

THE RELATIONSHIPS BETWEEN OBSESSIVE-COMPULSIVE DISORDER AND PSYCHOSIS: AN UNRESOLVED ISSUE

Stefania Palermo, Donatella Marazziti, Stefano Baroni, Filippo Maria Barberi, Federico Mucci

Abstract

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Objective: The aim of the present paper was to review and comment on available literature on the complex relationships between obsessive-compulsive disorder OCD and psychotic disorders, with a focus on diagnostic issues, as well as clinical and prognostic implications.

Method: The databases of PubMed, Scopus, Embase, PsycINFO and Google Scholar were accessed in order to research and collect articles published in English language only, according to the PRISMA guidelines. Free text terms and MeSH headings were combined as it follows: “Obsessive–compulsive disorder” OR “Obsessive-Compulsive Symptoms” AND “Schizophrenic Disorders” OR “Schizophrenic Symptoms” AND “Antipsychotic Treatment” OR “Second-Generation Antipsychotics “SGAs”.

Results: The relationships between obsessive-compulsive disorder (OCD) and schizophrenia spectrum disorders, intended as diagnostic categories, as well as the overlap between obsessive-compulsive and psychotic symptoms, represent an interesting example of how “neurosis” and “psychosis” actually stand along a longitudinal and transversal continuum, much more frequently than it was supposed in the past. It also poses a challenge for clinicians, since treating some symptoms of one disorder may trigger or worsen the other one.

Conclusions: The question of the symptom overlapping between OCD and psychoses remains unresolved, if considered within the stringent categorization of the available diagnostic systems, but even all the attempts to explain the heterogeneity of the clinical pictures, according to other theoretical constructs, result inconclusive. The controversial role of antipsychotics, especially of SGAs in the treatment of these complex patients is another problem to be clarified in future and more focused studies.

Key words: obsessive-compulsive disorder, psychosis, schizophrenia, second-generation antipsychotics

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Introduction

Obsessive-compulsive disorder (OCD) is a common psychiatric condition characterized by obsessions, compulsions, or both. Obsessions are recurrent, persistent, intrusive and unwanted thoughts, urges, or images that cause marked anxiety or distress. The individual tries to ignore or suppress such thoughts, urges, or images, or to neutralize them by performing a compulsion, which is a repetitive behavior or mental act. The aim of compulsions is to prevent or reduce anxiety or distress, and some dreaded events or situations, although not connected in a realistic way to what they are supposed to prevent or neutralize, or are clearly excessive (Diagnostic and Statistical Manual for Mental Disorders, 5th edition, DSM-5, APA, 2013). However, it is evident that OCD is a complex

pathology with a multiplicity of clinical pictures (and perhaps of pathophysiological mechanisms) that cannot be easily included in rigid categorical systems. As a result, different approaches have been proposed, based on dimensions or symptom peculiarities (Cordeiro, Sharma, Thennarasu, & Reddy, 2015; Stein et al., 2019).

The same issues also apply to those heterogeneous conditions that the DSM-5 groups together in the so-called schizophrenia (SZ) spectrum and other psychotic disorders. This is a wide category including schizotypal personality disorder, delusional disorder, brief psychotic disorder, schizophreniform disorder, SZ, schizoaffective disorder, substance and/or medication-induced psychotic disorder, psychotic disorder due to another medical condition, catatonia associated with another mental disorder, catatonic disorder due to another medical condition, unspecified catatonia,

other specified SZ spectrum and other psychotic disorder, unspecified SZ spectrum and other psychotic disorder. Not surprisingly, even for psychoses, different dimensional approaches have been proposed (Allardyce, Suppes, & van Os, 2007; Arciniegas, 2015).

The comorbidity of OCD with psychotic disorders, such as SZ, schizoaffective disorder or other, is widely reported in the literature with different prevalence rates (Bottas, Cooke, & Richter, 2005; Eisen, Beer, Pato, Venditto, & Rasmussen, 1997; Tibbo & Warneke, 1999). However, it should be pointed out that OCD patients were mainly diagnosed as schizophrenic, more or less until the eighties of the last century, when it was underlined that psychotic symptoms were quite frequent in this condition, and represented a common dimension shared by different disorders (Foa et al., 1995; Insel & Akiskal, 1986; Kozak & Foa, 1994; Marazziti, 2001). Interestingly, even bizarre psychotic symptoms in OCD patients were shown to improve with serotonergic drugs, while highlighting the relationship with the “core” disturbances (O’Dwyer & Marks, 2000).

This new conceptualization of OCD was first introduced in the 4th edition of the DSM (DSM-IV, APA, 1994), until the most comprehensive specification of this dimension in DSM-5. Indeed, the impressive bulk of data in OCD gathered in the last decades led to attribute nosological autonomy to this disorder and related conditions in the novel category of obsessive-compulsive and related disorders (OCRDs). The insight dimension became an important specifier distinguished along an increasing level of severity: “good or fair insight”, “poor insight”, or “absent insight/delusional beliefs”. Moreover, the “absent insight/delusional beliefs” specifier is associated with a worst prognosis, a chronic course, treatment resistance/refractoriness, and generally requiring the combination of different drugs including antipsychotics, according to current therapeutic guidelines (Kim, Ryba, Kalabalik, & Westrich, 2018; Marazziti, 2019; Marazziti, Catena, & Pallanti, 2006; NICE, 2005).

In any case, the relationship between OCD and psychotic disorders still represents a great challenge to psychological and psychiatric domains, as its deeper understanding might lead to more appropriate diagnoses and more tailored treatments of disorders that are frequently chronic and poorly responders to common therapeutic strategies.

The aim of this paper was at reviewing and commenting on the available literature exploring the relationship between OCD and psychosis.

Methods

According to the PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2009), the databases of PubMed, Scopus, Embase, PsycINFO and Google Scholar were accessed in order to research and collect articles that were published only in English language between January 1970 and January 2020. Free text terms and MeSH headings were combined as it follows: “Obsessive-Compulsive Disorder” OR “Obsessive-Compulsive Symptoms” AND “Schizophrenic disorders” OR “Schizophrenic Symptoms” AND “Antipsychotic Treatment” OR “Second-Generation Antipsychotics”. All the authors agreed to include in the review conference abstracts, posters and case reports if published in indexed journals. The following inclusion criteria were adopted: preclinical accurate studies carried out with standard/proven techniques, clinical studies carried out in

children/adults with reliable diagnosis of psychiatric disorders, according to structured interviews and standardized criteria, reliable assessment of outcome measures. All the authors equally contributed in identifying potential information specific to this topic amongst the titles and abstracts of the publications. The first selection excluded 4846 titles because: a) duplicates; b) not concerning the scope of the paper; c) not informative enough. The second selection excluded 515 abstracts after being read and reviewed, as the information reported did not fulfill the scope of our paper and/or the presented information did not seem relevant to the discussed topic. Subsequently, 108 more publications were excluded after being completely read and evaluated, as they did not provide enough information and/or resulted sufficiently in line with our review. Finally, 69 papers were included in the present review (figure 1). The search was last updated in March 2020.

OCD and psychotic disorders

The core components of OCD are obsessions and compulsions, both often posing a challenge in the differentiation from the clinical features of psychotic disorders (Badcock, Waters & Maybery, 2007). Indeed, distinguishing delusions from obsessions may be a great task (Poyurovsky et al., 2008). Generally, the degree of insight is of paramount importance (Poyurovsky, Weizman, & Weizman, 2004), but in some cases it can be difficult to ascertain whether an intrusive thought is an obsession in OCD with poor or no insight, or a delusion belonging to psychotic positive symptoms (Leung & Palmer, 2016). In addition, to complicate the question, some cognitive domains may fluctuate longitudinally between obsessions and delusions (Insel & Akiskal, 1986). A similar issue for the differential diagnosis involves the compulsions, since some positive symptoms of SZ may lead to repetitive behaviors (Faragian, Pashinian, Fuchs, & Poyurovsky, 2009).

All these considerations highlight the weakness of DSM organizational model implying constant additions of novel specifiers throughout the different editions of the manual. By contrast, novel approaches and conceptualizations of psychopathology and psychiatric disorders have been proposed, based on comorbidity dimensions, symptom patterns or spectrum models (Cassano, Pini, Saettoni, & Dell’Osso, 1999; Hollander, Kim, Khanna, & Pallanti, 2007; Spitzer, Endicott, & Robins, 1978), all with some merits, but unable to disentangle the crucial problem of overlapping clinical features. Therefore, nowadays, it is essential to consider psychopathological symptoms and features in both a categorical and a dimensional way, which allows to understand each patient and the complexity and heterogeneity of clinical pictures.

A recent study (Hagen, Solem, Opstad, Hansen, & Hagen, 2017) showed that, besides the comorbidity between OCD and psychotic disorders conceptualized as separated diagnostic categories, there exists even an important relationship between the symptoms of OCD and those of psychosis, with a consistent overlap between the different dimensions. The authors hypothesized that metacognition might play a crucial role in the development and maintenance of all psychological processes and psychopathological disorders, OCD and psychotic disorders included (Hagen et al., 2017). Indeed, metacognition has been associated with symptoms of a wide range of psychological disturbances, which suggests it might

represent a factor of vulnerability towards multiple forms of psychopathology (Wells & Carter, 2009). Metacognition refers to beliefs, processes and strategies that monitor, control or interpret thinking (Wells & Cartwright-Hatton, 2004), and, as such, has been proposed as a possible link between psychosis and OCD (Moritz, Peters, Larøi, & Lincoln, 2010). That is not surprising if we consider that both OCD and psychotic disorders are characterized by some identical cognitive patterns, like magical and bizarre thoughts (Rasmussen, Steketee, Silverman, & Wilhelm, 2013). In a study on the role of metacognition, a control group consisting of 194 people completed an internet survey assessing paranoid ideation, predisposition to hallucinations, symptoms of OCD, depression, anxiety, and metacognition (Hagen et al., 2017). Interestingly, metacognition showed strong positive correlations with all the other symptom measures. Further, obsessive-compulsive symptoms (OCS) showed a strong positive correlation with psychotic symptoms. In conclusion, the study showed a large overlap between psychotic (paranoia and hallucinations) or OCS and metacognition, the latter representing an important transdiagnostic cognitive dimension (Hagen et al., 2017). A recent cognitive investigation noted that OCS and delusions share specific metacognitive profiles, particularly through a heightened need to control thoughts (Tezenas du Montcel, Pelissolo, Schürhoff, & Pignon 2019). Other studies reported that psychotic symptoms like hallucinations, delusions, and thought disorders are more common in OCD patients than in the rest of population (Bortolon & Raffard, 2015; Eisen & Rasmussen, 1993).

Even early psychotic patients showed more OCS than healthy control subjects (Mariné et al., 2015). A Norwegian group reported that the OCD prevalence was 10.6% in patients with first-episode psychosis (Hagen, Hansen, Joa, & Larsen, 2013). Furthermore, an early diagnosis of OCD has been considered to be a risk factor for later development of psychosis (Van Dael et al., 2011).

The relationship between OCD and psychosis is indeed very complex, and several factors, such as common risk factors, course of illness, temporal association, pharmacological treatments, neuroimaging data (when available) should all be considered to help clarifying this question.

OCD and schizophrenia

The comorbidity OCS/OCD-SZ seems to be more frequent than previously supposed, as patients suffering from SZ seem to present OCS and OCD in, respectively, 25% and 12% of the cases (Schirmbeck & Zink, 2013). According to another study (Frias-Ibáñez, Palma-Sevillano, & Farriols-Hernando, 2014) this comorbidity would involve 12-15% of the patients with a primary diagnosis of psychotic spectrum, being this prevalence six times greater than that expected in the general population. Again, almost 30% of SZ patients might present OCS, with three main conditions identified: prodromal symptoms of SZ, co-occurrence of OCS and SZ, and antipsychotics-induced OCS (Tezenas du Montcel et al., 2019). Recent meta-analyses showed that approximately 12-14% of schizophrenic patients may meet the diagnostic criteria for OCD, and up to 30% of them report subclinical OCS (Achim et al., 2011; Swets et al., 2014). Percentages might be higher, with an OCS prevalence reaching the 64% in a sample of 100 SZ patients (Kayahan, Ozturk, Veznedaroglu,

& Eraslan, 2005), or amongst 396 patients closely related by consanguinity (Bener, Dafeeah, Abou-Saleh, Bhugra, & Ventriglio, 2018).

Throughout the years, the overlap between OCD and SZ has been labeled as “Obsessive psychosis” (Insel & Akiskal, 1986; Solyom, DiNicola, Phil, Sookman, & Luchins, 1985), “Obsessive delusions” (Porto, Bermanzohn, Pollack, Morrissey, & Siris, 1997), “Delusional OCD” (O’Dwyer & Marks, 2000), “Schizo-obsessive” (Hwang & Opler, 1994; Hwang & Hollander, 1993), until a clinical entity called “Schizo-obsessive disorder” (Attademo, De Giorgio, Quartesan, & Moretti, 2012; Hollander et al., 1999; Zohar, 1997) was coined and more widely accepted, referring to a disorder representing a nosological continuum between the two conditions (Poyurovsky et al., 2004). Therefore, the diagnosis of schizo-obsessive disorder requires the presence of both OCD and SZ (Schirmbeck & Zink, 2013), and its existence seems to be supported by epidemiologic, clinical and brain functional patterns (Poyurovsky, 2013; Poyurovsky et al. 2012). Moreover, several studies underlined how OCD and SZ share some similarities, such as course of illness, age at onset, and pathophysiological underpinnings, specifically structural and functional brain abnormalities, or serotonin and dopamine alterations (Poyurovsky et al., 2012; 2004). Again, gender distribution and age of onset are similar in SZ and OCD (Sharma & Reddy, 2019). A diagnosis of SZ may be wrongly made if the clinician overvalues the bizarre characteristics of obsessive-compulsive (OC) beliefs and rituals, often preceded by premonitory features of schizotypal personality, with primitive connotations of magical thinking, and with attribution of superstitious meanings to one’s thoughts and actions. Anyway, sensory phenomena and formal thoughts disorders are rare in OCD (Marazziti, 2020).

As already underlined, connections between OCD and SZ are multiple and at different levels. Transitions from OCD to SZ spectrum disorders have been described in the classic literature of the eighties and nineties of the last century (Allsopp & Verduyn, 1989; Berrios, 1989; Tien & Eaton, 1992). According to some authors (Sterk, Lankreijer, Linszen, & de Haan, 2011), OCS/OCD could develop in those subjects at ultra-high risk for psychosis, during prodromal psychotic state, in the first episode of SZ, during the course of chronic SZ, and after treatment with atypical antipsychotics (Sterk et al., 2011). A review analyzed this comorbidity from five perspectives: SZ with OCS, OCD with psychotic symptoms, OCS in SZ-spectrum personality disorders, OCS/OCD induced by second-generation antipsychotics (SGAs), and similarities in functional neural circuits in OCD and SZ (Frommhold, 2006). According to Frommhold, exploring the interface of schizophrenic and OCS was important for proper diagnosis, treatment and long-term prognosis. The author then suggested the need of further investigations in larger cohorts of schizophrenic and OCD patients, in order to identify a schizo-obsessive SZ and a schizotypal subtype of OCD (Frommhold, 2006). Similarly, four main theories and models were analyzed: OCD as a risk factor for SZ, OCD as a psychotic prodrome in SZ, the common risk factors between the two clinical entities in terms of neuroanatomy, neurophysiology, neuroendocrinology and neurocognition, and OCS/OCD inducement or exacerbation due to SGAs (Frias-Ibáñez et al., 2014). The comorbidity prevalence was much greater than expected by pure chance, and all the empirical evidence supported the newly created diagnostic entity called “schizo-obsessive disorder”, with the possible existence of several subtypes of “schizo-obsessive” patients.

Table 1. Studies showing obsessive-compulsive disorder (OCD) and obsessive-compulsive symptoms (OCS) prevalence amongst schizophrenia (SZ) patients

Type of study Authors and Year	Participants (n)	OCD	OCS
<u>Cohort-study</u> Kayahan et al. (2005)	100	30%	64%
<u>Cohort-study</u> El-Shiekh et al. (2017)	50	16%	62%
<u>Cohort-study</u> Bener et al. (2018)	396	26%	-
<u>Meta-analysis</u> Achim et al. (2011)	3007	12%	-
<u>Meta-analysis and meta-regression</u> Swets (2014)	3978	14%	30%
<u>Review article</u> Schirmbeck & Zink (2013)	-	12%	25%
<u>Review article</u> Frias-Ibanez et al. (2014)	-	12-15%	-
<u>Review article</u> Tezenas du Montcel et al. (2019)	-	-	30%

Furthermore, the differences between subtypes posed the question on whether OCS/OCD could represent a sort of coping with psychotic symptoms (Frias-Ibanez et al., 2014). A review suggested that proper distinctions should be made amongst OCS occurring only in the context of psychosis and that may overlap with psychotic phenomenology, those present only in the prodromal phase of SZ, OCS or OCD occurring comorbid with SZ, and antipsychotic-induced OCS or OCD (Bottas et al., 2005). A growing literature suggests that OC phenomena would represent a distinct dimension in SZ, independent from nuclear psychotic symptoms. Again, OC phenomena were reported to be indistinguishable in terms of their severity, resistance, interference, and control in 31 OCD patients and in 35 schizophrenic patients (Tonna et al., 2015). Furthermore, a “progression of the disorder” model has been underlined, that is to say, an egodystonic thought transitioning into a delusional egosyntonic ideation, together with a decrease of insight (Marazziti, Akiskal, Rossi, & Cassano, 1999; Scotti-Muzzi & Saide, 2018).

Clinical and prognostic implications

A population-based longitudinal and multigenerational family study reported that OCD patients showed a 12-fold increased risk of receiving a comorbid diagnosis of SZ, and that individuals first diagnosed with SZ had a 7 times higher risk of receiving a later diagnosis of OCD. These findings were largely independent from the prescription of medications that could lead to SGAs-induced OCS/OCD (Cederlöf et al., 2015). The study also revealed that OCD-affected relatives of OCD subjects showed a significantly increased risk for SZ and schizoaffective disorder. According to these authors, the high comorbidity, the sequential/longitudinal risk, and the shared familial

risk between OCD and SZ, would suggest a shared genetics, etiology and pathophysiology. Nonetheless, it was highlighted that other factors should be considered, including environmental influence, initial misdiagnosis, and dynamic brain changes over time, and how the comorbidity complicates the clinical management of these conditions (Cederlöf et al., 2015).

It is worth noting that in the middle of the last century, the presence of OCS in SZ was considered a protective factor against psychosis (Rosen, 1957), while subsequent studies led to different conclusions, with comorbid patients showing a poorer outcome than schizophrenic ones (Fenton & McGlashan, 1986). This notion has been increasingly supported by recent studies showing that OCD/OCS may influence the course of SZ, usually entailing greater severity and poorer prognosis (Sharma & Reddy, 2019). Moreover, patients with SZ and OCS seem to be characterized by more severe psychotic and depressive symptoms, higher suicidality and lower social functioning (Tezenas du Montcel et al., 2019). Amongst other clinical features, comorbid patients also showed an early-onset of the psychopathology, more negative symptoms, greater depressive mood and higher level of psychosocial dysfunctionality (Frias-Ibanez et al., 2014).

A comprehensive study reported that the rates of both OCS and OCD were higher in the schizophrenic sample: 62% of them showed OCS (versus 42% of the control group), and 16% were diagnosed with comorbid OCD (versus 4% of the control group) (El-Shiekh, Michail, Al-Said, & Ramadanet, 2017). The serotonin blood levels resulted lower in SZ patients without OCS, even lower in SZ patients with OCS, and lowest in SZ patients with full-blown OCD, as compared with the control group. In addition, the global functioning of the 50 SZ individuals was assessed: there was no significant difference between SZ with or without OCS, while there was a difference between SZ with and without

Table 2. Studies on clinical and prognostic findings of the association between obsessive-compulsive disorder (OCD)/obsessive-compulsive symptoms (OCS) and schizophrenia (SZ)

Type of study Authors and Year	Participants (n)	Clinical and prognostic findings
<u>Cohort-study</u> Tonna et al. (2015)	60	Functioning in SZ patients was positively related to mild OCS, and inversely related to moderate/severe OCS
<u>Cohort-study</u> El-Shiekh et al. (2017)	100	The serotonin blood levels resulted lower in SZ patients, even lower in SZ-OCS patients, and lowest in SZ-OCD patients, as compared with healthy subjects
<u>Cohort Longitudinal</u> Cederlof et al. (2015)	-	Increased risk for OCD patients to develop SZ and vice versa
<u>Retrospective</u> Fenton & McGlashan (1986)	21	OCD-SZ comorbid patients showed a poorer outcome than schizophrenic ones
<u>Retrospective chart review</u> Baytunca et al. (2017)	29	The mean antipsychotic doses used to treat the first episode resulted significantly lower in SZ patients than in comorbid ones. The OCD comorbidity seemed to be a predictor of treatment resistance
<u>Review article</u> Cunill et al. (2013)	-	More severe impairment in abstract thinking was detected in patients with SZ-OCS/OCD than in SZ patients without the OC comorbidity
<u>Review article</u> Frias-Ibanez et al. (2014)	-	Comorbid patients showed an early-onset of the psychopathology, more negative symptoms, greater depressive mood and higher level of psychosocial dysfunctionality
<u>Review article</u> Sharma & Reddy (2019)	-	OCD/OCS seemed to influence the course of SZ, usually entailing greater severity and poorer prognosis
<u>Review article</u> Tezenas du Montcel et al. (2019)	-	OCS/SZ comorbid patients showed more severe psychotic and depressive symptoms, higher suicidality and lower social functioning

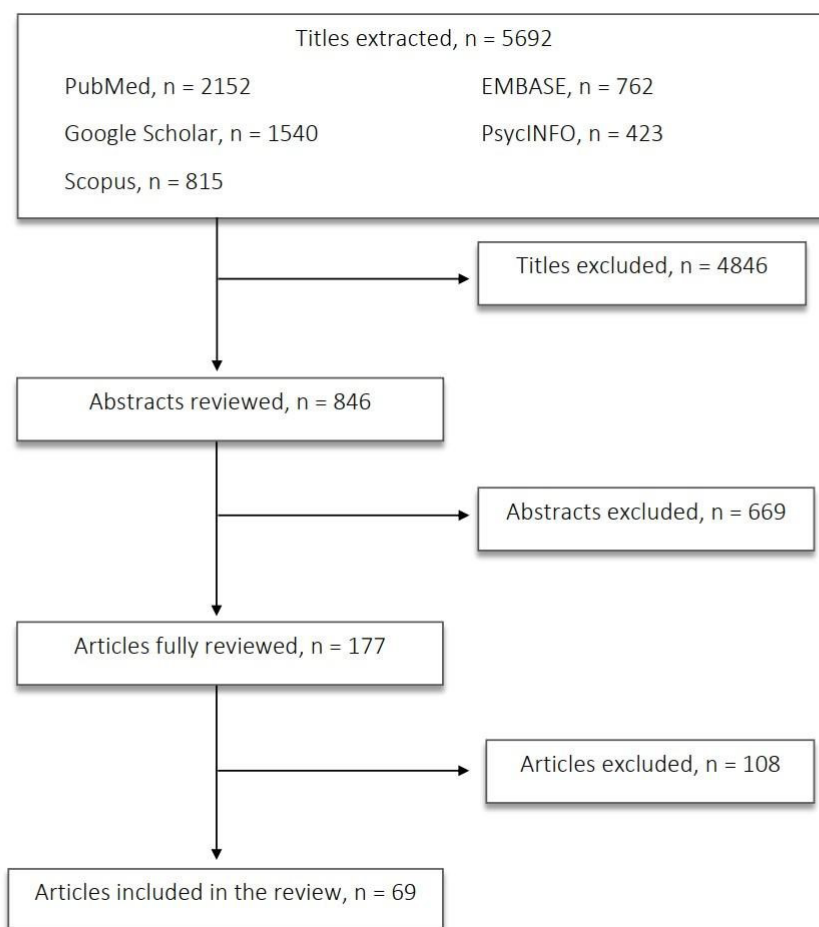
OCD, with the former showing a worst functioning (El-Shiekh et al., 2017).

An Italian study aimed at evaluating the effect of OCS/OCD on functioning in 60 schizophrenic patients, independently from SZ symptoms (Tonna et al., 2015). Along a severity gradient of OC dimension, the relationship between functioning and OCS was represented by a reverse U-shaped curve: functioning was positively related to mild OCS, and inversely related to moderate/severe OCS. These findings, named by the authors “Janus Bifrons effect”, might lead to the conclusion that routine and repetitive behaviors, when mild, would result in a certain order and organization in daily activities, providing stability and allowing to achieve prefixed goals; on the other hand, the interference of severe OCS on patients’ life might affect negatively the functioning, and become worsening rather than protective (Tonna et al., 2015). A more severe impairment in abstract thinking was also detected in patients with SZ-OCS/OCD than in patients with SZ without the OC comorbidity (Cunill, Huerta-Ramos, & Castells, 2013).

Interestingly, in 19 SZ patients without and 10 SZ patients with OCD, mainly adolescents with early-onset, the mean antipsychotic doses used to treat the first episode resulted significantly lower in the first than in the second group (290±209 mg/day versus 491±376 mg/day). Although the severity of the SZ was similar in the two groups, the OCD comorbidity in SZ seemed to be a predictor of treatment resistance (Baytunca et al., 2017).

The role of atypical antipsychotics

Occasionally, the comorbidity OCD-SZ is first recognized after the use of some SGAs, as OCD is commonly diagnosed in SZ patients treated with antipsychotics with significant anti-serotonergic activity (Grillault Laroche & Gaillard, 2016; Swets et al., 2014). Again, it is widely documented how the treatment with certain, but not all SGAs may worsen chronic OCD (Marazziti, 2020). The clinician should pay attention to what would sometimes represent an artificial comorbidity, since treatment for one may trigger the other disorder (Cederlöf et al., 2015). It is a shared hypothesis that the 5-HT_{2A} and 5-HT_{2C} receptor antagonism of SGAs, such as clozapine and olanzapine, could induce *de novo* or worsen pre-existing OCS (Grillault Laroche & Gaillard, 2016; Fonseka, Richter, & Müller, 2014; Schirmbeck et al., 2015). On the other hand, drugs with predominant dopaminergic blockade, such as that of amisulpride and aripiprazole are not associated with induction of OCS (Lopez-Gil, Artigas, & Adell, 2010). A cross sectional study assessed the severity of OCS and the incidence of OCD in 70 schizophrenic patients, amongst which 26 were treated with clozapine and 44 with another SGA. Significantly higher severity of OCS and incidence of OCD were both observed in the 26 patients treated with clozapine (Schreiter et al., 2016). In a group of 118 clozapine-treated schizophrenic patients, the OCD prevalence reached 47%. The authors, therefore, suggest to search for obsessive symptoms and compulsive behaviors in patients treated with clozapine and similar drugs with significant anti-serotonergic action (Fernandez-Egea,

Figure 1. Article selection flow chart

Worbe, Bernardo & Robbins, 2018). If it is possible that some SGAs may trigger OCD onset, it is also possible that undiagnosed OCD may precede psychosis onset, and then become more apparent with decreased psychosis and improved cognition (Veras et al., 2017). A retrospective selection of 142 inpatients who had started clozapine treatment, reported that no patients had developed a worsening of OCS as a result of this treatment. Although some fluctuations of OCS might have occurred, it was unclear whether those symptoms were related to psychotropic drugs or to variations in the natural history of illness, so that no definitive relationship between OCS and clozapine treatment could be established (Ghaemi, Zarate, Popli, Pillay, & Cole, 1995). An Indian study reviewed case records of 220 patients who received clozapine for at least 3 months. OCS/OCD were found in about one fifth ($n=42$) of patients, but the majority had been suffering from OCS/OCD prior to starting clozapine. About one fourth of these patients with pre-existing OCS/OCD showed a worsening with clozapine, while the remaining resulted unchanged (Grover, Hazari, Chakrabarti, & Avasthi, 2015).

There are also studies describing a positive effect of clozapine treatment in OC-SZ patients. Indeed, the effects of clozapine on OCS may range from improvement in some to worsening in other patients (Reznik et al., 2004). An open-label trial, involving 26 outpatients suffering from resistant OCD, examined the results of augmentation strategy with olanzapine in addition to serotonin reuptake inhibitors (SRIs).

Responders were defined as being those showing a reduction of at least 35% in the Yale-Brown obsessive-compulsive scale (Y-BOCS) total score: after 12 weeks of treatment 17 patients (68%) showed a significant reduction of OCS (Marazziti et al., 2005). Again, olanzapine was particularly useful in OCD patients suffering from severe OCD (Marazziti & Pallanti, 1999). Another report considered three schizophrenic patients with OCS who were unsuccessfully treated with different first-generation antipsychotics (FGAs) in combination with anti-obsessive agents, and who showed resistance or intolerance to clozapine. After olanzapine administration, all patients showed a significant improvement in both schizophrenic and OCS, as measured by the Brief Psychiatric Rating Scale (BPRS) and the Y-BOCS (Poyurovsky et al., 2000).

Conclusions

The relationships between OCD and psychotic disorders represent a “hot” topic widely debated within the psychiatric domain since decades. Generally, the frequency of one diagnosis respect to the other is based upon the prevalent paradigm of the time, therefore in the first half of the past century, SZ diagnosis was preferred, as OCD was considered rare and even a protective factor against psychosis. However, the subsequent increasing data in the OCD field revealed that this condition was common and more frequent than other psychotic disorders. Currently, the question of the

symptom overlapping between OCD and psychoses remains unresolved, if considered within the stringent categorization of the available diagnostic systems. As such, the comorbidity notion does not seem adequate enough to explain the heterogeneity of the clinical pictures, that even within each single disorder may be complex and multiform. In any case, these patients may pose hard problems to clinical management, with less favorable outcomes. The therapeutic choices must be continuously evaluated, especially in the case of SGAs that seem to be located on a tightrope, as they require to be constantly balanced between the improvement of negative psychotic symptoms and the possible worsening of OCS. Evidence so far seems to suggest that longitudinal course and complications of OCD would be significantly influenced from a disorder of the psychotic spectrum, although the opposite might also be true.

Further investigations are necessary taking into account dimensional rather than categorical models of both OCD and psychotic disorders. This will be essential to gather more solid evidence to provide patients a more targeted therapeutic approach, also addressing possible shared pathophysiological bases.

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