal, i.e., fluctuations in different frequencies, features. I here point out two such spatiotemporal mechanisms, i.e., "spatiotemporal binding and integration". Alterations in the resting state's spatial and temporal features lead to abnormal "spatiotemporal binding and integration" which results in abnormal contents in cognition as in the various psychopathological symptoms. This, together with concrete empirical evidence, is demonstrated in depression and schizophrenia. I therefore conclude that we need to develop a spatiotemporal approach to psychopathology, "spatiotemporal psychopathology:" as I call it.

## 1. Introduction

Neuroimaging has provided a novel method to investigate the biological mechanisms of altered brain activity in psychiatric disorders. In addition to task-evoked paradigm as related to cognitive, affective, social, or sensorimotor challenges, the investigation of the brain's resting state activity has gained considerable traction in psychiatric. Put in a nutshell, the brain's resting state activity is the neural activity we measure in the absence of any specific stimuli or tasks (Logothetis et al., 2009; Northoff, 2014a,b). The idea is that the measurement of resting state activity taps into the brain's intrinsically generated neural activity, its spontaneous activity. While the brain's spontaneous activity shows an elaborate spatiotemporal structure (Northoff, 2014a; Cabral et al., 2014; Raichle, 2015a,b), its exact role and function for especially psychopathological symptoms remains unclear so far.

Due to its unclear role and functions, the brain's resting state activity has been under critical scrutiny (Weinberger and Radulescu, 2016; Power et al., 2014). This shall not detract though from the features of the spontaneous activity itself, its elaborate spatiotemporal structure and its changes and abnormalities in psychiatric disorders. I here describe the spatiotemporal features of the brain's spontaneous activity in more detail and point out their role in binding and integrating different stimuli and contents in spatiotemporal terms – I therefore speak of "spatiotemporal binding and integration". Based on various findings, I suggest abnormal "spatiotemporal binding and integration" in the resting state in depression and schizophrenia which, in turn, leads to psychopathological symptoms like ruminations and hallucinations.

I postulate that the two features as introduced here, "spatiotemporal binding and integration", are hallmark features of what can be described as "Spatiotemporal Psychopathology" (Northoff, 2015a,b,c,d). The concept of "Spatiotemporal Psychopathology" refers to the fact that psychopathological symptoms are conceived primarily in spatiotemporal terms rather than in cognitive (as in Cognitive Psychopathology), phenomenological (as in Phenomenological Psychopathology), affective (as in Affective Psychopathology), or neuronal terms (as in Biological Psychiatry).

Cognitive Psychopathology, for instance, conceives psychopathological symptoms as consequence of cognitive dysfunction; the perceived contents are processed in an abnormal cognitive way leading to distortions as manifest in the symptoms (David and Halligan, 2000). Spatiotemporal Psychopathology, in contrast, searches for the spatial and temporal organisation of cognitive functions and their respective contents: psychopathological symptoms result from abnormal spatial

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and temporal organisation of cognitive functions and their contents rather than from the latter themselves.

How about experience as emphasized in Phenomenological Psychopathology (Parnas et al., 2013)? Phenomenological Psychopathology focuses on subjective experience of for instance time and space as well as of self, body, and world as central dimensions of symptoms. Spatiotemporal Psychopathology agrees with that but extends that claim to the neuronal level of spontaneous activity with its organisation and construction of the brain's time and space: the latter supposedly provides the neuronal basis for our experience of time and space and the subsequent shaping of self, body, and world (Northoff, 2014a). Finally, unlike Biological Psychiatry that approaches the brain is mainly neuronal terms of various functions (like sensory, motor, cognitive, etc.), Spatiotemporal Psychopathology views the brain in predominantly spatial and temporal terms: what are the temporal and spatial mechanisms, as based on the brain's spontaneous activity, that give rise and organize its various functions including affective functions as focused on in Affective Psychopathology (Panksepp, 2004).

The aim of this contribution is to demonstrate how changes in the resting state's spatiotemporal structure translate into psychopathological symptoms. In a first part I will describe "spatiotemporal binding and integration" in the brain's "normal" spontaneous activity; this is followed by showing their alterations in depression (second part) and schizophrenia (third part).

## 2. Part I: Spontaneous brain activity: Spatiotemporal features and "spatiotemporal binding and integration"

### 2.1. The brain's spontaneous activity – Spatial and temporal features

The brain's intrinsic activity (or spontaneous activity) can spatially be characterized by various neural networks that consist of regions showing close functional connectivity with each other. There is for instance the core default-mode network (DMN) that includes mainly the cortical midline structures (Northoff et al., 2006, Andrews-Hanna et al., 2016), which show strong low frequency fluctuations (Northoff, 2014a; Raichle, 2009, 2001). Other neural networks include the sensorimotor network, the salience network, the ventral and dorsal attention network, the cingulum-operculum network, and the central executive network (CEN) (see Menon (2011) for a review). These neural networks are related to each other in continuously dynamically changing constellations (de Pasquale et al., 2010, 2012), resulting in what may be described as spatial structure that, through its functional nature, supercedes the anatomical structure.

In addition to such spatial structure on the functional level, the spontaneous activity can also be characterized by fluctuations in its neural activity in different frequency bands ranging from infraslow (0.0001–0.1 Hz) over delta (1–4 Hz), theta (5–8 Hz), alpha (8–12 Hz) and beta (12–30 Hz) to gamma (30–180 Hz). Most importantly, these different frequency bands are coupled with each other, with for instance the phase of lower frequency bands being coupled to the phase or power of higher ones (Buzsaki, 2006; Buzsaki et al., 2013; Northoff, 2014a). This amounts to a complex temporal structure in the brain's intrinsic activity that, as shown most recently, is related in some yet unclear ways to the spatial structure and its various neural networks (e.g., Ganzetti and Mantini, 2013; Northoff, 2014a) (Fig. 1).

To be more specific, spontaneous BOLD fluctuations as observed in fMRI are found in lower frequency ranges including the delta band (1–4 Hz), up- and down-states (0.8 Hz) and infra-slow fluctuations (ISFs) (0.001–0.1 Hz) (Logothetis, 2008, Zhigalov et al., 2015). The slow frequency fluctuations observed in fMRI have been assumed to correspond to what is measured as slow cortical potentials (SCPs) in EEG (He and Raichle, 2009; Khader et al., 2008). These SCPs are not easy to obtain in EEG because they are subject to artifacts caused by sweating, movements, and electrode drift; their measurement therefore

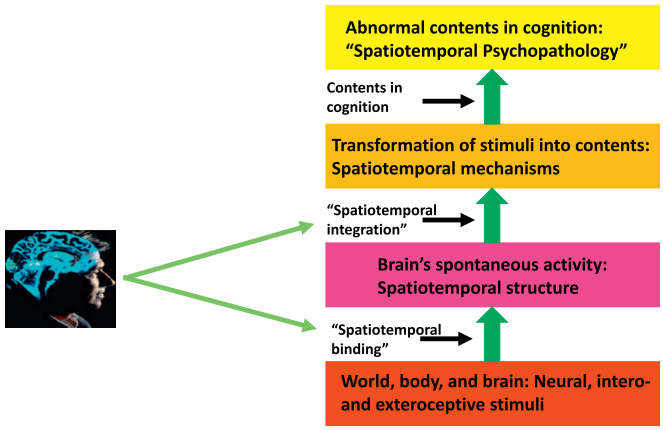


**Fig. 1.** The brain's spontaneous activity and "Spatiotemporal Psychopathology".The figure shows in the bottom that the various stimuli from world, body, and brain, i.e., neural and intero- and exteroceptive, are bind together based on their spatiotemporal features; i.e., "spatiotemporal binding". The resulting contents are integrated, i.e., "spatiotemporal integration". Abnormalities in the spatiotemporal features of the brain's spontaneous activity lead then to abnormal "spatiotemporal binding and integration" which, in turn, results abnormal contents in cognition and thus the various psychopathological symptoms (upper part).

requires a more direct approach by so-called direct current (DC) recording. There is some evidence that what is measured as SCP in EEG corresponds, or is even identical, to the low frequency fluctuations obtained in fMRI (He and Raichle, 2009; Khader et al., 2008).

In addition to such low frequency fluctuations, there are also higher frequency fluctuations in the brain's resting state activity. These cover 1 Hz and higher frequency ranges, thus including delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (> 30 Hz) (Mantini et al., 2007; Sadaghiani et al., 2010). This raises the question of how low and high frequencies are related to each other in the brain's resting state (Canolty and Knight, 2010; Fell and Axmacher, 2011; Fries, 2009; Sauseng and Klimesch, 2008). For instance, Vanhatalo et al. (2004) conducted an EEG study in healthy and epileptic subjects during sleep using DC-EEG to record low frequency oscillations. All subjects showed infraslow oscillations (0.02–0.2 Hz) cross all electrodes—and thus the whole brain—without any specific, visually obvious spatial distribution evident.

Most interestingly, Vanhatalo et al. (2004) observed phase-locking or phase-synchronization between the phase of slow (0.02–0.2 Hz) oscillations and the amplitudes of the faster (1–10 Hz) oscillations: the amplitudes of the higher frequency oscillations (1–10 Hz) were highest during the negative phases or deflection (e.g., during periods in the fluctuating cycle of the low frequency oscillation that show higher degrees of excitability for subsequent stimuli when compared to positive periods in the cycle) of the slow oscillations (0.02–0.2 Hz) (see Fig. 2).

Such phase-locking of high frequency oscillations' power to the

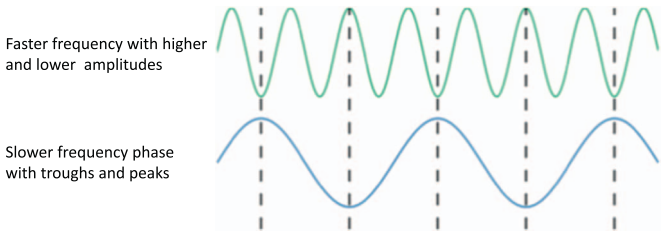


**Fig. 2.** Cross-frequency coupling.The figure illustrates in a schematic way how the phase (as featured by peaks and troughs) of the slower frequency (blue at bottom) couples to the level of amplitude of the faster frequency (green at top). The figures shows that the peaks of the slower frequency are always related to low levels in the amplitude of the faster frequency as indicated by the dotted vertical lines. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)