Resting State Activity and the "Stream of Consciousness" in Schizophrenia—Neurophenomenal Hypotheses

Georg Northoff*

Royal Ottawa Healthcare Group, University of Ottawa Institute of Mental Health Research, Ottawa, CA; Taipei Medical University, Graduate Institute of Humanities in Medicine, Taipei, Taiwan; Taipei Medical University-Shuang Ho Hospital, Brain and Consciousness Research Center, New Taipei City, Taiwan; National Chengchi University, Research Center for Mind, Brain and Learning, Taipei, Taiwan; Centre for Cognition and Brain Disorders (CCBD), Normal University Hangzhou, Hangzhou, China

*To whom correspondence should be addressed; Mind, Brain Imaging and Neuroethics, Canada Research Chair, EJLB-Michael Smith Chair for Neuroscience and Mental Health, Royal Ottawa Healthcare Group, University of Ottawa Institute of Mental Health Research, 1145 Carling Avenue, Room 6467, Ottawa, ON K1Z 7K4, Canada; tel: 613-722-6521 ext. 6870, fax: 613-798-2982, e-mail: georg.northoff@theroyal.ca

Schizophrenia is a multifaceted disorder with various symptoms including auditory hallucinations, egodisturbances, passivity phenomena, and delusions. Recent neurobiological approaches have focused on, especially, the abnormal contents of consciousness, the "substantive parts" as James said, to associate them with the neural mechanisms related to sensory, motor, and cognitive functions, and the brain's underlying stimulus-induced or task-evoked activity. This leaves open, however, the neural mechanisms that provide the temporal linkage or glue between the various contents, the transitive parts that makes possible the "stream of consciousness." Interestingly, schizophrenic patients seem to suffer from abnormalities specifically in the "transitive parts" when they experience contents as temporally disconnected or fragmented which in phenomenological psychiatry has been described as "temporal fragmentation." The aim of this article is to develop so-called neurophenomenal hypothesis about the direct relationship between phenomenal features of the "stream of consciousness," the "transitive parts," and the specific neuronal mechanisms in schizophrenia as based on healthy subjects. Rather than emphasizing stimulus-induced and task-evoked activity and sensory and lateral prefrontal cortical regions as in neurocognitive approaches with their focus on the "substantive parts," the focus shifts here to the brain's intrinsic activity, its resting state activity, which may account for the temporal linkage or glue between the contents of consciousness, the transitive parts.

Key words: schizophrenia/stream of consciousness/James/cortical midline structures/auditory

hallucinations/thought disturbances/frequency fluctuations/functional connectivity

Introduction

Schizophrenia is a multifaceted disorder including symptoms like delusions, passivity phenomena, auditory hallucinations, egodisorders, and thought disorder. These abnormal mental symptoms are directly given in experience. which is usually described as "phenomenal."[1] These experiences, as obtained in subjective first-person perspective by the patients, are supposed to be related and linked to third-person accessible, eg, objective psychological,[2] and neural (see in what follows) mechanisms. Although many abnormal experiences including those of aberrant experience of time, ie, an abnormal "stream of consciousness" in schizophrenia, have been reported (see in what follows for details), their linkage to neuronal mechanisms remains unclear at this point in time (see in what follows for some methodological issues concerning such neurophenomenal linkage).

James characterized consciousness by a strong temporal dimension when discussed about "stream of consciousness."[3,4] He characterized the "stream of consciousness" by different phenomenal features like the contents themselves, the "substantive parts," and the transitional periods, the "transitive parts" (which by themselves can be described by "sensible continuity" and "continuous change"; see in what follows). Although many researches in schizophrenia have focused on the "substantive parts" while investigating the cognitive and neural correlates of their abnormal contents, eg, neurocognitive hypotheses,[5]

the "transitive parts" that provide the temporal linkage or "temporal glue" between the different contents have rather been neglected. They may be central for constructing the temporal flow of consciousness that first and foremost makes possible to integrate the different contents into one "stream of consciousness."

How about the phenomenal side, the schizophrenic patients' subjective experience of the "transitive parts" in their "stream of consciousness"? The schizophrenic patients experience the various contents in a disjunct and temporally fragmented way with various "now-moments" that remain unlinked rather than as flow with multiple transitions between the different contents (as presupposed in the "normal" stream of consciousness." This has been described as "temporal fragmentation"[6] that signifies the disturbance of especially the "transitive parts" in the "stream of consciousness." Despite first attempt,[7,8] the neural mechanisms underlying "temporal fragmentation" and its disturbance of the "transitive parts" in the "stream of consciousness" remain nevertheless unclear.[5,6,9]

One may want to link phenomenal features of subjective experience and neural mechanisms leading to what can be described "neurophenomenal hypotheses."[9] Such neurophenomenal hypotheses aim to link subjective experiential, eg, phenomenal, features of experience, eg, consciousness, with objective neuronal mechanisms. They must be distinguished from neurocognitive hypotheses that search for the neural correlates of the contents, the cognitions, rather than focusing on the temporal structure in the "stream of consciousness" within which those with very same contents are abnormally integrated in schizophrenia.[9]

The aim of this article is to develop what I describe as "neurophenomenal hypotheses" (see in what follows as well as in ref. [9]) about the neural mechanisms related to the "transitive parts" in the "stream of consciousness" and how the abnormalities in "transitive parts" can be related to the various psychopathological symptoms in schizophrenia.[38] Based on recent findings in both healthy and schizophrenic subjects, the focus will be on cortical midline structures, the core regions of what is described as "default-mode network (DMN)."[10,11] I hypothesize that due to their extremely strong infraslow frequency fluctuations (eg, frequency fluctuations in extremely slow range around 0.0010.1; see in what follows for details), the cortical midline structures are ideal candidates for providing the "temporal linkage or glue" and thus the "transitive parts" between the various contents of consciousness. Alterations in cortical midline structures and their infraslow frequency fluctuations may then also account for the disturbance in the "transitive parts" and subsequent "temporal fragmentation" in schizophrenia. I consecutively divide my article into two parts: first part about the neuronal findings in schizophrenia especially in the cortical midline structures' resting state activity and the second part about neuronal and neurophenomenal hypotheses about the changes in the "stream of consciousness" and the structure of time experience in schizophrenia, before though, some brief methodological remarks shall be made.

Neurophenomenal Approach

What do I mean by neurophenomenal hypotheses? As described at the beginning of the introduction, the term "phenomenal" refers to subjective experience in first-person perspective as distinguished from objective observation in third-person perspective. In contrast, neural data as observed in, for instance, brain scanning are third-person data. How can we link phenomenal first-person experience to neural third-person data? For that I assume what I describe as neurophenomenal hypotheses that aim to link neuronal mechanisms and phenomenal features.[9]

More specifically, the neurophenomenal approach aims to link phenomenal features like the "stream of consciousness" including its distinction between "substantive parts" and "transitive parts" to particular neuronal features. Such neurophenomenal approach must be distinguished from neurocognitive, neuroaffective, and neurosocial (and neurosensorimotor) approaches. The latter focus on how the neural activity related to sensorimotor, affective, cognitive, and social functions, eg, task-related or stimulus-induced activity, and their respective contents are related to psychopathological symptoms like delusions, hallucinations, and so on.

That is different in the neurophenomenal approach. Instead of focusing on the various functions and their respective stimulus-induced or task-evoked activities, ie, extrinsic activity, the neurophenomenal approach targets the brain's resting state activity, its intrinsic activity including its spatial and temporal structure.[9,12–14] This implies that the focus on contents in experience (like affective, cognitive, social, or sensorimotor) is here replaced by the focus on the temporal and spatial structure of experience as obtained in first-person perspective. The main claim of neurophenomenal hypotheses is that the spatial and temporal structure of the brain's intrinsic activity may be related and linked to the spatial and temporal structure of experience.[9]

By considering the structure of experience, the neurophenomenal approach takes strong borrowing from phenomenological approaches that start with the phenomenon in question as, for instance, the distorted "stream of consciousness" in schizophrenia.[1] However, it should be noted, at the outset, that we can discuss some phenomenological features only in a rather coarse-grained way without being able to go into fine-grained phenomenological details. The rich phenomenological tradition on time experience in schizophrenia that dates back to the beginning of the 20th century with Eugen Minkowski, Erwin Strauss, Ludwig Binswanger, Victor von Gebsattel, and

others cannot be considered here. These earlier studies are continued these days by especially Josef Parnas, Lous Sass, and Thomas Fuchs with the latter focusing especially on abnormal experience of time on whom I therefore rely in the following. Space reasons preclude us from going into fine-grained phenomenological detail. In addition to such formal constraint, there may also be scientific constraints; there may be an imbalance in the degree of sophistication to which neuronal and phenomenal features are developed at this point in time. Therefore, the current neurophenomenal hypotheses may be considered tentative as suggestions for bridging the neurophenomenal gap which may be refined in the future by more direct and explicit experimental paradigms.

Resting State Activity in Schizophrenia

Neuronal Findings in Schizophrenia Ia: Abnormal Resting State Activity in Midline Regions. Various studies recently investigated the DMN in schizophrenia (see ref. [15] for a recent review). Recent imaging studies in schizophrenia reported abnormal resting state activity and functional connectivity in the anterior cortical midline structures (aCMS). A study[16] demonstrated that the aCMS and posterior CMS like the posterior cingulate cortex (PCC)/precuneus show decreased task-induced deactivation (TID) during a working memory task. This was observed in both schizophrenic patients and their relatives when compared with healthy subjects, which is indicative of decreased task-related suppression and possibly increased resting state activity.

Furthermore, the very same schizophrenic subjects also showed increased functional connectivity of the aCMS with other posterior regions of the CMS, such as the PCC. Both functional hyperconnectivity and decreased TID correlated negatively with each other. The more decreased the task-related suppression, the more increased the degree of functional connectivity. Finally, both decreased TID and increased functional connectivity in aCMS correlated with psychopathology, ie, the predominantly positive symptoms as measured with the PANSS scale (ie, the Positive and Negative Symptoms Scale).

Decreased TID in aCMS was also observed in an earlier study that investigated working memory.[17] Similar to the study described earlier, they let subjects perform a working memory task and observed abnormally decreased TID in aCMS in schizophrenic patients when compared with healthy subjects. Similar to the other study, they also observed abnormal task-related activation in the right dorsolateral prefrontal cortex in schizophrenic patients. Another study[18] also reported abnormal TID in aCMS as well as abnormal functional connectivity from aCMS and posterior CMS to the insula in schizophrenic patients.[19–22]

In addition to TID and functional connectivity, another abnormal measure of resting state activity is the temporal features, more specifically fluctuations or oscillations in certain temporal frequencies. For instance, low-frequency fluctuations in the resting state were increased in the aCMS (and the parahippocampal gyrus) in schizophrenic patients, while they were decreased in other regions like the insula.[23] Abnormally increased power of low-frequency oscillations (<0.06 Hz) in the aCMS (and posterior CMS regions and the auditory network) and their correlation with positive symptom severity were also observed in another study on schizophrenic patients.[24]

However, findings are not fully clear because a recent study showed decreased low-frequency power in midline regions in schizophrenia.[25,26] Most interestingly, they also observed that low-frequency power was no longer correlating, ie, decoupled, with functional connectivity. Finally, one recent study investigated the variability of neural activity (eg, amplitude of low-frequency fluctuations) in the low-frequency range in different frequency bands (slow 5: 0.010.027 Hz, slow 4: 0.0270.08 Hz) in schizophrenia; they observed significant reductions in variability in slow 5 in ventromedial prefrontal cortex (and basal ganglia and midbrain) in schizophrenia.[27]

In sum, there are clear changes in functional connectivity and low-frequency fluctuations in schizophrenia. Functional connectivity tends to be increased within cortical midline regions. In contrast, the exact direction of the changes in low-frequency fluctuations remains unclear with both reduction and increases being reported. Most interestingly, recent studies report decoupling between functional connectivity and low-frequency fluctuations as well as frequency-band specific decreases in variability of neural activity in anterior midline regions in schizophrenia. Overall, these findings suggest alterations in midline resting state activity in schizophrenia what Lloyd described as "dynamic temporal network,"[28] which one would assume to lead to alterations in temporal continuity and flow of neural activity (see in what follows).

Neuronal Findings in Schizophrenia Ib: Abnormal Balance Between Low- and High-frequency Fluctuations. Recent resting state electroencephalogram (EEG) showed increased coherence in basically all low- and high-frequency bands including delta, theta, alpha, and gamma bands within and between hemispheres in schizophrenia.[29–33] Most interestingly, the study by Spencer[33] could relate the increased gamma power in auditory cortex to reduced stimulus-evoked activity in response to auditory stimuli with the former predicting (ie, correlating) the latter. This suggests clear relationship between increased resting state gamma power and reduced task-evoked activity in gamma (see in what follows). Unfortunately, only a combined functional magnetic resonance imaging (fMRI)–EEG resting state study allowing for combined measurement of infraslow (0.0010.1 Hz), slow (012 Hz), and fast (1280 Hz) frequencies has been reported.[34] This study observed increased association of the DMN and the low-frequency fluctuations in the

midline regions as measured in fMRI with lower frequencies (delta and theta) as obtained in EEG in schizophrenia.[34]

Task-related electrophysiological findings have focused on especially beta and gamma oscillations where schizophrenic patients show severe impairments, eg, reductions in gamma power in response to sensory stimuli or other tasks (see recent articles [35] and [36–41]). In addition to gamma, other lower oscillations like delta, theta, and alpha have also been observed to be abnormal, eg, reduced during task-evoked activity in schizophrenia.[42,43]

In addition to these high- and low-frequency bands, as they can be measured with EEG, there are also lower, eg, infraslow bands that can be tapped into fMRI. We already reported that infraslow slow frequency power significantly differed in especially midline structures between schizophrenia and healthy subjects (see aforementioned discussion as well as #0;Yu, 2013 #2151;Yu, 2014 #2152), which has recently been further investigated. Infraslow frequency bands were subdivided into slow 4 (0.0270.08) and slow 5 (0.010.027). Schizophrenic patients showed frequency-specific abnormalities (in frequency band slow 4) in particular regions (like ventromedial prefrontal, cortex, basal ganglia, and midbrain).[25,27]

What remains unclear, however, is how these deficits in infraslow frequencies are related to the observed alterations in higher frequencies especially beta and gamma? Based on the observations in healthy subjects,[44] one would assume abnormal coupling from infraslow to high frequencies between infraslow frequency phase and high-frequency power.

Though not targeting the infraslow frequency fluctuations as measured with fMRI, recent EEG studies investigated the phase synchrony within and between frequency bands. A study by Uhlhaas et al[36–39] observed significantly reduced phase synchrony in especially the beta frequency band in schizophrenia during a Gestalt perception task (see also ref. [45] for review of high-frequency fluctuations in schizophrenia). A study by Spencer et al[46] reported that gamma-band power in auditory cortex (during an auditory task) was modulated by the phase of delta oscillations in a significantly lower degree in schizophrenic patients. This is complemented by White et al[47] who found reduced cross-frequency coupling between alpha and gamma bands in schizophrenia (see ref. [48] who could not observe decreases in cross-frequency coupling between theta and gamma; see refs [40,41,49] for reviews). Ideally, one would like to investigate direct phase–phase/power coupling between the infraslow frequency fluctuations of the midline regions and low- and high-frequency fluctuations in the same and other regions. This remains open, however.

Overall, despite being tentative and incomplete at this point, the findings strongly support altered temporal structure of neural activity in schizophrenia, eg, abnormal relationship between low- and high-frequency oscillations with their possible decoupling from each other.

Most interestingly, the low-frequency deficits seem to be related to the deficits in functional connectivity in especially the midline regions since both correlated in healthy subjects but were disconnected from each other in schizophrenia,[25,26] which suggests close though yet unclear disturbances in the linkage between temporal and spatial dimensions in resting state activity in schizophrenia. This may not only signify abnormalities in the temporal structure itself but also altered integration between temporal and spatial dimensions of resting state activity.

Resting State Activity and "Stream of Consciousness" in Schizophrenia

Neurophenomenal Hypothesis in Schizophrenia Ia: Dysbalance Between Temporal Continuity and Temporal Flow of Neural Activity in Midline Regions. Although at an early stage and not fully clear, the present findings on resting state midline activity in schizophrenia can nevertheless be summarized in a tentative way. Quite consistent seems to be the finding that functional connectivity within the midline regions is increased; this suggests an abnormally high degree of neuronal synchronization (as indicated by functional connectivity) among the different midline regions in schizophrenia. Such increased neuronal synchronization seems to be accompanied by decreased variability of neural activity—if they are more synchronized and coupled among each other, the different midline regions themselves can no longer be as variable in their neural activity. This is a tentative conclusion, however, because the exact relationship between functional connectivity and variability remains to be reported.

What does such abnormally high degree of neuronal synchronization within the midline regions imply for the degree of temporal continuity and temporal flow in neural activity? The concepts of temporal continuity and temporal flow describe neural activity by referring to one and the same dimension though from opposite ends, continuity or sameness, and flow or change. Temporal continuity describes the number of time points during which neuronal activity remains the same and does not change (refer aforementioned discussion): the higher the number of time points during which activity does not change, the higher the degree of temporal continuity. For instance, the long cycle durations of infraslow and low frequencies represent a period during which neural activity does not change entail a high degree of temporal continuity. In contrast, high-frequency fluctuations with their much shorter cycle duration entail higher degree of change in shorter time spans and thus lower degree of temporal continuity of neural activity. Temporal continuity can also be increased if the onsets of high-frequency fluctuations are related to the ones of low and infraslow frequency fluctuations.

A high degree of neuronal synchronization among the midline regions means that the neural activity remains the same and is consistent over time—there is a high degree

of temporal continuity of neural activity. Such neuronal synchronization, as it is increased in schizophrenia, increases the number of time points in time during which there is no change in neural activity and does therefore increases the degree of temporal continuity. Accordingly, it may be assumed that high degree of neuronal synchronization in schizophrenia entails high degree of temporal continuity of neural activity.

How about the opposite, temporal flow? Temporal flow describes the number of points in time after which neural activity changes. The lower the number of discrete points in time after which activity changes, the more change in neural activity and the higher the degree of temporal flow. That is well reflected in especially higher frequency fluctuations: due to their short cycle duration, the number of time points after which neural activity change is rather low, which leads to a higher degree of temporal flow (and lower degree of temporal continuity) of neural activity. Increase in neuronal synchronization between different points in time in neural activity (as for instance between time points from different, eg, low and high, frequency bands) leads to increase in the number of time points after which there is change in neural activity and consecutively decrease its degree of temporal flow. This seems to be the case where increased neuronal synchronization is reflected in increased functional connectivity and decreased variability in midline neural activity. Accordingly, it may be assumed that increased neuronal synchronization leads to decreased temporal flow of neural activity in midline regions in schizophrenia.

Overall, I hypothesize that the abnormally high degree of neuronal synchronization, eg, functional connectivity in midline regions, leads to dysbalance between temporal continuity and temporal flow of their neural activity in schizophrenia. Temporal continuity is increased and predominates over temporal flow that is decreased. This characterizes the resting state activity. Because of such increased neuronal synchronization, the resting state activity may therefore be less susceptible to activity changes during stimulus-induced or task-evoked activity which is consecutively decreased (as it is supported by the empirical data; see ref. [9] and figure 1a).

How about the infraslow frequency fluctuations in midline regions? The findings are somehow contradictory here. The earlier studies reported increase in power of infraslow frequency fluctuations in midline regions in schizophrenia, whereas the most recent ones seem to suggest rather reduced power. It is clear that there are some changes in the power of the infraslow frequency fluctuations in the midline regions. Moreover, it remains unclear how those changes are related to the increased neuronal synchronization, eg, functional connectivity.

Although preliminary at this point, this suggests that the balance between infraslow and low- and high-frequency fluctuations may be altered in schizophrenia. One

may hypothesize that the balance is tilted more towards the infraslow frequency fluctuations and their increased degree of neuronal synchronization entailing increased temporal continuity. This makes them less susceptible to neuronal changes, eg, temporal flow as related to low- and high-frequency fluctuations during stimulus-induced or task-evoked activity. The latter is well compatible with the well-established gamma deficit during task-evoked activity in schizophrenia (see the aforementioned discussion). Accordingly, the neuronal balance is shifted towards the infraslow frequency fluctuations in the resting state at the expense of the high-frequency fluctuations during stimulus-induced or task-evoked activity (see figure 1b).

Neurophenomenal Hypothesis in Schizophrenia Ib: Reduced Temporal Extension of Stimulus-induced Neural Activity in Midline Regions. How does the dysbalance between temporal continuity and flow as well as the one between infraslow and high-frequency fluctuations manifest in the stream of consciousness? Before reaching to the phenomenal side, we need to take one more intermediate step, the one related to temporal extension. Temporal extension refers to the degree to which a particular stimulus or task at one particular point in time is extended across different points in time during its encounter with the long phase durations of the infraslow frequency fluctuations in the midline regions.

How do the increased degrees of neuronal synchronization and temporal continuity impact temporal extension of particular stimuli in time as for instance during mental time travel with prospection and retrospection (see refs [50] and [51]). Firstly, prospection and retrospection refer to mental travel in time that has be distinguished from the more cognitive and content-based concepts of anticipation/remembering particular events in past and future as well as from the rather phenomenologically based terms protention/retention.[50] Let us now sketch the neuronal scenario. The extrinsic stimulus encounters an intrinsic resting state activity with increased neuronal synchronization and temporal continuity where, as presumed, the long phase durations of low-frequency fluctuations predominate. One would then suggest that the extrinsic stimuli should be more extended in time by the long phase durations. Such temporal extension is possible, however, only if the extrinsic stimuli interact with and induce some change, eg, temporal flow in the ongoing midline resting state activity.

The ability to induce change in the midline regions by extrinsic stimuli is reduced; however, due to their high degree of neuronal synchronization, eg, functional connectivity, with the high degree of temporal continuity, the midline regions' resting state activity is less susceptible to change, eg, temporal flow, induced by the extrinsic stimuli. The extrinsic stimuli is processed but can no longer induce as much change in the midline's neural activity and can therefore no longer be extended beyond its particular point in time. Accordingly, increased temporal continuity during resting state activity

a   Dysbalance between temporal continuity and temporal flow of neural
activity in cortical midline regions in schizophrenia
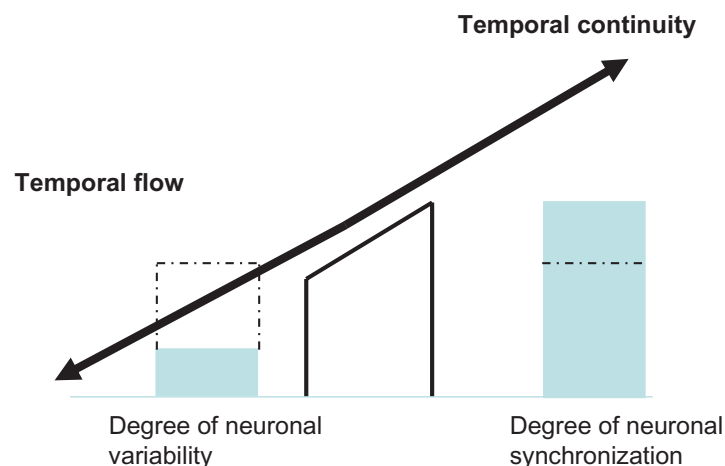
b   Temporal continuity and flow of neural activity and low and high
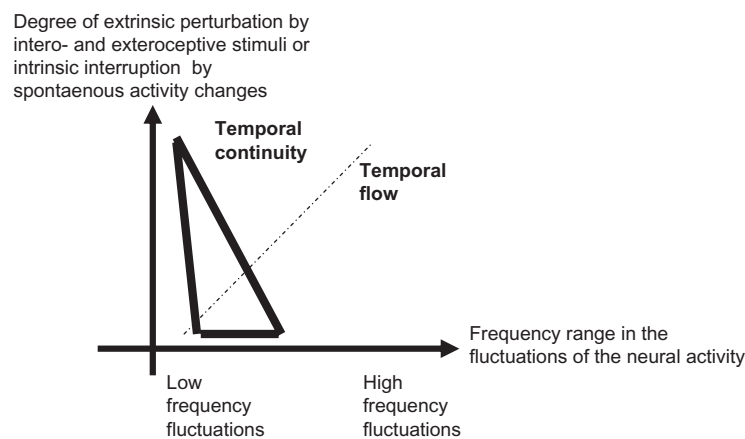frequency fluctuations in the neural activity's fluctuations in schizophrenia

Fig. 1. Balance in neural activity between temporal continuity and flow (a) in relation to low- and high-frequency fluctuations (b) in schizophrenia. (a) Balance between temporal continuity and flow of neural activity in midline regions is abnormally shifted towards temporal continuity in schizophrenia, indicated by the abnormally tilted horizontal arrows (upper part). Temporal continuity of neural activity in midline regions is abnormally strong in schizophrenia (as related to increased neuronal synchronization, eg, functional connectivity) and decreased neuronal variability as indicated by the bar diagrams in lower part). (b) Balance between temporal continuity (thick lines) and temporal flow (thin dotted line) is abnormally shifted towards the former at the expense of the latter. Most importantly that shift goes along with a shift from high- to low-frequency fluctuations with extrinsic stimuli no longer inducing high-frequency fluctuations in the intrinsic activity and its predominant low-frequency fluctuations.
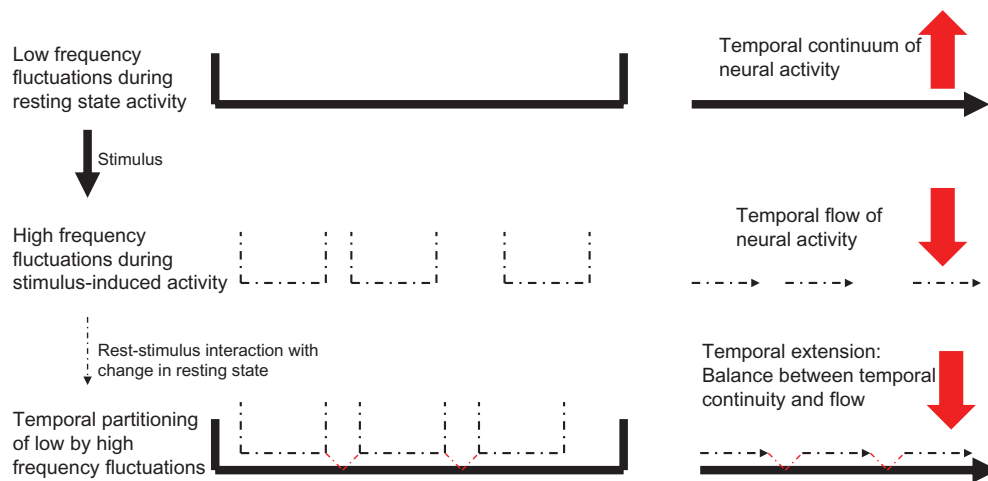
entails reduced temporal extension during task-evoked or stimulus-induced activity. Owing to the changes in opposite directions, one may say that temporal continuity and temporal extension of midline neural activity dissociate from each other in schizophrenia (see figures 2a and 2b).

Neurophenomenal Hypothesis in Schizophrenia IIa: From Reduced Temporal Extension to Reduced "Sensible Continuity" and Increased "Temporal Fragmentation" in the "Stream of Consciousness."   How does the dissociation between increased temporal continuity and decreased temporal extension of neural activity in

midline regions affects the construction of time in consciousness, the "stream of consciousness"? Following James, we characterized the "stream of consciousness" by "transitive parts" that provide the transition between the different contents in consciousness. The 'transitive parts' themselves can be characterized by "sensible continuity" and "continuous changes."

Let us focus on the first, "sensible continuity," which describes that no phenomenal state and its contents vanishes and perishes completely before the onset of the next one (see the aforementioned discussion). Taken in this sense, sensible continuity is obviously closely related to temporal

a Neural activity and temporal extension in schizophrenia

Low frequency
fluctuations during
resting state activity

Stimulus

Temporal continuum of
neural activity

High frequency
fluctuations during
stimulus-induced activity

Temporal flow of
neural activity

Rest-stimulus interaction with
change in resting state

Temporal partitioning
of low by high
frequency fluctuations

Temporal extension:
Balance between temporal
continuity and flow

b Neuronal continuum and temporal extension in healthy (dotted
line) and schizophrenic (red line) subjects

Degree of temporal extension
of time into past and future

Healthy subjects

Schizophrenic subjects

Neuronal continuum
between temporal
continuity and temporal
flow in neural activity

Temporal continuity

No activity change

Low frequency fluctuations

Temporal flow

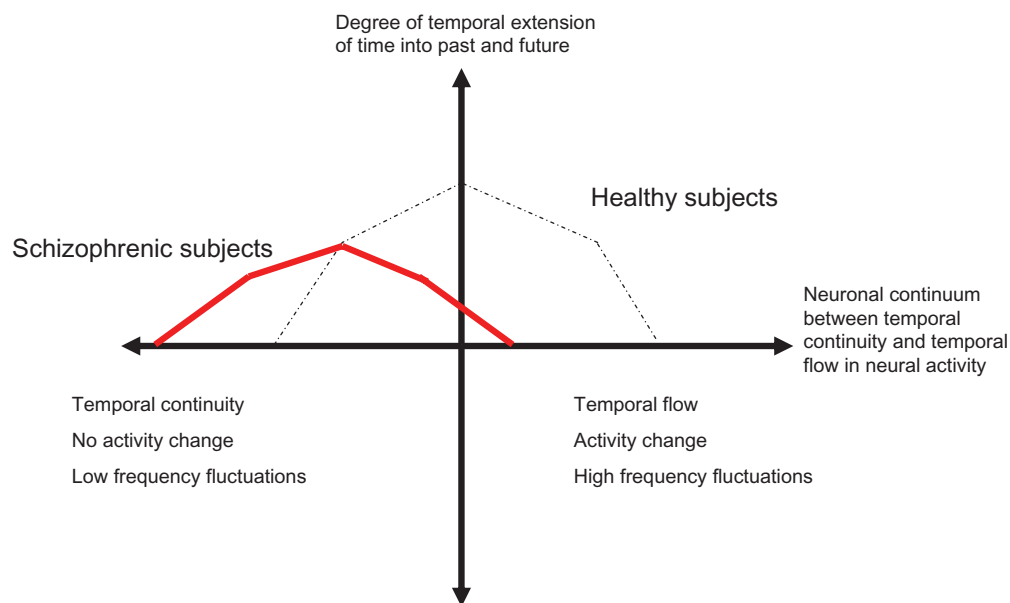Activity change

High frequency fluctuations

Fig. 2. Abnormal relationship between changes in neural activity and temporal extension and how they are modulated by high- and low-frequency fluctuations (a) and the abnormal continuum of changes in neural activity (b) in schizophrenia. (a) Abnormally strong resting state's low-frequency fluctuations (upper left) provide abnormally strong temporal continuity (upper right) on the basis of their long phase durations as symbolized by the length of the interval (left) and arrow (right). The low-frequency fluctuations are then complemented by the stimulus-related high-frequency fluctuations (middle left) that show much shorter phase durations and allow for temporal flow of neural activity (middle right), which is significantly reduced in schizophrenia (dotted thin lines). Combination of both implies an abnormally low degree of temporal partitioning of the resting state's long phase durations (lower left), which leads to reduced temporal extension of the stimulus' present time point into the past and future (lower right) in schizophrenia. (b) Relationship between the degree of temporal extension into past and future (*y*-axis) and the neuronal balance or continuum between temporal flow and continuity of neural activity (*x*-axis). Temporal extension is based on a balance between temporal flow and continuity of neural activity as reflected in the inverted u-shape curve (dotted lines in healthy subjects). This inverted u-shape curve is shifted abnormally towards the left in schizophrenia (red curve), which entails reduced temporal extension of the stimulus' present time point into past and future ones.

extension: the higher the degree of temporal extension of neural activity as related to particular stimuli or tasks, the more that stimulus or tasks can be extended neurally in time, and the higher the degree of subsequent sensible continuity on the phenomenal level of consciousness.

Therefore, temporal extension and sensible continuity are positively and directly proportional related to each other. Reduced degree of temporal extension should entail reduced sensible continuity. The stimulus or task can no longer be extended in time and is therefore less continuous with previous mental contents (as associated with the preceding stimuli and tasks) on the phenomenal level of consciousness. The contents of consciousness as resulting externally from the stimuli and tasks should consequently be less continuous in time and with each other—they should be more segregated from each other in subjective experience.

This is exactly one form and way how schizophrenic patients experience time (besides other ways that cannot be described in detail here; see my hint at the end of the Methodological Remark section). These patients do indeed experience disruption in temporal continuity between the different (internal and external) mental contents: the different contents are no longer linked or glued to each by an underlying temporal continuity and are instead segregated from each other temporally which leads to what has been described as "temporal fragmentation" (see refs [6],[9](ch. 17)). In the following text, we will focus on such "temporal fragmentation" and how it can be linked to specific neuronal mechanisms. Although we leave other forms and ways of time experience in schizophrenia as described in subtle details by psychiatrists (like Minkowski, Gebsattel, Binswanger, and Strauss) as mentioned earlier, there is a more refined neurophenomenal investigation kept aside for future..

Let us specify experience of temporal fragmentation in the following text. Decreased temporal extension may lead to decreased temporal extension of the respective stimulus or task in the neural activity. Thus, there is decreased temporal linkage or "temporal glue" and consequently less neural continuity between the different stimuli or tasks and their respective different discrete points in time which, therefore, can no longer be properly linked and glued to each other. The various mental contents occurring at different discrete points in time can consequently no longer be connected, linked, and glued temporally to each other. Instead of being connected as distinct parts of a homogenous stream of consciousness, the different mental contents are now experienced as temporally disconnected or fragmented with no temporal linkage or glue connecting them anymore in consciousness.

The lack of temporal linkage or glue between the different contents has been described as "temporal fragmentation" as it is well reflected in experience of schizophrenic patients.[6,52] Accordingly, I hypothesize that what phenomenally is described as "temporal fragmentation" and indicative of reduced sensible continuity in the stream of consciousness may be related neurally to reduced temporal extension during stimulus-induced activity and increased temporal continuity in resting state activity of the midline regions.

Such fragmentation of the contents and the underlying disruption in sensible continuity in the stream of consciousness is well reflected in the following quote by a schizophrenic patient by Fuchs[53]: "When I move quickly, it is a strain on me. Things go too quickly for my mind. They get blurred and it is like being blind. It's as if you were seeing a picture one moment and another picture the next." The schizophrenic patient describes here that the contents, eg; the different pictures, are no longer linked and glued temporally together. There are no longer any temporal transitions between the different discrete points in time and space associated with the different contents, eg, pictures. Instead of temporal transitions, there are temporal gaps, which lead to temporal delays in linking the different contents and putting them together. Metaphorically speaking, the pictures are, as it were, experienced as pearls without an underlying chain. Because the underlying chain—the resting state's spatiotemporal continuity— seems to be disrupted within itself, the pearls—the different contents— can no longer be put together, ordered, structured, and organized in consciousness.

Here is an another example in what follows: "Each scene jumps over into the next, there is no coherence. Time is running strangely. It fells apart and no longer progresses. There arise only innumerable separate now, now, now — quite crazy and without rules or order. It is the same with myself. From moment to moment, various 'selves' arise and disappear entirely at random. There is no connection between my present ego and the one before."[4,6,8]

The lacking temporal extension of the resting state activity makes it impossible to temporally integrate the various stimuli and their respective contents and thus to provide temporal linkage or glue. This, in turn, leads to "temporal gaps" and "temporal fragmentation" during the experience of the various contents which are then only experienced at different now-moments without any temporal linkage or glue. This is, for instance, well reflected in the following quote from a schizophrenia patient: "Time splits up and doesn't run forward anymore. These arise uncountable disparate now, all crazy and without rule or order."[7]

Neurophenomenal Hypothesis in Schizophrenia IIb: From Reduced "Sensible Continuity" and Increased "Temporal Fragmentation" to Psychopathological Symptoms. How is such "temporal fragmentation" in "stream of consciousness" related to the various psychopathological symptoms in schizophrenia? The occurrence of temporal fragmentation may most likely underlie various symptoms like passivity phenomena, thought insertion, and thought withdrawal, which may thus be traced back to temporal fragmentation as the underlying basic, eg, temporal symptoms.

For instance, a recent study by Angelopoulos et al[54] investigated the electrophysiological correlates of resting state during thought blocks. Thought blocks were

characterized by patients as "a rock in my head," "blank page in my mind," "spontaneous block of my thought," and "loss of mind" which usually occurred automatically during the hallucinatory state. Using EEG, they observed significantly decreased phase synchrony in theta and alpha range in left temporal and frontal electrodes during thought blocks in schizophrenic patients with chronic auditory hallucinations. In contrast, recovery from thought blocks was accompanied by immediate increase in phase synchrony.

Although tentatively these data clearly suggest that the decreased phase synchrony between temporal and frontal areas in the ongoing resting state activity is closely related to thought blocks on the symptomatic side: the decrease in phase synchrony signals decreased temporal extension of the usually ongoing flow of thought leading to a thought block. The seemingly cognitive symptom, eg, thought block, may turn out as temporal symptom, eg, the reduction of temporal extension of neural activity that interrupts the usually ongoing flow between different thoughts, eg, their "sensible continuity" in the "stream of consciousness."

Accordingly, the decrease in temporal extension of neural activity may affect the mental contents in consciousness that originate in the external world, eg, external contents. External mental contents are no longer temporally extended in time and are henceforth experienced as less continuous indicating temporal fragmentation. This is well

manifest in perception and action that show both reduced sensible continuity as visible, for instance, in abnormal perception and awkward movements (eg, motor signs). The abnormal perceptions may prone the subject to make abnormal cognitive inferences leading to delusions.

The same applies to internal mental contents like one's thoughts, the own self, and the own memories that are also experienced in a less continuous way. For instance, a psychological study by Zalla et al[55] showed videotaped movies to healthy and schizophrenic subjects who were required to detect the transitions between the different events shown in the movie. Afterwards, subjects were asked to recall the events. Interestingly, schizophrenic patients recalled the events in a temporary much more fragmentary way when compared with healthy subjects and had major difficulties in recalling longer lasting events. This psychological study clearly shows how the abnormal "stream of consciousness" with increased temporal fragmentation impacts a cognitive function like memory recall. Analogous temporal mechanisms, eg, temporal fragmentation, may underlie and concern the own thought which lead to thought disturbances as well as the own self which then may be experienced in a fragmentary and delayed way (see figure 3).

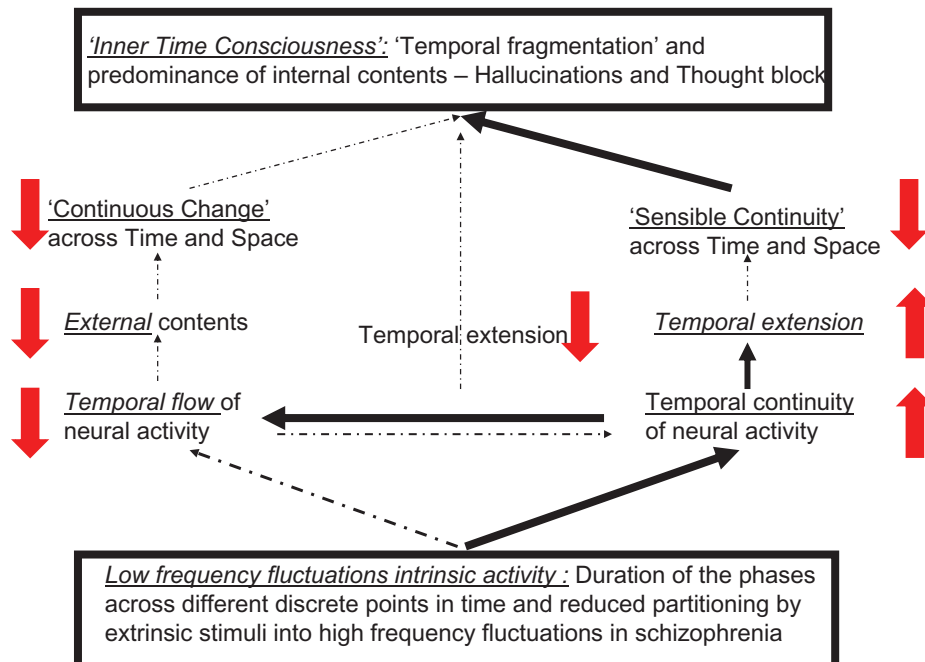Finally, the sense of self is altered in schizophrenia resulting in egodisorders (see refs [9,56–58] for details).

Fig. 3. Abnormalities in the two main components of the "stream of consciousness," "sensible continuity," and "continuous change" (upper part) depend supposedly on duration of the phases of the low-frequency fluctuations in the brain's abnormal neural activity during both resting state and stimulus-induced activity (lower part) in schizophrenia. Reduced "continuous change" on the phenomenal level of consciousness is related to the decreased temporal flow of neural activity across different discrete points in time (middle left), although reduced "sensible continuity" may corresponds to the increased temporal continuity of neural activity (middle right). Dysbalance between temporal continuity and temporal flow of neural activity that are already present in the brain's intrinsic activity in schizophrenia are central in constituting decreased "sensible continuity" and "continuous change" in the "stream of consciousness" which leads to abnormal predominance of internal contents and temporal fragmentation in conscious experience.

The sense of self is closely associated with neural activity in the midline structures[59] which is also implicated in allowing for mental time travel as in prospection and retrospection (see ref. [9(ch. 13)] for details). One may now assume that temporal fragmentation may also affect the sense of self especially the identity of the self across time: if there is temporal discontinuity in neural activity, the different senses of self at the different points in time can no longer be linked together. The self can consecutively no longer be properly temporalized which, in turn, makes identity of self across time impossible. The different sense of self at distinct points in time is henceforth associated with different persons or ego resulting in what psychopathology describes as egodisorder. Although tentative (and speculative to a certain degree), this hypothesis can nevertheless be tested by linking mental time travel to self-related paradigms: one would expect that reduced midline neural activity during mental time travel predicts the degree of reduced self-related processing and subsequently the degree of egodisorder in schizophrenic patients.

Conclusion

In this study, we investigated the neural abnormalities in schizophrenia based on recent findings and linked them to phenomenal abnormalities in "sensible continuity" and "continuous change" in their "stream of consciousness." We pointed out that such neurophenomenal approach to time, eg, the "stream of consciousness," yields experimentally testable hypotheses and, even more important, may well account for some of the schizophrenic symptoms like thought block, auditory hallucinations, and delayed self (see the aforementioned section.). However, other symptoms like egodisturbances remain unexplained.

What do we gain clinically from the suggested neurophenomenal hypotheses? At the outset, they put forward experimentally testable hypotheses about the relationship between specific neural features like cortical midline variability and particular phenomenal features like "sensible continuity" and "continuous change." This will contribute to better understanding of the neurophenomenal relationships of the "stream of consciousness" in both healthy and schizophrenic subjects. Secondly, the specification of neurophenomenal relationships on both sides neurally and phenomenally may make possible the development of different diagnostic markers for the various phenomenal abnormalities and psychopathological symptoms in schizophrenia.

References

1. Parnas J, Sass LA, Zahavi D. Rediscovering psychopathology: the epistemology and phenomenology of the psychiatric object. *Schizophr Bull*. 2013;39:270–277.
2. Mesholam-Gately RI, Giuliano AJ, Goff KP, Faraone SV, Seidman LJ. Neurocognition in first-episode schizophrenia: a meta-analytic review. *Neuropsychology*. 2009;23:315–336.
3. James W. *The Principles of Psychology*. Vol 1. New York, NY: Holt; 1890.
4. James W. *The Principles of Psychology*. Vol 2. New York, NY: Holt; 1890.
5. Frith CD. *The Cognitive Neuropsychology of Schizophrenia*. London: Psychology Press; 1992.
6. Fuchs T. Temporality and psychopathology. *Phenomenol Cogn Sci*. 2013;12:75–104.
7. Martin B, Giersch A, Huron C, van Wassenhove V. Temporal event structure and timing in schizophrenia: preserved binding in a longer "now". *Neuropsychologia*. 2013;51:358–371.
8. Vogeley K, Kupke C. Disturbances of time consciousness from a phenomenological and a neuroscientific perspective. *Schizophr Bull*. 2007;33:157–165.
9. Northoff G. *Unlocking the Brain. Volume II: Consciousness*. Oxford: Oxford University Press; 2014.
10. Northoff G, Bermpohl F. Cortical midline structures and the self. *Trends Cognit Sci*. 2004;8:102–107.
11. Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. *Proc Natl Acad Sci USA*. 2001;98:676–682.
12. Northoff G. What the brain's intrinsic activity can tell us about consciousness? A tridimensional view. *Neurosci Biobehav Rev*. 2013;37:726–738.
13. Northoff G. Gene, brains, and environment-genetic neuroimaging of depression. *Curr Opin Neurobiol*. 2013;23:133–142.
14. Northoff G. *Unlocking the Brain: Volume 1: Coding*. Oxford: Oxford University Press; 2014.
15. Kühn S, Gallinat J. Resting-state brain activity in schizophrenia and major depression: a quantitative meta-analysis. *Schizophr Bull*. 2013;39:358–365.
16. Whitfield-Gabrieli S, Thermenos HW, Milanovic S, et al. Hyperactivity and hyperconnectivity of the default network in schizophrenia and in first-degree relatives of persons with schizophrenia. *Proc Natl Acad Sci USA*. 2009;106:1279–1284.
17. Pomarol-Clotet E, Honey GD, Murray GK, et al. Psychological effects of ketamine in healthy volunteers. Phenomenological study. *Br J Psychiatr*. 2006;189:173–179.
18. Mannell MV, Franco AR, Calhoun VD, Cañive JM, Thoma RJ, Mayer AR. Resting state and task-induced deactivation: a methodological comparison in patients with schizophrenia and healthy controls. *Hum Brain Mapp*. 2010;31:424–437.
19. Calhoun VD, Maciejewski PK, Pearlson GD, Kiehl KA. Temporal lobe and "default" hemodynamic brain modes discriminate between schizophrenia and bipolar disorder. *Hum Brain Mapp*. 2008;29:1265–1275.
20. Jafri MJ, Pearlson GD, Stevens M, Calhoun VD. A method for functional network connectivity among spatially independent resting-state components in schizophrenia. *Neuroimage*. 2008;39:1666–1681.

21. Park IH, Kim JJ, Chun J, et al. Medial prefrontal default-mode hypoactivity affecting trait physical anhedonia in schizophrenia. *Psychiatr Res*. 2009;171:155–165.

22. Williamson P. Are anticorrelated networks in the brain relevant to schizophrenia? *Schizophr Bull*. 2007;33:994–1003.

23. Hoptman MJ, Zuo XN, Butler PD, et al. Amplitude of low-frequency oscillations in schizophrenia: a resting state fMRI study. *Schizophr Res*. 2010;117:13–20.

24. Rotarska-Jagiela A, van de Ven V, Oertel-Knöchel V, Uhlhaas PJ, Vogeley K, Linden DE. Resting-state functional network correlates of psychotic symptoms in schizophrenia. *Schizophr Res*. 2010;117:21–30.

25. Yu Q, Sui J, Liu J, et al. Disrupted correlation between low frequency power and connectivity strength of resting state brain networks in schizophrenia. *Schizophr Res*. 2013;143:165–171.

26. Yu Y, Shen H, Zeng LL, Ma Q, Hu D. Convergent and divergent functional connectivity patterns in schizophrenia and depression. *PLoS One*. 2013;8:e68250.

27. Yu R, Chien YL, Wang HL, et al. Frequency-specific alternations in the amplitude of low-frequency fluctuations in schizophrenia. *Hum Brain Mapp*. 2014;35:627–637.

28. Lloyd D. Neural correlates of temporality: default mode variability and temporal awareness. *Conscious Cogn*. 2012;21:695–703.

29. Hanslmayr S, Backes H, Straub S, et al. Enhanced resting-state oscillations in schizophrenia are associated with decreased synchronization during inattentional blindness. *Hum Brain Mapp*. 2013;34:2266–2275.

30. Kam JW, Bolbecker AR, O'Donnell BF, Hetrick WP, Brenner CA. Resting state EEG power and coherence abnormalities in bipolar disorder and schizophrenia. *J Psychiatr Res*. 2013;47:1893–1901.

31. Kikuchi M, Hashimoto T, Nagasawa T, et al. Frontal areas contribute to reduced global coordination of resting-state gamma activities in drug-naïve patients with schizophrenia. *Schizophr Res*. 2011;130:187–194.

32. Ranlund S, Nottage J, Shaikh M, et al. Resting EEG in psychosis and at-risk populations a possible endophenotype? *Schizophr Res*. 2014;153:96–102.

33. Spencer KM. Baseline gamma power during auditory steady-state stimulation in schizophrenia. *Front Hum Neurosci*. 2011;5:190.

34. Razavi N, Jann K, Koenig T, et al. Shifted coupling of EEG driving frequencies and fMRI resting state networks in schizophrenia spectrum disorders. *PLoS One*. 2013;8:e76604.

35. Sun L, Castellanos N, Grützner C, et al. Evidence for dysregulated high-frequency oscillations during sensory processing in medication-naïve, first episode schizophrenia. *Schizophr Res*. 2013;150:519–525.

36. Uhlhaas PJ, Linden DE, Singer W, et al. Dysfunctional long-range coordination of neural activity during Gestalt perception in schizophrenia. *J Neurosci*. 2006;26:8168–8175.

37. Uhlhaas PJ, Phillips WA, Mitchell G, Silverstein SM. Perceptual grouping in disorganized schizophrenia. *Psychiatry Res*. 2006;145:105–117.

38. Uhlhaas PJ, Phillips WA, Schenkel LS, Silverstein SM. Theory of mind and perceptual context-processing in schizophrenia. *Cognit Neuropsychiatry*. 2006;11:416–436.

39. Uhlhaas PJ, Singer W. Neural synchrony in brain disorders: relevance for cognitive dysfunctions and pathophysiology. *Neuron*. 2006;52:155–168.

40. Uhlhaas PJ, Singer W. Abnormal neural oscillations and synchrony in schizophrenia. *Nat Rev Neurosci*. 2010;11:100–113.

41. Uhlhaas PJ, Singer W. Neuronal dynamics and neuropsychiatric disorders: toward a translational paradigm for dysfunctional large-scale networks. *Neuron*. 2012;75:963–980.

42. Ford JM, Dierks T, Fisher DJ, et al. Neurophysiological studies of auditory verbal hallucinations. *Schizophr Bull*. 2012;38:715–723.

43. Moran LV, Hong LE. High vs low frequency neural oscillations in schizophrenia. *Schizophr Bull*. 2011;37:659–663.

44. Buzsaki G. *Rhythms of the Brain*. Oxford: Oxford University Press; 2006.

45. Tan HR, Lana L, Uhlhaas PJ. High-frequency neural oscillations and visual processing deficits in schizophrenia. *Front Psychol*. 2013;4:621.

46. Spencer KM, Niznikiewicz MA, Nestor PG, Shenton ME, McCarley RW. Left auditory cortex gamma synchronization and auditory hallucination symptoms in schizophrenia. *BMC Neurosci*. 2009;10:85.

47. White TP, Joseph V, O'Regan E, Head KE, Francis ST, Liddle PF. Alpha-gamma interactions are disturbed in schizophrenia: a fusion of electroencephalography and functional magnetic resonance imaging. *Clin Neurophysiol*. 2010;121:1427–1437.

48. Kirihara K, Rissling AJ, Swerdlow NR, Braff DL, Light GA. Hierarchical organization of gamma and theta oscillatory dynamics in schizophrenia. *Biol Psychiatr*. 2012;71:873–880.

49. Uhlhaas PJ, Singer W. High-frequency oscillations and the neurobiology of schizophrenia. *Dialog Clin Neurosci*. 2013;15:301–313.

50. Suddendorf T, Addis DR, Corballis MC. Mental time travel and the shaping of the human mind. *Philos Trans R Soc Lond B Biol Sci*. 2009;364:1317–1324.

51. Botzung A, Denkova E, Manning L. Experiencing past and future personal events: functional neuroimaging evidence on the neural bases of mental time travel. *Brain Cognit*. 2008;66:202–212.

52. Fuchs T. Das Gehirn-ein Beziehungsorgan: eine phänomenologisch-ökologische. Stuttgart, Germany: Konzeption. W. Kohlhammer Verlag; 2009.

53. Fuchs T. The temporal structure of intentionality and its disturbance in schizophrenia. *Psychopathology*. 2007;40:229–235.

54. Angelopoulos E, Koutsoukos E, Maillis A, Papadimitriou GN, Stefanis C. Brain functional connectivity during the experience of thought blocks in schizophrenic patients with persistent auditory verbal hallucinations: an EEG study. *Schizophr Res*. 2014;153:109–112.

55. Zalla T, Verlut I, Franck N, Puzenat D, Sirigu A. Perception of dynamic action in patients with schizophrenia. *Psychiatr Res*. 2004;128:39–51.

56. Abraham A, Schubotz RI, von Cramon DY. Thinking about the future versus the past in personal and nonpersonal contexts. *Brain Res*. 2008;1233:106–119.

57. Nelson B, Whitford TJ, Lavoie S, Sass LA. What are the neurocognitive correlates of basic self-disturbance in schizophrenia?: integrating phenomenology and neurocognition. Part 1 (Source monitoring deficits). *Schizophr Res*. 2014;152:12–19.

58. Nelson B, Whitford TJ, Lavoie S, Sass LA. What are the neurocognitive correlates of basic self-disturbance in schizophrenia? Integrating phenomenology and neurocognition: part 2 (aberrant salience). *Schizophr Res*. 2014;152:20–27.

59. Northoff G, Heinzel A, de Greck M, Bermpohl F, Dobrowolny H, Panksepp J. Self-referential processing in our brain–a meta-analysis of imaging studies on the self. *NeuroImage*. 2006;31:440–457.