Obsessive-compulsive symptoms in schizophrenia: implications for future psychiatric classifications

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Abstract

Although obsessive-compulsive symptoms are not considered primary features, they are prevalent, independent of psychosis, and substantially modify clinical characteristics, course, treatment and prognosis of schizophrenia. The authors highlight the clinical significance of obsessive-compulsive symptoms in schizophrenia, provide diagnostic criteria for “schizo-obsessive” patients and address future directions for research.
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Schizophrenia and obsessive-compulsive disorder (OCD) are distinct nosological entities with discrete underlying brain mechanisms, clinical presentations and treatments. Nevertheless, they share some demographic and clinical characteristics and, apparently, some pathophysiological underpinnings. Both schizophrenia and OCD are characterized by similar distributions between men and women, age of onset during adolescence or early adulthood, and earlier age of onset in men. Increasingly sophisticated translational, neurophysiological and neuroimaging research shows a substantial overlap between schizophrenia and OCD in structural and functional brain abnormalities and in the involvement of dopamine, serotonin and glutamate neurotransmitter systems in the pathophysiology underlying these disorders. Thus, it is not surprising that obsessive-compulsive and schizophrenic symptoms coexist in a greater proportion of patients than would be expected from random co-occurrence of the two disorders.

In contrast to positive, negative and cognitive symptoms, obsessive-compulsive symptoms are not considered primary features of schizophrenia [1]. Some of the founders of modern psychiatry (Westphal, Mayer-Gross, Bleuler) clearly identified obsessive-compulsive symptoms in schizophrenia and deemed them a feature of the disorder’s prodromal or active phases. The authors argue that current advances in understanding the clinical and neurobiological significance of obsessive-compulsive symptoms in schizophrenia justify their introduction in future psychiatric classifications.

Initially, obsessive-compulsive symptoms were thought to occur in a minority of schizophrenia patients (1%-3.5%) and were considered to be a protective factor [2]. A seminal work by Fenton and McGlashan challenged this “positive” view by showing a considerable rate of obsessive-compulsive symptoms in schizophrenia patients (12.9%), with a poorer outcome for schizo-obsessive patients [3]. The Diagnostic and Statistical Manual, Third Edition (DSM-III)
did not allow a diagnosis of obsessive-compulsive disorder (OCD) in the presence of schizophrenia, since the OCD was considered “due to” a disorder higher in the hierarchy. DSM-IV allowed the diagnosis of co-occurring schizophrenia and clinically meaningful and potentially treatable secondary syndromes (e.g., depression, panic disorder). The term “schizo-obsessive” was suggested in order to draw attention to those schizophrenia patients with clinically significant obsessive-compulsive symptoms [4].

We now know that valid and reliable identification of obsessive-compulsive symptoms in schizophrenia patients is feasible, despite a symptomatic overlap between the two disorders (e.g., between obsessions and delusions). Utilizing instruments developed to evaluate OCD (e.g., the Yale-Brown Obsessive-Compulsive Scale), studies have consistently shown that in a majority of schizo-obsessive patients, obsessive-compulsive symptoms precede initial psychotic symptoms, are associated with fair to good insight, exhibit symptom dimensions comparable to those seen in “pure” OCD, and are typically moderate to severe [5,6]. These findings, and the documented substantial distress and functional impairment associated with them, lend support to the independent nature and clinical significance of obsessive-compulsive symptoms in schizophrenia.

In a recent meta-analysis based on 34 epidemiological and clinical studies with a total of 3000 patients, the prevalence of OCD in schizophrenia was estimated to be 12.1% (95% Confidence Interval, 7%-17.1%), a rate considerably higher than in the general population (2%-3%) [7]. Relaxing the diagnostic threshold for obsessive-compulsive symptoms led to an even higher rate (weighted average 25%) [8]. It has become clear that obsessive-compulsive symptoms in schizophrenia are not a sequel to chronic illness or to antipsychotic treatment, since a comparable prevalence rate is revealed in individuals at ultra-high risk for psychosis, in the prodromal phase of schizophrenia, and in first-episode drug-naïve schizophrenia patients [9,10]. Detection of obsessive-compulsive symptoms across the life span in adolescent, adult and elderly patients further highlights the broad prevalence and persistence of obsessive-compulsive phenomena in schizophrenia [11,12].

As in “pure” OCD, there is remarkable consistency in the reported rates of OCD in schizophrenia samples across the globe (e.g., North America, Australia, Europe, Japan, Israel, Kenya, Mexico) [7]. Cross-cultural prevalence rates of OCD are stable in patients with and without schizophrenia.

Compared with schizophrenia patients, schizo-obsessive patients have distinct clinical features. Schizo-obsessive patients exhibit an earlier age at onset, more depressive symptoms and suicide attempts, increased rates of hospitalization, decreased likelihood of being employed or married, lower quality of life and greater disability [13,14]. A meta-analysis revealed that the presence of obsessive-compulsive symptoms is associated with higher global, positive and negative schizophrenia symptom severity [15]. Compared with schizophrenia patients, schizo-obsessive patients show a different pattern of comorbidity, with a preferential aggregation of OCD-spectrum disorders, namely body dysmorphic disorder, eating disorders and tic disorders, but not of major depressive, substance abuse or anxiety disorders [16]. Important differences are also found in first-degree relatives of schizophrenia patients with and without obsessive-compulsive symptoms. Compared with relatives (N = 210) of schizophrenia probands, relatives (N = 182) of schizo-obsessive probands had a significantly higher morbid risk for schizo-obsessive disorder, obsessive-compulsive personality disorder and, at a trend level, for an increased rate of OCD, while no between-group differences were found in the rate of schizophrenia-spectrum disorders [17]. Differential familial aggregation of OCD-related disorders further supports the validity of recognizing a distinct schizo-obsessive subgroup in the schizophrenia-spectrum.

The neurobiological underpinnings of obsessive-compulsive symptoms in schizophrenia patients are far from definitively known, but preliminary reports suggest a distinct neuro-anatomical profile. Magnetic resonance imaging studies have identified significantly reduced volumes of the left hippocampus, frontal lobes and anterior horn of the lateral and third ventricles in a small group of schizo-obsessive patients compared with schizophrenia patients [18]. A neurophysiological investigation using event-related potentials (ERPs) during a discriminative response task found a distinct ERP pattern, with abnormally increased target activation and reduced P300 amplitudes in a schizo-obsessive group versus both schizophrenia and OCD groups [19]. A generalized neurocognitive deficit in schizophrenia and a more selective neurocognitive deficit in OCD have consistently been shown (20). Several studies have found that subgroups of schizophrenia patients with OCD or obsessive-compulsive symptoms exhibit more soft neurological signs and neurocognitive deficits, primarily in abstraction and executive function, than do schizophrenia patients without obsessive-compulsive phenomena or “pure” OCD [20]. However, a lack of difference or even better performance of schizo-obsessive patients than of schizophrenia patients, particularly during the initial stages of illness, has also been reported [13]. Further comparative evaluation of cognitive deficits in schizophrenia patients with and without OCD is imperative, considering the central role of cognitive impairment in schizophrenia and its impact on patients’ functional outcome and prognosis.

Although large-scale, controlled studies are lacking, there is general consensus that schizo-obsessive patients are difficult-to-treat and differentially responsive to specific treatment interventions. Indeed, monotherapy with typical antipsychotics appears to be ineffective and associated with increased sensitivity to extrapyramidal side effects. Second-generation antipsychotics may be effective as monotherapy in the amelioration of both schizophrenic and obsessive-compulsive symptoms in some patients, but a combination with serotonin reuptake inhibitors (SRIs) is usually required.
Pharmacotherapeutic complexity is further highlighted by the bi-directional effect of atypical antipsychotics, both improving and exacerbating obsessive-compulsive symptoms in schizophrenia patients [22].

Overall, these substantial bodies of evidence indicate that obsessive-compulsive symptoms represent a clinically meaningful dimension of psychopathology in schizophrenia, and that schizophrenia patients with obsessive-compulsive symptoms have distinct clinical and neurobiological characteristics, family inheritance, treatment response and prognosis. We suggest provisional diagnostic criteria for the identification of an obsessive-compulsive symptom subgroup ("schizo-obssesive") of schizophrenia (Appendix A).

Additional research is needed to delineate the etiology, genetics, neurobiology, psychopathology and treatment of the subset of schizophrenia patients with obsessive-compulsive symptoms. Large-scale follow-up studies are needed to address course-dependent interrelationships between obsessive-compulsive and schizophrenia symptoms, and diagnostic stability during long-term follow-up. Valid and reliable diagnostic instruments for assessing psychotic-related obsessive-compulsive symptoms in schizophrenia patients, in addition to typical ego-dystonic obsessive-compulsive symptoms, should be developed.

The definition of obsessions and compulsions in the nosological context of schizophrenia and the differential diagnosis distinguishing these symptoms from delusions and delusionally motivated repetitive behaviors are essential to clarify whether the presence of obsessive-compulsive symptoms is another important goal. A pharmacogenetic approach is promising for the development of personalized treatment. There is preliminary evidence pointing toward association of the glutamate transporter gene SLC1A1 with atypical antipsychotic-induced obsessive-compulsive symptoms in schizophrenia patients [24]. Conceivably, patients who manifest obsessive-compulsive symptoms associated with atypical antipsychotics have a genetic predisposition, which is "unmasked" by treatment. It is also possible that genetic predisposition, albeit with a differential "load", exists in schizophrenia patients who exhibit obsessive-compulsive symptoms that are unrelated to treatment with atypical antipsychotic agents. Finally, large-scale controlled trials to evaluate the therapeutic efficacy of antipsychotic agents alone and in combination with SRIs or other potentially effective compounds (e.g., glutamatergic drugs) are essential to establish evidence-based treatment guidelines for schizophrenia patients with obsessive-compulsive symptoms, a group that remains diagnostically challenging and difficult-to-treat.

Overall, growing evidence points towards the existence of a schizo-obssesive subgroup of schizophrenia. However, further longitudinal studies with larger samples of patients are essential to clarify whether the presence of obsessive-compulsive symptoms in schizophrenia represents a comorbidity between the two disorders or a distinct "schizo-obssesive" subtype of schizophrenia.

Appendix A. Proposed diagnostic criteria for an obsessive-compulsive symptom subgroup ("schizo-obssesive") of schizophrenia

A. Symptoms are present that meet Criterion A for obsessive-compulsive disorder at some time point during the course of the schizophrenia.
B. If the content of the obsessions and/or compulsions is interrelated with the content of delusions and/or hallucinations (e.g., compulsive hand washing due to command auditory hallucinations), additional typical OCD obsessions and compulsions recognized by the person as unreasonable and excessive are required.
C. Symptoms of obsessive-compulsive disorder are present for a substantial portion of the total duration of the prodromal, active and/or the residual period of schizophrenia.
D. The obsessions and compulsions are time-consuming (more than 1 hour a day), cause distress or significantly interfere with the person’s normal routine, in addition to the functional impairment associated with schizophrenia.
E. The obsessions and compulsions in the patient with schizophrenia are not due to the direct effect of antipsychotic agents, a substance of abuse (e.g., cocaine), or an organic factor (e.g., head trauma).
References


