

REVIEW ARTICLE

Phenomenology and the Role of Selfhood Disorders

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Abstract: Schizophrenia remains challenging to fully comprehend due to insufficient attention to its characteristic overall pattern, or "Gestalt," which defines its psychopathological structure. Schizophrenia is a chronic psychiatric condition influenced by diverse genetic and neurobiological factors impacting early brain development. It manifests through psychotic symptoms including hallucinations, delusions, disorganization, and cognitive impairments. Although gross brain pathology is absent, subtle pathological changes occur in specific neural cell populations and their communication. Neuroimaging reveals functional abnormalities in information processing among both first-episode and chronic patients. While pharmacological treatments can alleviate psychotic symptoms, they often do not significantly enhance social, cognitive, or occupational functioning. Psychosocial interventions such as cognitive-behavioral therapy, cognitive remediation, and supported education and employment programs offer value but are inconsistently applied. Early identification and preventive strategies are crucial due to the disorder's early onset and varying prevalence influenced by urbanization and immigration patterns. This article argues that disorders of selfhood are pivotal in shaping this Gestalt. Initially, it provides a phenomenological exploration of the self, followed by an examination of common complaints in schizophrenia that reflect disturbances in self-perception, often tracing back to childhood experiences. The characteristic features of schizophrenic psychosis, such as "double bookkeeping," hallucinations, and delusions, are then discussed in relation to their association with instability in self-representation. The article briefly recounts an encounter with a schizophrenia patient, highlighting the diagnostic significance of self-disorders.

Keywords: Schizophrenia; Selfhood; Phenomenology; Psychosis; Neurobiology.

1. Introduction

Schizophrenia is a complex psychiatric condition affecting approximately 1% of the global population and ranking among the top 10 causes of disability worldwide [1]. It is characterized by a spectrum of symptoms, including positive psychotic symptoms such as hallucinations and delusions, negative symptoms like reduced motivation, and cognitive impairments affecting memory and mental processing speed [2]. These symptoms vary widely among individuals, contributing to significant disability and hindering full recovery. Many patients also face social isolation, stigma, and high unemployment rates [3,4]. The disorder's impact extends beyond symptoms, influencing life expectancy, which is shortened by 13 to 15 years due to factors like poor diet, substance use, and associated health issues [4,5]. Additionally, the risk of suicide among those with schizophrenia is notably high, affecting 5% to 10% of patients during their lifetime [6]. Despite its prevalence, schizophrenia's diagnostic criteria, causes, and pathophysiology remain incompletely understood, complicating treatment approaches. While current therapies focus primarily on managing psychotic symptoms, negative and cognitive symptoms often respond inadequately to antipsychotic medications [2,4].

Historically, schizophrenia has been viewed through different lenses, with early descriptions emphasizing broader aspects beyond just positive symptoms like delusions and hallucinations [4]. Diagnosis involves a thorough psychiatric evaluation to exclude other potential causes of psychosis, considering risk factors such as birth complications, family history, and environmental influences like cannabis use and childhood trauma [6,7]. Recent research also suggests a significant role for neuroinflammation and immune dysregulation in the pathogenesis of schizophrenia, with evidence of altered cytokine levels and microglial activation in the brains of affected individuals [8,9].

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2. Aetiology

Schizophrenia sometimes runs in families, affecting less than 1 percent of the general population but rising to 10 percent among those with first-degree relatives who have the disorder. Environmental factors like prenatal exposure to viruses, malnutrition, and birth complications may contribute. Scientists note structural brain differences in those with schizophrenia, such as larger ventricles and elevated dopamine levels, though the exact mechanisms remain unclear [8]. Recent advances have greatly enhanced our understanding of schizophrenia's etiology. Although no single cause has been identified, insights into brain physiology have grown. Schizophrenia is now widely seen as a neurodevelopmental disorder [10], with key etiological factors being genetic influences, brain abnormalities, and environmental factors [9,11].

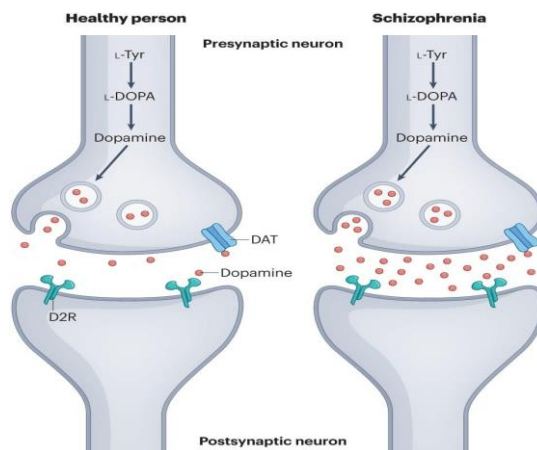


Figure 1. Pathophysiology of schizophrenia-dopamine pathway

Genetic studies have identified numerous risk loci associated with schizophrenia, with the largest genome-wide association study to date implicating over 100 genetic regions [12]. These findings suggest a highly polygenic architecture, with many common variants of small effect contributing to risk. Rare copy number variants and de novo mutations have also been implicated, particularly in cases with an early onset [13]. Gene expression studies point to disruptions in pathways related to synaptic function, neurodevelopment, and immune regulation [14]. Environmental factors, particularly those operating during critical periods of brain development, are also thought to play a significant role. Prenatal exposures to maternal infection, malnutrition, and obstetric complications have been associated with increased risk [15]. Urban birth and upbringing, as well as migration, have also been consistently linked to elevated rates of schizophrenia, possibly reflecting the impact of social adversity and marginalization [16]. Cannabis use, especially during adolescence, has emerged as another important environmental risk factor [17]. Integrating these genetic and environmental influences, the neurodevelopmental hypothesis posits that schizophrenia arises from subtle disruptions in brain development, beginning prenatally and continuing through adolescence [10]. These disruptions are thought to affect the formation and refinement of neural circuits, particularly those involving the prefrontal cortex and its connections with subcortical regions [18]. The resulting alterations in brain structure and function may then interact with later environmental stressors to trigger the onset of psychotic symptoms [19]. While much progress has been made, the precise interplay of genetic, environmental, and neurodevelopmental factors in the etiology of schizophrenia remains an active area of research. Continued efforts to elucidate these complex pathways will be crucial for developing targeted preventive and therapeutic strategies

3. Pathophysiology

The primary positive, negative, and cognitive symptoms of schizophrenia have been associated with many neurotransmitters, but subcortical dopamine dysfunction remains a key factor in psychotic symptoms. Presynaptic dopamine dysfunction appears to mediate psychosis in schizophrenia. Stimulants such as amphetamines enhance dopamine effects and may induce psychotic symptoms in healthy individuals. When people with schizophrenia take stimulants, they are more sensitive to psychotic effects due to increased subcortical synaptic dopamine content, dopamine synthesis, and abnormally high dopamine release following amphetamine administration. Positron emission tomography (PET) studies have shown that the increased synaptic dopamine content is localized in the striatum. In patients with schizophrenia, alterations in dopamine function within the striatum cause delusions and psychosis [9]. The thalamus is the central relay station that transmits all information to and from the cerebral cortex. The primary circuit responsible for psychotic symptoms forms between the thalamus, cerebral cortex, and associative striatum, where changes in any of these regions can impair the whole network (Figure 1). Many more pathways are involved directly or indirectly with this circuit, such as the amygdala and hippocampus, which are responsible for perception and emotion regulation. Dysfunction of the thalamus and cerebral cortex largely affects the striatum and D2 receptors, causing hallucinations and delusional symptoms [9].

Studies have shown that dopamine neurons not only release dopamine in a synaptic signal mode but also release co-transmitters glutamate and gamma-aminobutyric acid (GABA). Glutamate in the excitatory pathway and GABA in the inhibitory pathway transmit various patterns of dopamine neuron activity to the striatum. The N-methyl-D-aspartate (NMDA) receptor antagonists such as ketamine and phencyclidine (PCP) can disrupt the thalamus circuit and lead to cognitive dysfunction and psychotic symptoms [9]. Similar to amphetamine, individuals with schizophrenia are more sensitive to the effect of these medications. Hypofunction of NMDA receptors may be associated with the pathogenesis of schizophrenia; therefore, treatment with D-serine, glycine, and sarcosine, which modulate NMDA receptors, can be beneficial, especially for negative symptoms [10]. GABA interneurons such as chandelier neurons have reduced immunostaining for the GABA transporter, which is related to decreased brain-derived neurotrophic factor (BDNF) signalling or NMDA receptor hypofunction. BDNF enhances glutamatergic transmission and reduces GABAergic transmission, causing alterations in neuron survival and central nervous system (CNS) function [11]. The extent to which these changes contribute to the pathophysiology of schizophrenia remains unclear.

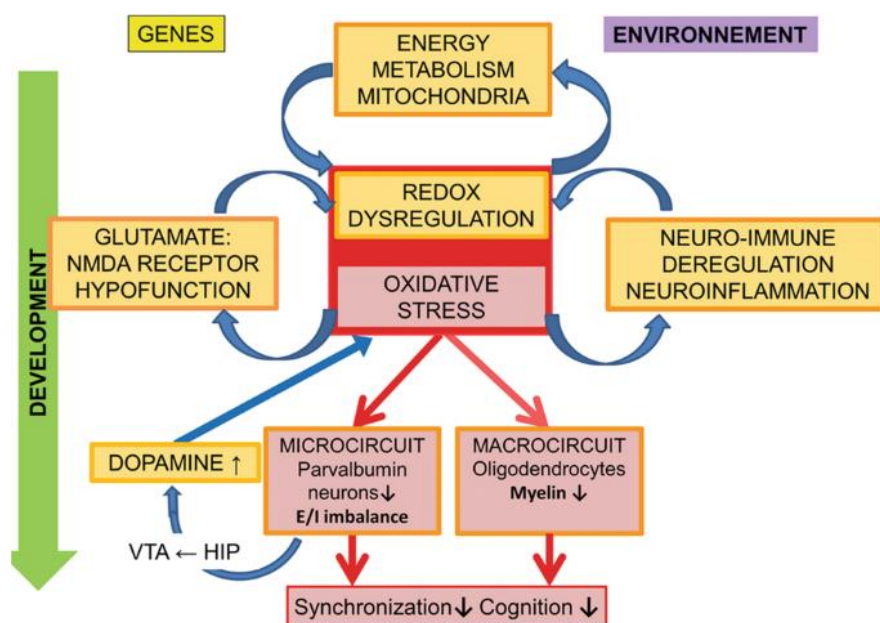


Figure 2. Oxidative stress in schizophrenia

Recent research has also highlighted the role of neuroinflammation and immune dysregulation in the pathophysiology of schizophrenia [20,21]. Post-mortem studies have revealed increased microglial activation and elevated levels of pro-inflammatory cytokines in the brains of individuals with schizophrenia [22]. These findings are supported by in vivo PET imaging studies demonstrating increased microglial activation in both medication-naïve and treated patients [23]. Peripheral markers of inflammation, such as C-reactive protein and interleukin-6, have also been found to be elevated in individuals with schizophrenia [24].

The neuroinflammatory processes observed in schizophrenia are thought to interact with the neurodevelopmental and neurotransmitter abnormalities described above. For example, maternal infection during pregnancy, a well-established risk factor for schizophrenia, may lead to fetal neuroinflammation and altered neurodevelopment [25]. Inflammatory mediators can also modulate neurotransmitter systems, particularly dopamine and glutamate, contributing to the emergence of psychotic symptoms [26]. While the precise mechanisms linking neuroinflammation to the clinical manifestations of schizophrenia remain to be fully elucidated, these findings suggest that targeting immune dysregulation may represent a promising therapeutic avenue. Anti-inflammatory agents, such as non-steroidal anti-inflammatory drugs and minocycline, have shown some preliminary efficacy in reducing symptom severity in schizophrenia [27,28].

4. Phenomenological Approach to Schizophrenia

The empiricist perspective on recovery from schizophrenia prioritizes objective measurement tools like the BPRS, PANSS, GAF, and SOFA to assess symptom severity, vocational functioning, independent living, and social relationships. While these tools are essential for quantifying progress, they may inadvertently sideline subjective experiences and the broader social contexts crucial to understanding recovery. In contrast, phenomenology offers a complementary approach by delving into the lived experiences and personal meanings associated with schizophrenia recovery [29]. This philosophical tradition highlights remission and functional improvement but also appreciates the subjective dimensions of recovery. This holistic approach fosters more tailored and supportive

treatment strategies that encompass the diverse aspects of individuals' experiences and aspirations in their journey towards recovery. The importance of first-person perspectives, emphasizing individual growth, subjective well-being, and the significance of personal relationships within recovery processes, is increasingly recognized [30].

Phenomenological research in schizophrenia has focused on exploring the alterations in self-experience that lie at the core of the disorder [31]. These alterations, often referred to as "self-disorders" or "ipseity disturbances," are thought to precede the onset of positive symptoms and contribute to the characteristic fragmentation of the self observed in schizophrenia [32]. Self-disorders encompass a range of experiences, including a diminished sense of self-presence, a loss of agency, and a disruption of the basic sense of being a unified, embodied subject [33]. Qualitative studies employing phenomenological interviews have provided rich descriptions of these self-disorders, revealing their pervasive impact on individuals' lives [34]. Patients often report feeling disconnected from their own thoughts, emotions, and bodily sensations, as if they were passive observers of their own mental life [35]. They may also experience a profound sense of alienation from the world and others, struggling to maintain a stable and coherent sense of identity [36].

Incorporating these first-person accounts into the conceptualization of schizophrenia has important implications for both research and clinical practice. By attending to the subjective dimensions of the disorder, phenomenological approaches can help bridge the gap between the neurobiological and experiential aspects of schizophrenia [37]. This integrative perspective may guide the development of more personalized and recovery-oriented interventions that target the core disturbances in self-experience [38]. Moreover, phenomenological research can inform the refinement of diagnostic criteria and assessment tools, ensuring that they adequately capture the lived experience of individuals with schizophrenia [39]. The inclusion of self-disorders as a key feature of schizophrenia in the DSM-5 and ICD-11 reflects the growing recognition of their diagnostic and prognostic significance [40].

5. Core phenomenological symptoms

The core phenomenological symptoms of schizophrenia encompass a range of experiences that reflect the profound disruption of self-experience and the loss of contact with shared reality. These symptoms are often described as "first-rank" symptoms, based on the work of German psychiatrist Kurt Schneider, who considered them to be particularly characteristic of schizophrenia [41]. One of the most prominent first-rank symptoms is the experience of thought insertion, where individuals feel that thoughts are being placed into their minds by an external force or entity [42]. This can be accompanied by the related phenomena of thought withdrawal, where one's thoughts seem to be removed or "pulled out" of the mind, and thought broadcasting, where one's thoughts are experienced as being audible or accessible to others [43]. Another key symptom is the experience of passivity phenomena or delusions of control, where individuals feel that their actions, emotions, or bodily sensations are being controlled or influenced by external agents [44]. This can manifest as the sense that one's movements are being directed by outside forces or that one's feelings and impulses are not one's own [45].

Auditory hallucinations, particularly in the form of commenting or conversing voices, are also considered a first-rank symptom [46]. These voices are often experienced as distinct from one's own inner speech and may provide a running commentary on the person's actions or engage in dialogue with each other [47]. Delusions, particularly those with bizarre or impossible content, are another core feature of schizophrenia [48]. These can include delusions of reference, where neutral environmental cues are imbued with personal significance, and delusions of persecution, where individuals believe they are being targeted or plotted against by others [49]. The negative symptoms of schizophrenia, such as blunted affect, *alogia* (poverty of speech), and *avolition* (lack of motivation), are also important from a phenomenological perspective [50]. These symptoms reflect a profound alteration in the basic sense of self, characterized by a diminished capacity for spontaneous thought, emotion, and action [51]. Cognitive symptoms, including impairments in attention, memory, and executive function, are increasingly recognized as core features of schizophrenia [52]. These deficits can contribute to the fragmentation of self-experience by disrupting the continuity and coherence of mental life [53]. Finally, the phenomenon of "double bookkeeping," where individuals maintain a paradoxical coexistence of mutually incompatible beliefs or experiences, is a key feature of schizophrenic psychosis [54]. This can manifest as a simultaneous acknowledgment and denial of one's illness or a persistence of delusional beliefs alongside an intellectual recognition of their implausibility [55].

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6. Brain Connectivity in Schizophrenia

Recent advances in neuroimaging techniques have provided unprecedented insights into the brain connectivity abnormalities associated with schizophrenia. These findings have led to a reconceptualization of the disorder as one of dysconnectivity, characterized by alterations in the functional and structural connections between brain regions [56]. Functional connectivity studies, which examine the temporal correlation of neural activity across different brain areas, have consistently revealed a disruption of large-scale brain networks in schizophrenia [57]. The default mode network (DMN), which is involved in self-referential processing and is typically deactivated during goal-directed tasks, has been found to show reduced connectivity and failure to deactivate in individuals with schizophrenia [58]. This abnormal DMN activity has been linked to the positive symptoms of the disorder, such as hallucinations and delusions [59]. Other functional networks, such as the salience network, which is involved in detecting and orienting to salient stimuli, and the central executive network, which is involved in higher-order cognitive functions, have also been found to show altered connectivity in schizophrenia [60]. The disruption of these networks may contribute to the cognitive deficits and difficulty in distinguishing between internally and externally generated stimuli that are characteristic of the disorder [61].

Structural connectivity studies, which use diffusion tensor imaging (DTI) to examine the integrity of white matter tracts connecting different brain regions, have also revealed abnormalities in schizophrenia [62]. Reduced fractional anisotropy, a measure of white matter integrity, has been found in multiple tracts, including the uncinate fasciculus, cingulum bundle, and corpus callosum [63]. These structural alterations are thought to underlie the functional dysconnectivity observed in the disorder [64]. Graph theoretical analyses, which model the brain as a complex network of nodes (brain regions) and edges (connections between regions), have provided further evidence of dysconnectivity in schizophrenia [65]. These studies have revealed a disruption of the small-world topology that characterizes healthy brain networks, with reduced local clustering and increased path length between nodes [66]. This alteration in network organization may contribute to the inefficient information processing and cognitive fragmentation observed in the disorder [67]. The etiology of these connectivity abnormalities in schizophrenia is likely to be multifactorial, involving a complex interplay of genetic, environmental, and neurodevelopmental factors [68]. Genetic studies have identified several risk variants associated with schizophrenia that are involved in synaptic plasticity and neuronal migration, processes that are crucial for the establishment of functional and structural brain connectivity [69]. Environmental insults, such as prenatal infection and early life stress, have also been shown to impact brain development and connectivity [70]. The neurodevelopmental hypothesis of schizophrenia posits that these genetic and environmental factors interact to disrupt the normal trajectory of brain maturation, leading to the emergence of connectivity abnormalities and clinical symptoms in adolescence or early adulthood [71]. This view is supported by longitudinal neuroimaging studies showing progressive changes in brain structure and function in individuals at high risk for psychosis [72].

The identification of brain connectivity abnormalities in schizophrenia has important implications for the development of novel therapeutic interventions. For example, non-invasive brain stimulation techniques, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), have been explored as potential tools for modulating abnormal network activity in the disorder [73]. These interventions have shown promising results in reducing symptom severity and improving cognitive function, though further research is needed to establish their long-term efficacy [74]. In addition, pharmacological agents targeting the neurotransmitter systems involved in synaptic plasticity and network function, such as the glutamatergic and GABAergic systems, are being investigated as potential treatments for schizophrenia [75]. These compounds aim to restore the balance of excitatory and inhibitory neurotransmission that is thought to be disrupted in the disorder [76]. Finally, cognitive remediation and social skills training interventions, which aim to enhance cognitive and social functioning in individuals with schizophrenia, have been shown to induce neuroplastic changes in brain connectivity [77]. These findings suggest that behavioural interventions can have a meaningful impact on the neural substrate of the disorder and may complement pharmacological treatments in promoting recovery [78].

7. Models of Selfhood

The concept of selfhood is central to the phenomenological understanding of schizophrenia, as the disorder is characterized by profound alterations in the basic sense of self. Several models have been proposed to account for these alterations, each emphasizing different aspects of self-experience and their disruption in schizophrenia. One influential model is the ipseity disturbance model, proposed by Josef Parnas and colleagues [79]. According to this model, the core feature of schizophrenia is a disturbance in the basic sense of self-presence or ipseity, which refers to the implicit, pre-reflective awareness of being a unified, embodied subject of

experience [80]. In schizophrenia, this basic sense of self is fragmented, leading to experiences of depersonalization, altered bodily sensations, and a loss of the sense of ownership over one's thoughts and actions [81]. Another important model is the narrative self model, which emphasizes the role of autobiographical memory and self-narrative in the construction and maintenance of a coherent sense of self [82]. According to this model, the self is not a static entity but rather an ongoing process of integrating past experiences, present circumstances, and future aspirations into a meaningful life story [83]. In schizophrenia, this process of narrative self-construction is disrupted, leading to a fragmentation of personal identity and a loss of continuity in the sense of self over time [84].

The dialogical self model, proposed by Hubert Hermans and colleagues, conceptualizes the self as a dynamic multiplicity of relatively autonomous I-positions, each representing different aspects of the individual's identity [85]. These I-positions engage in dialogical relationships with each other and with the external world, contributing to the richness and complexity of self-experience [86]. In schizophrenia, the dialogical structure of the self is thought to be disrupted, with certain I-positions becoming dominant or dissociated from the rest of the self-system, leading to experiences of inner fragmentation and loss of personal agency [87]. The embodied self model, rooted in the phenomenological work of philosophers such as Maurice Merleau-Ponty, emphasizes the central role of the body in the constitution of self-experience [88].

According to this model, the sense of self is fundamentally grounded in the pre-reflective experience of embodiment, which provides the basic sense of being a unified, situated subject of perception and action [89]. In schizophrenia, this embodied sense of self is disrupted, leading to experiences of disembodiment, altered bodily sensations, and a loss of the sense of being grounded in the world [90]. The minimal self model, proposed by Dan Zahavi and colleagues, distinguishes between the basic, pre-reflective sense of self (the minimal self) and the more complex, narratively structured sense of self (the narrative self) [91]. According to this model, the minimal self is the fundamental structure of experience, providing the basic sense of ownership and agency that is necessary for any form of self-awareness [92]. In schizophrenia, it is this minimal sense of self that is primarily disturbed, leading to a range of anomalous self-experiences that may later give rise to the more explicit symptoms of the disorder [93].

While these models differ in their specific emphasis and conceptual framework, they all converge on the idea that schizophrenia involves a fundamental disturbance in the basic structure of self-experience. By providing a detailed and nuanced account of these alterations, these models can help guide the development of targeted therapeutic interventions aimed at restoring the sense of self and promoting recovery in individuals with schizophrenia.

For example, interventions based on the ipseity disturbance model may focus on helping individuals regain a stable and coherent sense of self-presence through techniques such as body-oriented psychotherapy [94] and mindfulness-based approaches [95]. Interventions based on the narrative self-model may emphasize the importance of reconstructing a coherent and meaningful life story through narrative therapy [96] and autobiographical memory training [97]. Similarly, interventions based on the dialogical self-model may aim to promote the integration and coordination of different I-positions through techniques such as role-playing and internal dialogue [98]. Interventions based on the embodied self model may focus on restoring the sense of bodily integrity and agency through body-oriented approaches such as yoga [99] and dance therapy [100]. Finally, interventions based on the minimal self model may aim to strengthen the basic sense of ownership and agency through techniques such as metacognitive training [101] and self-monitoring [102].

Schizophrenia remains a complex disorder, challenging both those affected and researchers. While progress has been made in understanding its biological basis, much remains unknown about its etiology and pathophysiology. The phenomenological approach complements empirical research by providing insight into the subjective experience, particularly self-disturbances. Neuroimaging and genetics have revealed brain connectivity abnormalities and molecular mechanisms underlying the disorder. Future research should integrate subjective experiences with neural and molecular findings to develop a comprehensive framework. A multidisciplinary approach is crucial, placing individuals' lived experiences at the center to develop more effective, personalized treatments aimed at helping those with schizophrenia lead fulfilling lives. The key concepts and their implications in Schizophrenia research and treatment are shown in Table 1 below:

Table 1. Key concepts and their implications in schizophrenia research and treatment

Concept	Description	Implications
Phenomenology	The study of subjective experience and consciousness	Provides a rich, detailed account of the lived experience of schizophrenia, particularly alterations in self-experience
Iipseity disturbance	Disruption of the basic sense of self-presence or pre-reflective self-awareness	Underlies experiences of depersonalization, altered bodily sensations, and loss of agency in schizophrenia
Narrative self	The sense of self constructed through the integration of past experiences, present circumstances, and future aspirations into a coherent life story	Disrupted in schizophrenia, leading to fragmentation of personal identity and loss of continuity in the sense of self over time
Dialogical self	The self as a dynamic multiplicity of relatively autonomous I-positions engaging in dialogical relationships	Disrupted in schizophrenia, with certain I-positions becoming dominant or dissociated, leading to inner fragmentation and loss of agency
Embodied self	The sense of self grounded in the pre-reflective experience of embodiment	Disrupted in schizophrenia, leading to experiences of disembodiment, altered bodily sensations, and loss of being grounded in the world
Minimal self	The basic, pre-reflective sense of self, providing the fundamental sense of ownership and agency	Primarily disturbed in schizophrenia, giving rise to anomalous self-experiences and later explicit symptoms
Brain connectivity	The functional and structural connections between brain regions	Altered in schizophrenia, leading to a reconceptualization of the disorder as one of dysconnectivity
Neurodevelopment	The process of brain development from prenatal stages through adolescence and early adulthood	Disrupted in schizophrenia, with genetic and environmental factors interacting to alter the normal trajectory of brain maturation
Therapeutic interventions	Strategies aimed at reducing symptoms, improving functioning, and promoting recovery in schizophrenia	Can be tailored to address specific alterations in self-experience and brain connectivity, guided by phenomenological and neurobiological models

References

- [1] Parnas J, Sass LA. Self, solipsism, and schizophrenic delusions. *Philos Psychiatry Psychol.* 2001;8(2-3):101-120.
- [2] Sass LA, Parnas J. Schizophrenia, consciousness, and the self. *Schizophr Bull.* 2003;29(3):427-444.
- [3] Lysaker PH, Lysaker JT. Schizophrenia and alterations in self-experience: a comparison of 6 perspectives. *Schizophr Bull.* 2010;36(2):331-340.
- [4] Zahavi D. *Subjectivity and selfhood: investigating the first-person perspective.* Cambridge, MA: MIT Press; 2005.
- [5] Gallagher S. Philosophical conceptions of the self: implications for cognitive science. *Trends Cogn Sci.* 2000;4(1):14-21.
- [6] Nelson B, Parnas J, Sass LA. Disturbance of minimal self (ipseity) in schizophrenia: clarification and current status. *Schizophr Bull.* 2014;40(3):479-482.
- [7] Uhlhaas PJ, Singer W. Abnormal neural oscillations and synchrony in schizophrenia. *Nat Rev Neurosci.* 2010;11(2):100-113.
- [8] Friston KJ, Frith CD. Schizophrenia: a disconnection syndrome? *Clin Neurosci.* 1995;3(2):89-97.
- [9] van den Heuvel MP, Fornito A. Brain networks in schizophrenia. *Neuropsychol Rev.* 2014;24(1):32-48.
- [10] Rubinov M, Bullmore E. Schizophrenia and abnormal brain network hubs. *Dialogues Clin Neurosci.* 2013;15(3):339-349.
- [11] Rapoport JL, Giedd JN, Gogtay N. Neurodevelopmental model of schizophrenia: update 2012. *Mol Psychiatry.* 2012;17(12):1228-1238.
- [12] Owen MJ, O'Donovan MC, Thapar A, Craddock N. Neurodevelopmental hypothesis of schizophrenia. *Br J Psychiatry.* 2011;198(3):173-175.
- [13] Insel TR. Rethinking schizophrenia. *Nature.* 2010;468(7321):187-193.

- [14] Howes OD, Murray RM. Schizophrenia: an integrated sociodevelopmental-cognitive model. *Lancet*. 2014;383(9929):1677-1687.
- [15] Cannon TD. How schizophrenia develops: cognitive and brain mechanisms underlying onset of psychosis. *Trends Cogn Sci*. 2015;19(12):744-756.
- [16] Keshavan MS, Nasrallah HA, Tandon R. Schizophrenia, "Just the Facts" 6. Moving ahead with the schizophrenia concept: from the elephant to the mouse. *Schizophr Res*. 2011;127(1-3):3-13.
- [17] Tandon R, Nasrallah HA, Keshavan MS. Schizophrenia, "just the facts" 4. Clinical features and conceptualization. *Schizophr Res*. 2009;110(1-3):1-23.
- [18] Tandon R, Keshavan MS, Nasrallah HA. Schizophrenia, "Just the Facts": what we know in 2008 part 1: overview. *Schizophr Res*. 2008;100(1-3):4-19.
- [19] Sass L, Parnas J, Zahavi D. Phenomenological psychopathology and schizophrenia: contemporary approaches and misunderstandings. *Philos Psychiatry Psychol*. 2011;18(1):1-23.
- [20] Sass LA, Parnas J. Thought disorder, subjectivity, and the self. *Schizophr Bull*. 2017;43(3):497-502.
- [21] Parnas J, Henriksen MG. Disordered self in the schizophrenia spectrum: a clinical and research perspective. *Harv Rev Psychiatry*. 2014;22(5):251-265.
- [22] Nelson B, Sass LA, Škodlar B. The phenomenological model of psychotic vulnerability and its possible implications for psychological interventions in the ultra-high risk (prodromal) population. *Psychopathology*. 2009;42(5):283-292.
- [23] Raballo A, Sæbye D, Parnas J. Looking at the schizophrenia spectrum through the prism of self-disorders: an empirical study. *Schizophr Bull*. 2011;37(2):344-351.
- [24] Parnas J, Møller P, Kircher T, Thalbitzer J, Jansson L, Handest P, Zahavi D. EASE: Examination of Anomalous Self-Experience. *Psychopathology*. 2005;38(5):236-258.
- [25] Henriksen MG, Parnas J. Clinical manifestations of self-disorders and the Gestalt of schizophrenia. *Schizophr Bull*. 2012;38(4):657-660.
- [26] Parnas J, Handest P. Phenomenology of anomalous self-experience in early schizophrenia. *Compr Psychiatry*. 2003;44(2):121-134.
- [27] Sass LA. Self-disturbance and schizophrenia: structure, specificity, pathogenesis (Current issues, New directions). *Schizophr Res*. 2014;152(1):5-11.
- [28] Lysaker PH, Lysaker JT. Narrative structure in psychosis: schizophrenia and disruptions in the dialogical self. *Theory Psychol*. 2002;12(2):207-220.
- [29] Lysaker PH, Lysaker JT. Psychosis and the disintegration of dialogical self-structure: Problems posed by schizophrenia for the maintenance of dialogue. *Br J Med Psychol*. 2001;74(1):23-33.
- [30] Lysaker PH, Lysaker JT. Schizophrenia and the collapse of the dialogical self: recovery, narrative and psychotherapy. *Psychother Theory Res Pract Train*. 2001;38(3):252-261.
- [31] Holma J, Aaltonen J. Narrative understanding in acute psychosis. *Contemp Fam Ther*. 1998;20(3):253-263.
- [32] Gallagher S. The natural philosophy of agency. *Philos Compass*. 2007;2(2):347-357.
- [33] Gallagher S. Neurocognitive models of schizophrenia: a neurophenomenological critique. *Psychopathology*. 2004;37(1):8-19.
- [34] Gallagher S. Self-reference and schizophrenia: a cognitive model of immunity to error through misidentification. In: Zahavi D, editor. *Exploring the self: philosophical and psychopathological perspectives on self-experience*. Amsterdam: John Benjamins Publishing Company; 2000. p. 203-239.
- [35] Fuchs T. Corporealized and disembodied minds: a phenomenological view of the body in melancholia and schizophrenia. *Philos Psychiatry Psychol*. 2005;12(2):95-107.
- [36] Stanghellini G. *Disembodied spirits and deanimated bodies: the psychopathology of common sense*. Oxford: Oxford University Press; 2004.
- [37] Cermolacce M, Naudin J, Parnas J. The "minimal self" in psychopathology: re-examining the self-disorders in the schizophrenia spectrum. *Conscious Cogn*. 2007;16(3):703-714.

- [38] Pérez-Álvarez M, García-Montes JM, Vallina-Fernández O, Perona-Garcelán S, Cuevas-Yust C. New life for schizophrenia psychotherapy in the light of phenomenology. *Clin Psychol Psychother*. 2011;18(3):187-201.
- [39] Nelson B, Yung AR. Psychotic-like experiences as overdetermined phenomena: when do they increase risk for psychotic disorder? *Schizophr Res*. 2009;108(1-3):303-304.
- [40] Irrázaval L. The lived body in schizophrenia: transition from basic self-disorders to full-blown psychosis. *Front Psychiatry*. 2015;6:9.
- [41] Fuchs T, Schlimme JE. Embodiment and psychopathology: a phenomenological perspective. *Curr Opin Psychiatry*. 2009;22(6):570-575.
- [42] Krueger J. Schizophrenia and the scaffolded self. *Topoi*. 2020;39(3):597-609.
- [43] Moe AM, Docherty NM. Schizophrenia and the sense of self. *Schizophr Bull*. 2014;40(1):161-168.
- [44] Stephensen H, Parnas J. What can self-disorders in schizophrenia tell us about the nature of subjectivity? A psychopathological investigation. *Phenomenol Cogn Sci*. 2018;17(4):629-642.
- [45] Nischk D, Rusch J, Merz P. Self-concepts and delusions: the role of the self in delusions of reference. *Psychopathology*. 2017;50(4):273-278.
- [46] Mishara AL. Is minimal self preserved in schizophrenia? A subcomponents view. *Conscious Cogn*. 2007;16(3):715-721.
- [47] Sarella PN, Vipparthi AK, Valluri S, Vegi S, Vendi VK. Nanorobotics: Pioneering Drug Delivery and Development in Pharmaceuticals. *Research Journal of Pharmaceutical Dosage Forms and Technology*. 2024 Feb 22;16(1):81-90.
- [48] Sass L, Parnas J. Schizophrenia, consciousness, and the self. *Schizophr Bull*. 2003;29(3):427-444.
- [49] Sass LA. Self-disturbance and schizophrenia: structure, specificity, pathogenesis (Current issues, New directions). *Schizophr Res*. 2014;152(1):5-11.
- [50] Sarella PN, Vegi S, Vendi VK, Vipparthi AK, Valluri S. Exploring Aquasomes: A Promising Frontier in Nanotechnology-based Drug Delivery. *Asian Journal of Pharmaceutical Research*. 2024 May 28;14(2):153-61..
- [51] 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(1):20-27.
- [52] Sass L, Borda JP, Madeira L, Pienkos E, Nelson B. Varieties of self disorder: a bio-pheno-social model of schizophrenia. *Schizophr Bull*. 2018;44(4):720-727.
- [53] Parnas J, Sass LA. Self, solipsism, and schizophrenic delusions. *Philos Psychiatry Psychol*. 2001;8(2-3):101-120.
- [54] Parnas J, Handest P. Phenomenology of anomalous self-experience in early schizophrenia. *Compr Psychiatry*. 2003;44(2):121-134.
- [55] Nelson B, Thompson A, Yung AR. Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. *Schizophr Bull*. 2012;38(6):1277-1287.
- [56] Pettersson-Yeo W, Allen P, Benetti S, McGuire P, Mechelli A. Dysconnectivity in schizophrenia: where are we now? *Neurosci Biobehav Rev*. 2011;35(5):1110-1124.
- [57] Fornito A, Zalesky A, Pantelis C, Bullmore ET. Schizophrenia, neuroimaging and connectomics. *Neuroimage*. 2012;62(4):2296-2314.
- [58] Whitfield-Gabrieli S, Ford JM. Default mode network activity and connectivity in psychopathology. *Annu Rev Clin Psychol*. 2012;8:49-76.
- [59] 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(1):21-30.
- [60] Palaniyappan L, Liddle PF. Does the salience network play a cardinal role in psychosis? An emerging hypothesis of insular dysfunction. *J Psychiatry Neurosci*. 2012;37(1):17-27.
- [61] Manoliu A, Riedl V, Zherdin A, Mühlau M, Schwerthöffer D, Scherr M, et al. Aberrant dependence of default mode/central executive network interactions on anterior insular salience network activity in schizophrenia. *Schizophr Bull*. 2014;40(2):428-437.
- [62] Ellison-Wright I, Bullmore E. Meta-analysis of diffusion tensor imaging studies in schizophrenia. *Schizophr Res*. 2009;108(1-3):3-10.

- [63] Kubicki M, McCarley R, Westin CF, Park HJ, Maier S, Kikinis R, et al. A review of diffusion tensor imaging studies in schizophrenia. *J Psychiatr Res.* 2007;41(1-2):15-30.
- [64] Kubicki M, Shenton ME. Diffusion tensor imaging findings and their implications in schizophrenia. *Curr Opin Psychiatry.* 2014;27(3):179-184.
- [65] van den Heuvel MP, Fornito A. Brain networks in schizophrenia. *Neuropsychol Rev.* 2014;24(1):32-48.
- [66] Liu Y, Liang M, Zhou Y, He Y, Hao Y, Song M, et al. Disrupted small-world networks in schizophrenia. *Brain.* 2008;131(Pt 4):945-961.
- [67] Alexander-Bloch AF, Vértes PE, Stidd R, Lalonde F, Clasen L, Rapoport J, et al. The anatomical distance of functional connections predicts brain network topology in health and schizophrenia. *Cereb Cortex.* 2013;23(1):127-138.
- [68] Stephan KE, Friston KJ, Frith CD. Dysconnection in schizophrenia: from abnormal synaptic plasticity to failures of self-monitoring. *Schizophr Bull.* 2009;35(3):509-527.
- [69] Harrison PJ, Weinberger DR. Schizophrenia genes, gene expression, and neuropathology: on the matter of their convergence. *Mol Psychiatry.* 2005;10(1):40-68.
- [70] Brown AS. The environment and susceptibility to schizophrenia. *Prog Neurobiol.* 2011;93(1):23-58.
- [71] Fatemi SH, Folsom TD. The neurodevelopmental hypothesis of schizophrenia, revisited. *Schizophr Bull.* 2009;35(3):528-548.
- [72] Sarella PN, Mangam VT. AI-Driven Natural Language Processing in Healthcare: Transforming Patient-Provider Communication. *Indian Journal of Pharmacy Practice.* 2024;17(1).
- [73] Brunelin J, Mondino M, Gassab L, Haesebaert F, Gaha L, Suaud-Chagny MF, et al. Examining transcranial direct-current stimulation (tDCS) as a treatment for hallucinations in schizophrenia. *Am J Psychiatry.* 2012;169(7):719-724.
- [74] Harani A, VijayaRatnam J, Dipankar B, Kumar DS, Lalitha MB, Kumar SP. Molecular interaction studies of phosphatidylcholine as drug delivery substrate for asenapine maleate. *Current Science.* 2018 Aug 10;115(3):499-504.
- [75] Javitt DC. Glutamatergic theories of schizophrenia. *Isr J Psychiatry Relat Sci.* 2010;47(1):4-16.
- [76] Moghaddam B, Javitt D. From revolution to evolution: the glutamate hypothesis of schizophrenia and its implication for treatment. *Neuropsychopharmacology.* 2012;37(1):4-15.
- [77] Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatry.* 2011;168(5):472-485.
- [78] Eack SM, Hogarty GE, Cho RY, Prasad KM, Greenwald DP, Hogarty SS, et al. Neuroprotective effects of cognitive enhancement therapy against gray matter loss in early schizophrenia: results from a 2-year randomized controlled trial. *Arch Gen Psychiatry.* 2010;67(7):674-682.
- [79] Fuchs T. The intersubjectivity of delusions. *World Psychiatry.* 2015;14(2):178-179.
- [80] Nelson B, Sass LA, Parnas J. Basic self disturbance in the schizophrenia spectrum: a review and future directions. In: Mishara AL, Corlett PR, Fletcher PC, Schwartz MA, editors. *Phenomenological neuropsychiatry: bridging the clinic and clinical neuroscience.* New York: Springer; 2016. p. 237-256.
- [81] Henriksen MG, Parnas J. Self-disorders and schizophrenia: a phenomenological reappraisal of poor insight and noncompliance. *Schizophr Bull.* 2014;40(3):542-547.
- [82] Lysaker PH, Lysaker JT. Schizophrenia and alterations in self-experience: a comparison of 6 perspectives. *Schizophr Bull.* 2010;36(2):331-340.
- [83] Lysaker PH, Clements CA, Plascak-Hallberg CD, Knipscheer SJ, Wright DE. Insight and personal narratives of illness in schizophrenia. *Psychiatry.* 2002;65(3):197-206.
- [84] Raffard S, D'Argembeau A, Lardi C, Bayard S, Boulenger JP, Van der Linden M. Narrative identity in schizophrenia. *Conscious Cogn.* 2010;19(1):328-340.
- [85] Sarella PN, Dadishetti JP, Asogwa PO, Kakarparthy R. A Case Report on Organic Psychosis Induced by Antitubercular Drugs in A Young Female. *Asian Journal of Hospital Pharmacy.* 2023 May 28:1-3.
- [86] Lysaker PH, Hermans HJM. The dialogical self in psychotherapy for persons with schizophrenia: a case study. *J Clin Psychol.* 2007;63(2):129-139.

- [87] Mancuso F, Horan WP, Kern RS, Green MF. Social cognition in psychosis: multidimensional structure, clinical correlates, and relationship with functional outcome. *Schizophr Res.* 2011;125(2-3):143-151.
- [88] Stanghellini G, Ballerini M, Prezenza S, Mancini M, Northoff G, Cutting J. Abnormal time experiences in schizophrenia: an empirical qualitative study. *Psychopathology.* 2016;49(1):27-32.
- [89] Stanghellini G, Ballerini M, Prezenza S, Mancini M, Raballo A, Blasi S, et al. Psychopathology of lived time: abnormal time experience in persons with schizophrenia. *Schizophr Bull.* 2016;42(1):45-55.
- [90] Fuchs T. The self in schizophrenia: Jaspers, Schneider and beyond. In: Stanghellini G, Fuchs T, editors. *One century of Karl Jaspers' general psychopathology.* Oxford: Oxford University Press; 2013. p. 245-257.
- [91] Zahavi D. Schizophrenia and self-awareness. *Philos Psychiatry Psychol.* 2001;8(4):339-341.
- [92] Zahavi D. *Subjectivity and selfhood: investigating the first-person perspective.* Cambridge, MA: MIT Press; 2005.
- [93] Møller P, Husby R. The initial prodrome in schizophrenia: searching for naturalistic core dimensions of experience and behavior. *Schizophr Bull.* 2000;26(1):217-232.
- [94] Röhricht F, Papadopoulos N, Holden S, Clarke T, Priebe S. Therapeutic processes and clinical outcomes of body psychotherapy in chronic schizophrenia – an open clinical trial. *Arts Psychother.* 2011;38(3):196-203.
- [95] Chadwick P. *Person-based cognitive therapy for distressing psychosis.* Chichester: John Wiley & Sons; 2006.
- [96] Lysaker PH, Lysaker JT. Narrative identity in schizophrenia: a bridge between phenomenological and neurocognitive approaches to understanding the self. *Theory Psychol.* 2020;30(4):494-513.
- [97] Ricarte JJ, Hernández-Viadel JV, Latorre JM, Ros L. Effects of event-specific memory training on autobiographical memory retrieval and depressive symptoms in schizophrenic patients. *J Behav Ther Exp Psychiatry.* 2012;43 Suppl 1:S12-20.
- [98] Hermans HJM, Dimaggio G, editors. *The dialogical self in psychotherapy.* Hove: Brunner-Routledge; 2004.
- [99] Visceglia E, Lewis S. Yoga therapy as an adjunctive treatment for schizophrenia: a randomized, controlled pilot study. *J Altern Complement Med.* 2011;17(7):601-607.
- [100] Röhricht F, Priebe S. Effect of body-oriented psychological therapy on negative symptoms in schizophrenia: a randomized controlled trial. *Psychol Med.* 2006;36(5):669-678.
- [101] Moritz S, Andreou C, Schneider BC, Wittekind CE, Menon M, Balzan RP, et al. Sowing the seeds of doubt: a narrative review on metacognitive training in schizophrenia. *Clin Psychol Rev.* 2014;34(4):358-366.
- [102] van der Meer L, de Vos AE, Stiekema AP, Pijnenborg GH, van Tol MJ, Nolen WA, et al. Insight in schizophrenia: involvement of self-reflection networks? *Schizophr Bull.* 2013;39(6):1288-1295

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