

# How Is Our Self Altered in Psychiatric Disorders? A Neurophenomenal Approach to Psychopathological Symptoms

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## Key Words

Consciousness · Cortical midline region · Stimulus processing

## Abstract

The self is central in our experience and has often been assumed to be necessary for any kind of consciousness in philosophy. Recent investigations in neuroscience demonstrate a particular set of regions such as the cortical midline regions to be associated with the processing of stimuli specifically related to the self as distinguished from those remaining unrelated to the self. Furthermore, findings show a close overlap between self-related activity and high levels of resting state activity in especially anterior midline regions. Interestingly, recent findings in psychiatric disorders such as depression and schizophrenia show resting state abnormalities in exactly these regions, that is in the cortical midline structures. Based on phenomenal and neural observations, I here suggest a neurophenomenal approach that directly links neuronal and phenomenal features (without sandwiching cognitive or sensorimotor functions) to psychopathological symptoms of self in depression and schizophrenia.

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## Introduction

You read these lines. You find them boring and your experience is thus signified by boredom. Who experiences this boredom? You. You are the subject of the experience of boredom. Without you as subject of this experience, you could not experience anything at all, not even boredom. This subject of experience has been described as the 'self'. It is your 'self' that makes it possible for you to experience things.

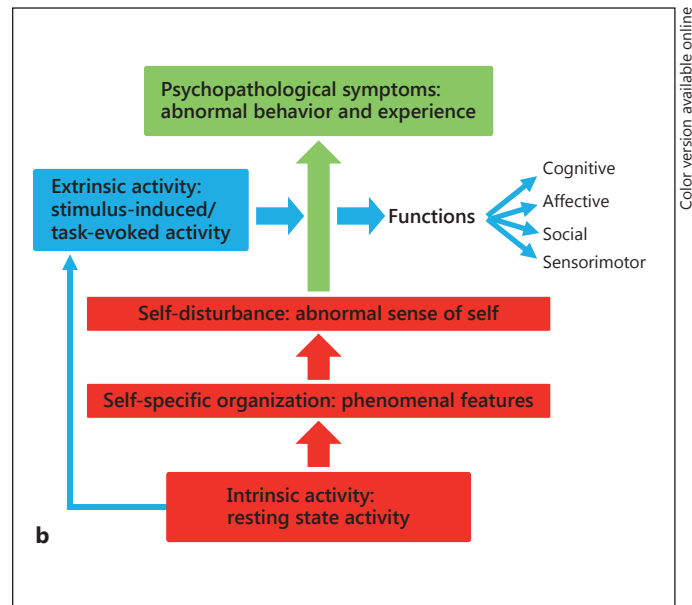
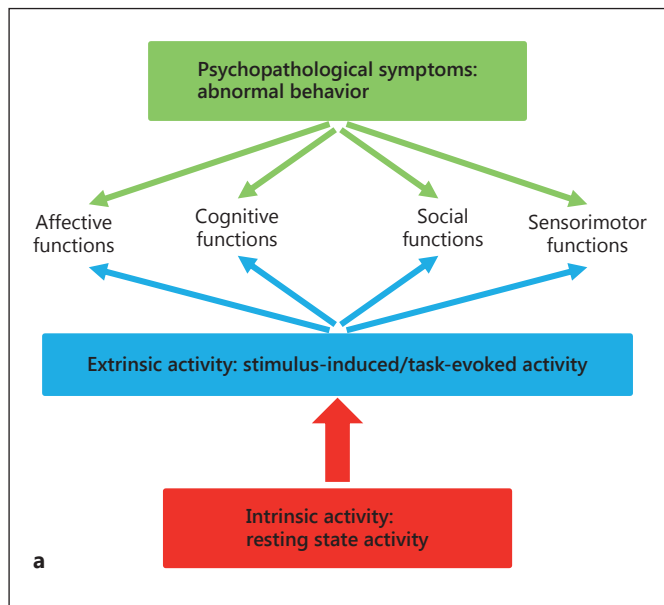
The self is a necessary condition for the possible constitution of experience and thus also consciousness. It is clear therefore that there is much at stake when it comes to the self. We thus need to discuss how to characterize and define the concept of self. Why is the self so important? Because we usually assume that somebody must have consciousness. Somebody speaks a language. And somebody acquires a second language when coming for instance to a new country. Without somebody we may remain unable to do all these things. Who though is this somebody? This is what is traditionally called self. Hence the self is of central relevance. Who though is this self, and how is it altered in the psychopathology of psychiatric disorders like depression and schizophrenia?

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**Fig. 1.** Neurocognitive and neurophenomenal approaches to psychopathology. **a** The neurocognitive approach considers the content of the various functions (affective, cognitive, social and sensorimotor) to be related to the various psychopathological symptoms (upper part). This attributes a central role to extrinsic activity, task-evoked or stimulus-induced activity. In contrast, the brain's intrinsic activity (lower part) bears no direct relationship to the psychopathological symptoms except for a yet unclear indirect one. While this approach can explain the psychopathological symptoms in terms of the functions and their extrinsic activity, the neural mechanisms underlying the abnormal sense of self in particular and subjective experience, e.g. consciousness of the environment, in general remain unclear in the neurocognitive ap-

proach. **b** The neurophenomenal approach attributes a central role to the brain's intrinsic activity in that it characterizes it by self-specific organization which is supposed to make possible, e.g. predispose, the sense of self in particular and subjective experience, e.g. consciousness, in general. Alterations in resting state activity in psychiatric disorders consequently entail an abnormal sense of self (lower part). That, in conjunction with abnormal extrinsic activity, as based on abnormal resting activity (left thin arrow), and the consecutively abnormal functions (cognitive, social, affective, sensorimotor; middle part), leads the various psychopathological symptoms including abnormal experience, e.g. consciousness of the environment (upper part).

This is the topic of the present contribution. Rather than going into much conceptual detail about the self [1–3], I here start right away with a definition of the self in the first part which is followed by discussing alterations of self in depression (part 2) and schizophrenia (part 3).

### Part 1: Definition and Neuroanatomy of the Self

#### *Definition of Self and 'Neurophenomenal Approach'*

The self is often conceptualized as cognitive, affective, social or sensorimotor, and as such associated with the respective functions in the brain [1, 2]. Phenomenological approaches emphasize the experience of self, the sense of self which is the definition I will presuppose in the following.

Most importantly, I presume that such a phenomenological approach to the self, the experience or sense of self, can

neuroscientifically be directly linked to neural features and relates to the brain's intrinsic activity, its resting state activity. I assume that the brain's intrinsic activity can account for phenomenal features of consciousness like the experience of self, the sense of self. Most importantly, I assume this neurophenomenal linkage to be direct without being mediated by sensorimotor, affective, cognitive and social functions as related to the brain's extrinsic activity, its stimulus-induced or task-evoked activity [4, 5]. Therefore, such a neurophenomenal approach focusing on the brain's intrinsic activity is to be distinguished from neurocognitive, neuroaffective, neurosocial, and neurosensorimotor approaches to the self and their focus on extrinsic activity (fig. 1a, b).

Most importantly I assume that such a neurophenomenal approach can better account for the disturbances of the self and its various psychopathological symptoms in psychiatric disorders such as depression and schizophre-

nia. This will be the focus in the following. Reasons of space will prevent me from giving a more general overview of the psychopathology of the self in other psychiatric disorders such as in addiction (see for instance de Greck et al. [6, 7]) and personality disorders (see Doering et al. [8]).

### *Self and Midline Regions*

Neuroanatomically, self-specificity has been investigated by applying self- and non-self-specific stimuli (like one's own name and names of others) during brain imaging. This yielded strong activity changes in especially the cortical midline regions [4, 5, 9].

Is there a subcortical-cortical midline system mediating the self? There is indeed some neuroanatomical ground justifying the assumption of such a subcortical-cortical midline system (see though the critical stance of Christoff et al. [10], Gillihan and Farah [11] and Legrand and Ruby [12], who consider the midline regions to be too unspecific while they presuppose a different more cognitive notion of the self as presupposed here). This is well documented in the threefold radial-concentric anatomical organization, with inner, middle and outer rings, that spans from the subcortical to cortical regions [1, 2, 13].

On the subcortical level the three rings group around the third ventricle. Most adjacent to it is the inner ring, the median part that extends to the aforementioned regions on the cortical level. This is followed by the paramedian and lateral core as middle ring and finally by the most outer lateral part, with both finding their continuation onto the cortical level. The threefold anatomical organization thus suggests integrated subcortical-cortical systems.

Simply put, the inner ring includes all cortical and subcortical regions directly adjacent to the ventricles such as the anterior and posterior cingulate on the cortical level, while the outer ring contains all regions that are visible on the outer surface of the brain such as the lateral prefrontal and parietal cortex and the sensory and motor cortices. The middle ring is sandwiched in between and contains on the cortical level the ventromedial prefrontal cortex (VMPFC), the dorsomedial prefrontal cortex (DMPFC) and the precuneus.

How is such a threefold subcortical-cortical neuroanatomical distinction related to the self? Does it map self-specificity better and more congruently than the traditional dichotomous medial-lateral distinction?

For answers to these questions, neurologist Todd Feinberg relies, much like traditional neurologists such as Charles Sherrington, on the careful study of neurological

patients. These patients suffer from lesions in particular regions of the brain and often experience bizarre changes in their phenomenal consciousness, including their sense of self. Feinberg attempts to explain his patients' unusual experience of the self with the concept of the threefold anatomical organization [14–16].

Feinberg [14] and Feinberg et al. [16] now assume that the inner ring reflects the bodily or 'interoself', while the outer ring may be rather related to the environmental self or the 'exteroself'. The middle ring is more related to the integration between both and thus the self proper, the 'integrative self', that spans across intero- and exteroceptive stimuli and thus body and environment. Moreover, results show that neural activity during self-related processing in especially inner and middle rings strongly overlaps with the level of resting state activity in especially anterior midline regions (such as VMPFC and perigenual anterior cingulate cortex, PACC; see chapter 23 in Northoff [5] for details).

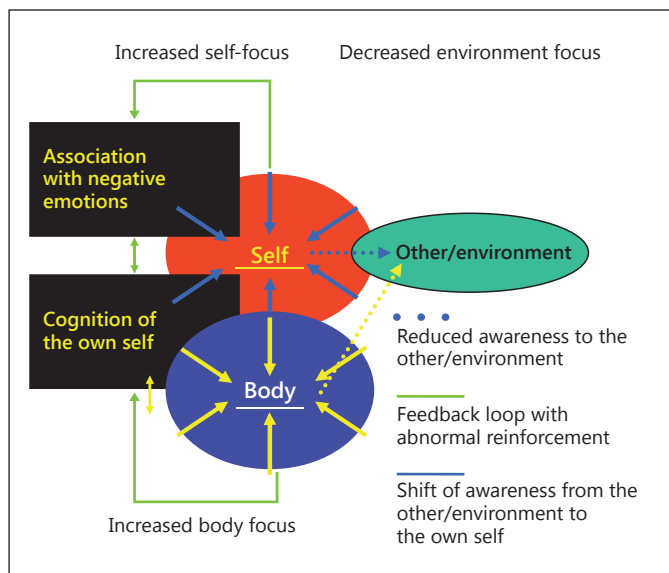
The overlap between resting state and self-related activity suggests that the former, the resting state activity, contains and encodes some yet unclear information about the self – this may conceptually be described as the resting state's 'self-specific organization' (see Northoff [5] for details). The resting state's self-specific organization is most relevant also for psychiatric disorders such as depression and schizophrenia that show abnormalities in both resting state and self.

## **Part 2: Self in Depression**

### *Psychopathological Symptoms: 'Increased Self-Focus' and 'Decreased Environment Focus' in Depression*

Major depressive disorder (MDD) is a psychiatric disorder that is characterized by extremely negative emotions, suicidal thoughts, hopelessness, diffuse bodily symptoms, lack of pleasure, that is anhedonia, ruminations and enhanced stress sensitivity [3, 13, 17, 18].

How do depressed patients experience their symptoms? This is dealt with in phenomenology that, loosely (and rather broadly) defined [for details, see Northoff [19]], describes the subjective experience of the depressive symptoms from the first person. Such a phenomenological approach has to be distinguished from the psychopathological approach that targets the depressive symptoms in the rather objective terms of observation in third-person perspective. To illustrate the subjective experience I want to start with a quote from a recent paper that nicely describes the alterations of the self in depression:



Color version available online

**Fig. 2.** Self, body and environment in depression: relationship between the different directions of phenomenal consciousness (here denoted as awareness) in depression. Phenomenal consciousness can be directed either externally towards the environment or internally towards either the own self or the body. In depression, there is increased directedness towards the own self and the body ('increased self- and body focus'), while the directedness towards the environment is decreased ('decreased environment focus'). The increased self- and body focus is symbolized by larger circles and inward arrows; the decreased relationship of both self and body to the environment is illustrated by dotted arrows. The consequences of the increased self-focus for subsequent psychological functions are indicated on the very left leading to increased association with negative emotions and increased cognitions of the own self.

She sat by the window, looking inward rather than looking out. Her thoughts were consumed with her sadness. She viewed her life as a broken one, and yet she could not place her finger on the exact moment it fell apart. 'How did I get to feel this way?' she repeatedly asked herself. By asking, she hoped to transcend her depressed state; through understanding, she hoped to repair it. Instead, her questions led her deeper and deeper inside herself – further away from the path that would lead to her recovery [20].

This description of a depressed patient shows three crucial characteristics concerning the self which shall be conceptualized as *increased self-focus*, *association of the self with negative emotions* and *increased cognitive processing of the own self* [21].

Let me start with the *increased self-focus*. Similar to our patient, almost all depressed patients look rather inward than outward, they focus very much on themselves while no longer being able to shift their focus on others (see arrows towards the self in fig. 2). Social-psychological the-

ory speaks of self-focused attention as focus on internal perceptual events, that is information from those sensory perceptions that react to changes in bodily activity [22]. The self-focus may also concern enhanced awareness of one's present or past physical behavior, that is heightened cognizance of what one is doing or what one is like. In addition to such an increased self-focus, the depressed patient's focus is often also on his/her own body. Depressed patients show heightened awareness of their own body which phenomenologically results in the subjective perception of diffuse bodily symptoms [23]. The increased self-focus may consequently be accompanied by what I call 'increased body focus'.

The increased self- and body focus implies that the depressed subject's attention is no longer focused on its relation to the environment and environmental events, as in healthy subjects, but rather on itself as the prime focus with the environment shifting into the background. Hence the increased self-focus goes along with what one may call 'decreased environment focus'.

The concept of the *decreased environment focus* describes that the patient's subjective experience and perception are no longer directed towards the environment and its respective persons and events. Instead, the patient's subjective perception and experience are rather directed at his/her own body and own cognition, thus resulting in what I here describe as 'increased self-focus'. This means that the balance between the environment focus and the self-focus is unilaterally shifted to the latter in depression at the expense of the former. Therefore, the decreased environment focus entails the increased self-focus (and vice versa; fig. 2).

This is also supported by recent empirical data. Empirical research clearly indicates heightened self-focused attention in depression. A variety of studies assessing self-focused attention with diverse measures and methodologies all converge on the finding of an increased and perhaps prolonged level of self-focused attention in depression [22]. What remains unclear though is whether this increased self-focus is purely explicit and thus conscious or whether it is already present on an implicit and thus unconscious level.

Another characteristic is the attribution of negative emotions to the own self, *the association of the own self with negative emotions*. The own self is associated with abnormal sadness, guilt, mistakes, inabilities, death, illness, etc. which may ultimately result in delusions of guilt. A recent study investigating symptom clusters in the Beck Depression Inventory observed 3 factors, among them the self-blame factor [24]. Interestingly, depressed pa-



tients with previous suicide attempts showed significantly higher scores on the Beck Depression Inventory self-blame factor than those without suicide attempts. Moreover, the self-blame factor significantly correlated with the total number of suicide attempts and with known risk factors for suicidal behavior [for a review, see 21]. Such self-blame possibly results from the association of the self with predominantly negative emotions in depression while at the same time these patients remain apparently unable to attribute any kind of positive emotions to their self.

Finally, there is also *increased cognitive processing of the own self*. Our patient described above typically suffers from increased cognitive processing, she thinks about herself and her mood and tries desperately to discover the reasons for her depression and thereby gets only deeper and deeper into the depressed mood (see arrows from negative cognitions to the self in fig. 2). This cognitive processing of the own self is described as rumination and is often considered a method of coping with negative mood that involves increased self-focused attention and self-reflection [22].

#### *Neuronal Findings: Resting State and Its Anatomical Organization*

Let me first describe the findings of altered resting state activity in MDD. Because of several excellent reviews about the structural and functional brain changes in MDD [25–30], we here briefly highlight only the main findings and conclusions from these various reviews and then relate them to functional networks as delineated in normal-healthy brains [for recent reviews, see 3, 17].

Alcaro et al. [25] conducted a meta-analysis of all imaging studies in human MDD that had focused on resting state activity. This yielded hyperactive regions in the PACC, the VMPFC, thalamic regions such as the dorsomedial thalamus and the pulvinar, pallidum/putamen and midbrain regions such as the ventral tegmental area, substantia nigra, the tectum and the periaqueductal gray. In contrast, resting state activity was hypoactive and thus reduced in the dorsolateral prefrontal cortex (DLPFC), the posterior cingulate cortex (PCC) and adjacent precuneus/cuneus [25].

These results are well in accordance with other meta-analyses [30–33], which emphasized the role of the hippocampus, parahippocampus and the amygdala where resting state hyperactivity was also evident in MDD. Interestingly, the very same regions and the PACC also show structural abnormalities with reduced gray matter volume in imaging studies and reduced cell count mark-

ers of cellular function in postmortem studies [30, 32, 33]. Involvement of these regions in MDD is further corroborated by the investigation of resting state activity in animal models of MDD. Reviewing evidence for resting state hyperactivity in various animal models yielded diverse participating brain regions – the anterior cingulate cortex, the central and basolateral nuclei of the amygdala, the bed nucleus of the stria terminalis, the dorsal raphe, the habenula, the hippocampus, the hypothalamus, the nucleus accumbens, the PAG, the dorsomedial thalamus (DMT), the nucleus of the solitary tract, and the piriform and prelimbic cortex [25]. In contrast, evidence of hypoactive resting state activity in animal models remains sparse with no clear results [25].

Taken together, these findings indicate *abnormally high resting state activity in extended subcortical and cortical medial regions* of the brain. This has led authors like Phillips [34], Mayberg [26–28] and Drevets and colleagues [30, 32, 33] to assume dysfunction in the limbic system in depression or more specifically in the ‘limbic-corticostriatopallidothalamic circuit’ with reciprocal interactions between medial prefrontal and limbic regions being crucial [30].

#### *Neuronal Findings: Resting State Imbalance between Inner and Outer Rings*

How do these findings fit into the delineated anatomical characterization of the healthy brain as characterized by inner, middle and outer rings? What was conceptualized as inner and middle rings at the cortical level, the paralimbic areas and the cortical midline structures generally shows hyperactivity during the resting state in MDD.

Another observation fits well with this anatomical model in the healthy brain. The outer ring covers the lateral regions on the cortical level such as the DLPFC and the sensory and motor regions. Especially in the DLPFC and in part also in the motor cortex [25], resting state hypoactivity has been consistently observed, especially in MDD.

Considering these findings together, resting state activity in MDD may be characterized by a *subcortical-cortical imbalance between inner/middle and lateral rings*. More specifically, the inner and middle rings’ regions seem to be hyperactive in the resting state. In contrast, subcortical and especially cortical regions of the lateral-cognitive ring, such as the lateral prefrontal cortex and the sensorimotor cortices, seem to show hypoactivity in the resting state [13].

### *Neuropsychopathological Hypothesis I: Resting State Hyperactivity and Increased Self-Focus in Depression*

The aforementioned findings indicate an imbalance in the resting state activity between inner/middle and outer rings. More specifically, they show that resting state activity in the anterior portions of the inner ring and also to some degree in the middle ring is abnormally elevated, while the outer ring's resting state activity is decreased. This means that there is a dysbalance in the resting state activity in depression along the aforementioned inner-to-outer and anterior-to-posterior gradients.

I now assume the balance between the three anatomical rings and their corresponding functional connectivity to be central in constituting the balance between self- and non-self-specific, e.g. internal and external, contents in our mental states. The neural balance between midline and lateral networks is central in designating contents as internal or external (see chapter 25 in Northoff [5] for details). Since the neuronal balance between the three anatomical rings is altered in depression, one would expect a shift toward increased internal contents and decreased external contents. This indeed is the case and surfaces on the phenomenal level, as I describe in the following.

Phenomenally, a core symptom in MDD is the extremely increased focus on the own self. All thoughts and feelings are circulating around the own self, the own person, which we described as increased self-focus [3, 21]; see also Lemogne [35], who distinguishes such an increased self-focus as associated with phasic VMPFC hyperactivity from its phasic DMPFC-mediated cognitive elaboration. Such an increased self-focus goes along with detachment from the environment, that is from the persons, objects and events, with the patients feeling disconnected. We described this as 'decreased environment focus' [13]. The question is now how the shift in the focus from the environment to the self, that is decreased environment focus and increased self-focus, is generated. For that, we turn to the resting state activity in MDD.

One would consequently expect elevated resting state activity in the midline regions to lead to increased self-specificity and hence to abnormally increased personal concerns in patients with MDD during both resting state and stimulus-induced activity. While it remains to be demonstrated for the resting state activity, it holds true indeed for stimulus-induced activity. Grimm et al. [36, 37] from our group (and others such as Lemogne et al. [35, 38–40] who also distinguish between phasic and tonic activity) observed that depressed patients assigned a higher self-relatedness score (than healthy subjects) to especially negative emotional pictures. Neuronally this

went along with decreased signal changes during self-specific stimuli in anterior cortical midline regions. This supposedly reflects the abnormally high resting state activity and its increased assignment of self-specificity to stimuli.

The assumption of increased self-specificity on the phenomenal level is further supported by the observation of a correlation between the increased behavioral scores of self-specificity and the decreased stimulus-induced activity in especially the anterior midline structures. One may consequently hypothesize that the increased self-specificity as observed behaviorally stems from the abnormally increased resting state activity in the midline regions and their apparently increased self-specific processing [36, 37].

What do these findings imply in neurophenomenal regard? We observed decreased stimulus-induced activity in the anterior midline regions, while at the same time the stimuli were assigned increased degrees of self-specificity. How is it possible that decreased stimulus-induced activity goes along with increased self-specificity? I assume that this is due to the carryover and transfer of the increased resting-state activity and its abnormal self-specific organization onto subsequent stimulus-induced activity.

Let me be more specific. The increased resting state activity makes it impossible for the stimulus to induce major activity changes, hence the decreased stimulus-induced activity. And the associated carryover and transfer of the resting state's abnormal self-specific organization is increased and consecutively leads to the assignment of abnormally high degrees of self-specificity to the stimuli, hence the conjunction of neuronal decreases in stimulus-induced activity and behavioral increases in self-specificity.

### *Neuronal Findings: Abnormal Exteroceptive Processing in Depression*

Patients with MDD often suffer from generalized bodily symptoms such as heart pounding, increased breathing (with yawning) and multiple-diffuse bodily aches. This seems to go along with abnormally increased awareness of their own bodily processes (body perception), including sensitivity to stress and autonomic-vegetative changes as demonstrated in a recent work [23].

The same study also investigated the neuronal activity during exteroceptive and interoceptive awareness (tone and heartbeat counting) in relation to the brain's resting state activity. Interoceptive stimuli by themselves (e.g. the heartbeat) induced a 'normal' degree of brain signal changes (activation) in the bilateral anterior insula in de-

pressed patients when considered relative to the preceding resting state activity levels. This suggests that there is no abnormality in interoceptive stimulus processing itself in depression.

In contrast to stimulus-induced activity during interoceptive stimuli, we observed abnormally reduced activity during exteroceptive stimuli. More specifically, we observed that exteroceptive stimuli induced decreased stimulus-induced activity in the insula in depressed patients when compared to healthy subjects. This let us further question whether such a reduced activity is related either to the exteroceptive stimulus itself or rather to abnormal resting state activity levels. The latter was indeed the case, as we observed increased resting state activity in the insula itself. This is well in line with the resting state hyperactivity in the inner ring, the core-paralimbic system to which the insula belongs.

To test for independent changes in exteroceptively related stimulus-induced activity, we then calculated the exteroceptively related stimulus-induced activity relative to the preceding resting state activity level. Interestingly, the initially observed difference between healthy and depressed patients in 'absolute', for example, resting-state-independent, signal changes during exteroceptive stimuli when calculating them in such a 'relative' way is dependent on the preceding resting state activity level. Hence, when including the resting state activity level, there was no difference anymore between healthy and depressed subjects in signal changes during exteroceptive processing.

In contrast to the exteroceptive stimuli, no differences between healthy and depressed subjects were evident in interoceptive stimuli in both relative and absolute signal changes. This difference between interoceptive and exteroceptive stimuli with regard to relative and absolute signal changes suggests a differential interaction of both kinds of stimuli with resting state activity. Either rest-stimulus interaction is reduced during exteroceptive stimuli or rest-stimulus interaction is increased during interoceptive stimuli, which cannot be differentiated on the basis of our findings.

What is clear is that there is imbalanced activity between intero- and exteroceptive stimulus processing, including their respective interaction with the resting state activity level. Because of the paucity of work in this area, additional imaging studies need to investigate changes in interoceptive processing in depression.

The study by Wiebking et al. [23] also investigated psychological measures of body perception, employing the body perception questionnaire. They found the body per-

ception questionnaire scores to be significantly increased in depressed patients as being indicative of increased bodily awareness. Most interestingly, unlike in healthy subjects, the increased body perception questionnaire scores no longer correlated with the signal changes during the resting state and the exteroceptive condition.

This suggests that depressed patients no longer properly modulate their degree of neuronal activity. They remain apparently unable to properly downmodulate the perception and awareness of their own body and to shift attention from the body to the environment. This may explain the many somatic complaints that characterize MDD. Though tentative, such a lack of correlations with abnormally increased neuronal activity has also been seen for other psychological measures in depression like excessive negative affect, self-specificity and negativistic temporal projections to future possibilities [23, 35, 37, 40].

#### *Neuropsychopathological Hypothesis II: Dysbalance between Internal and External Mental Contents in Depression*

These findings are indicative of an imbalance in the neural processing between interoceptive and exteroceptive stimuli, with only the latter but not the former inducing decreased neural activity. This may consecutively lead to relatively increased neural processing of interoceptive processing and rest-interoceptive interaction when compared to the apparently absolutely reduced exteroceptive processing and rest-exteroceptive interaction. As already noted, this abnormal shift toward interoceptive processing may psychopathologically promote increased bodily awareness and subsequent concerns with undesired bodily symptoms.

Meanwhile, the decreased exteroceptive processing may be accompanied by reduced awareness of and concern with environmental changes, especially positive events that could beneficially impact depression (fig. 2). This means that, phenomenally, one may want to speak not only of an increased self-focus, but also of an increased bodily focus and a decreased environment focus (see also Northoff et al. [13]).

Why though are rest-exteroceptive interaction and external awareness reduced when compared to rest-interoceptive interaction and internal (i.e. self- and bodily) awareness? Recall that I assumed the increased self-focus and increased self-specificity during stimulus-induced activity to be traced back to the increased resting state activity and the anterior regions of the inner ring, the midline network. At the same time, however, the resting state

data also showed decreased resting state activity in the lateral regions of the outer ring (see earlier).

Taken together, the resting state's abnormally high activity and strong self-specific organization are manifest in increased self-specificity and increased internal contents in mental states at the expense of external contents. This is reflected in the description of an increased self-focus and a decreased environment focus (see earlier). That is possible only if the resting state's organization is dysbalanced toward internal contents, which I assume to correspond to the abnormal neural balance between midline and lateral networks, that is between inner/middle and outer rings.

### Part 3: Self in Schizophrenia

#### *Psychopathological Symptoms: Abnormalities of Self in Schizophrenia*

Early psychiatrists like E. Kraepelin and E. Bleuler at the beginning of the 20th century assumed abnormality of the self to be basic in schizophrenia. Unlike in our times, these early psychiatrists had to rely on nothing but clinical observation. Based on that, they assumed an abnormal change of the self to be fundamental in schizophrenia.

More specifically, Kraepelin [41] characterized schizophrenia as 'the peculiar destruction of the *inner coherence of the personality*' with a *'disunity of consciousness' ('orchestra without conductor')*. Bleuler [42] also pointed out that schizophrenia is a 'disorder of the personality by splitting, dissociation' where the 'I is never completely intact'.

A contemporary of Bleuler and Kraepelin, Berze [43] even referred to schizophrenia as 'basic alteration of self-consciousness'. Jaspers [44] also noticed 'incoherence, dissociation, fragmenting of consciousness, intrapsychic ataxia, weakness of apperception, insufficiency of psychic activity and disturbance of association, etc.' to be basic as unifying 'central factors' in schizophrenia.

The early descriptions of a disrupted self are complemented by current phenomenological accounts that focus predominantly on the experience of the own self in relation to the world. Parnas [45] and Parnas et al. [46] describe what they call 'presence' as being altered in schizophrenia. The experience of the world and its objects is not accompanied by a prereflective self-awareness anymore.

Let me specify this point. The own self, the self that experiences the experience of the world, is no longer included in that very experience:

The prominent feature of altered presence in the pre-onset stages of schizophrenia is disturbed ipseity, a disturbance in which the sense of self no longer saturates the experience. For instance, the sense of mineness of experience may become subtly affected: one of our patients reported that this feeling of his experience as his own experience only 'appeared a split-second delayed' [45].

The patients remain unable to refer to themselves in their experience of the world. It is as if the experience of the world is no longer their own experience of their own self. This leads in later stages to passivity phenomena, e.g. delusions of passivity, and ego disturbances where their experience may belong to and be experienced by someone else rather than being associated with the own self. Due to the absence (as opposed to presence) of the own self in their experience of the world, patients with schizophrenia become detached, alienated and estranged from their own experience. Such a detachment of the experiences from their own self makes it impossible for them to experience their experiences as subjective and thus as belonging to their own self.

The experiencing self is consequently no longer affected by its own experiences, which Sass and Parnas [47] describe as 'disorder of self-affectivity': the own self is no longer experienced as the own self and most importantly is no longer experienced as the vital center and source of the own experiences, actions, perceptions, thoughts and so on. This reflects what Sass and Parnas [47] call the 'diminished self-affectation', meaning that the self is no longer affected by its own experiences.

If, however, the self is not affected anymore by its own experience, the self stands apart from the objects and the events in the world that are experienced. A gulf, a phenomenological distance as Parnas [45] says, opens up between world and self. The objects and events of the world no longer make intuitive sense and are thus not meaningful anymore to the experiencing subject. The own self becomes thus almost objective and mechanical in its experience and perception of the world.

#### *Neuronal Findings: Resting State in Schizophrenia*

Various studies investigated recently the default mode network in schizophrenia (see Kuhn and Gallinat [18], for a recent review). Recent imaging studies in schizophrenia reported abnormal resting state activity and functional connectivity in the anterior cortical midline structures (CMS). One study [48] demonstrated that the anterior CMS (and posterior CMS such as the PCC/pre-cuneus) show decreased task-induced deactivation (TID) during a working memory task. This was observed in both schizophrenic patients and their relatives when



compared to healthy subjects. That 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 anterior CMS 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 task-related suppression, the more increased the degree of functional connectivity. Finally, both decreased TID and increased functional connectivity in anterior CMS correlated with psychopathology, that is, the predominantly positive symptoms as measured with the Positive and Negative Syndrome scale.

Decreased TID in anterior CMS was also observed in an earlier study that investigated working memory [49]. Similar to the study described earlier, they let subjects perform a working memory task and observed abnormally decreased TID in anterior CMS in schizophrenic patients when compared to healthy subjects. And similar to the other study, they also observed abnormal task-related activation in the right dorsolateral prefrontal cortex in schizophrenic patients. Another study [50] also reported abnormal TID in anterior CMS as well as abnormal functional connectivity from anterior CMS and posterior CMS to the insula in schizophrenic patients [51–54].

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, Hoptman et al. [55] demonstrated that low-frequency fluctuations in the resting state were increased in the anterior CMS (and the parahippocampal gyrus) in schizophrenic patients, while they were decreased in other regions such as the insula. Abnormally increased low-frequency oscillations (<0.06 Hz) in the anterior CMS (and posterior CMS regions and the auditory network) and their correlation with positive symptom severity were also observed in another study on schizophrenic patients [56].

#### *Neuronal Findings: Self-Specificity in Schizophrenia*

This concerns alterations in the resting state activity. How about changes during stimulus-induced activity and their relation to self-specificity?

A recent imaging study by Holt et al. [57] showed that abnormal anterior-to-posterior midline connectivity is related to self-specificity. They investigated schizophrenic patients during a word task where subjects had to judge trait adjectives according to their degree of self-specificity

(and also two other tasks: other reflection, i.e. relation of that word to another person) and perception reflection (i.e. word printed in uppercase or lowercase letters).

How about their results? Schizophrenic patients showed significantly elevated activity in posterior midline regions such as the mid- and posterior cingulate cortex during self-reflection, while signal changes in the anterior midline regions such as the medial prefrontal cortex were significantly reduced when compared to healthy subjects. Finally, functional connectivity was abnormally elevated from the posterior to the anterior midline regions in schizophrenic patients. Analogous results of altered midline activity with a dysbalance between anterior and posterior midline regions are also observed in other studies on self-specificity in schizophrenia [58].

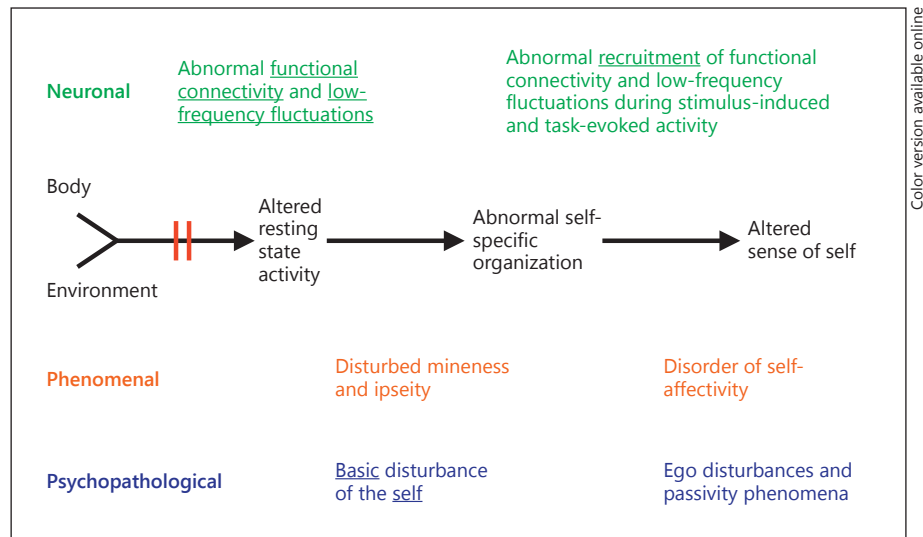
Taken together, these results demonstrate *abnormal resting state activity in especially the anterior and posterior midline network in schizophrenia* (see Kuhn and Gallinat [18] for a recent meta-analysis). The very same network also shows *alterations in the balance between anterior and posterior midline regions when probing for self-specific stimuli*.

#### *Neuropsychopathological Hypothesis Ia: 'Basic Disturbance of the Self' in Schizophrenia*

How do these findings relate to the psychopathological and phenomenological descriptions? I assume that what the early psychiatrists described as 'the peculiar destruction of the inner coherence of the personality' or 'basic alteration of self-consciousness' may correspond to what here refers to the changes in the resting state's self-specific organization. Let me spell this out in further detail.

Following the early descriptions, the basic disturbance in the self is supposed to impact all other subsequent functions and domains of the personality. Analogously, I assume the resting state's self-specific organization to also affect any subsequent stimulus-induced activity and consecutively all functions, including sensory, motor, affective and cognitive functions (as it seems indeed to be the case in cognitive, affective, sensory and motor functions). In the same way the basic disturbance of the self is present everywhere, the resting state, metaphorically speaking, 'has its hands' in all kinds of neural processing.

How is such overall presence of the 'basic disturbance of the self' possible? It must indeed be very basic. As basic as, for instance, the resting state is basic to any kind of subsequent stimulus-induced activity. And it must be carried over and transferred to the subsequent stimulus and its associated contents and functions. I thus assume that what the early psychiatrists described as 'basic distur-



**Fig. 3.** Resting state activity and the ‘basic disturbance of self’ in schizophrenia. The middle part with the arrows shows different stages in the constitution of an altered sense of self in schizophrenia. Based on empirical findings, I assume the constitution of the brain’s resting state activity, as based on the continuous input from body and environment, to be abnormal in schizophrenia. That leads to altered resting state activity including alterations in its self-specific organization which ultimately leads to an altered sense of self. *Neuronally* (upper part) this is mediated by abnormal low-frequency fluctuations and functional connectivity in the resting state. That, in turn, leads to abnormal recruitment of the resting state activity during stimulus-induced or task-evoked activity

(right part). *Phenomenally*, the altered self-specific organization of the resting state may be related to what phenomenologically has been described as ‘basic disturbances of mineness and ipseity’ where the own experiences and mental states are no longer linked to and suffused by the subjectivity of the own self. That ultimately leads to a ‘disorder of self-affectivity’ where the own self is no longer affected by external stimuli and tasks in subjective experience as it is related neuronally to abnormal stimulus-induced or task-evoked activity. *Psychopathologically*, the resting state’s abnormal self-specific organization may reflect the ‘basic disturbances of self’ which is central in predisposing ego disturbances and passivity phenomena during exposure to external stimuli and tasks.

bance of the self’ is carried over and transferred to every domain of the subject’s mental life. In the very same way the resting state’s abnormal self-specific organization is carried over and transferred to the subsequent stimulus-induced activity and its associated functions (fig. 3).

I now assume the resting state and its abnormal self-specific organization to be carried over and transferred to subsequent stimulus-induced activity and thus any kind of neural processing. This may then be manifest in the various neural abnormalities in schizophrenia related to sensorimotor, affective, cognitive and social functions, e.g. its extrinsic or stimulus-induced/task-evoked activity.

*Neuropsychopathological Hypothesis Ib: Abnormal Self-Specific Organization in Schizophrenia and Its Manifestation in Experience*

How do these phenomenal descriptions relate to the here postulated neuronal mechanisms? I assume that they reflect an abnormal self-specific organization in the rest-

ing state as it is carried over and transferred to subsequent stimulus-induced activity. This is in accordance with the earlier described neuronal results of an abnormal resting state and abnormal neural activity during self-specific stimuli.

Let me be more specific. Due to the resting-state abnormalities, the stimulus cannot be properly integrated into the resting state’s self-specific organization. The lack of the stimulus’s integration into the resting state’s self-specific organization leads then to a lack of self-specificity of the stimulus itself during stimulus-induced activity.

This decreased or lacking assignment of self-specificity to the stimulus is then phenomenally manifest in what is described as decreases in both self-affectation and sense of mineness and belongingness. That amounts to exactly the way Parnas and others characterize experience in schizophrenia by ‘disturbed mineness and ipseity’ and the ‘disorder of self-affectivity’ which psychopathologically is reflected in ‘basic disturbance of self’ (and ego disturbances and passivity phenomena; see above and fig. 3).

## Conclusion

I focused on the abnormalities of resting state activity across different regions in MDD and schizophrenia.

Both disorders and their respective symptoms point out the central role of the resting state in these disorders in general and its particular relationship to the abnormalities of the self. Most importantly, in our neuropsychological approach, the direct linkage between resting state activity and phenomenal features can well account for the various psychopathological symptoms related to the self in both schizophrenia and depression. Though

these are the first steps in this direction, such a neuropsychological approach may prove useful in the future in providing diagnostic and therapeutic markers and, ideally, novel forms of resting state-based therapies in psychiatric disorders.

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