

## Cognitive-behavioural therapy for obsessive-compulsive disorder co-occurring with psychosis: Systematic review of evidence

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### Abstract

#### AIM

To review available evidence on the use of cognitive behavioural therapy (CBT) for treating obsessive compulsive disorder co-occurring with psychosis.

#### METHODS

In this paper we present a detailed and comprehensive review of the current literature focusing on CBT treatment of obsessive compulsive disorder (OCD) co-occurring with schizophrenia or schizoaffective disorder. We identified relevant literature published between 2001 and May 2016 through MEDLINE/PubMed search using as search string (“obsessive compulsive disorders” or “obsessive compulsive symptoms”) and (“schizophrenia” or “schizoaffective disorder” or “psychosis”) and (“cognitive behavioural therapy”). Other citations of interest were further identified from references reported in the accessed articles. The search was limited to studies written in English and carried out in adult patients. A total of 9 studies, 8 case reports and 1 case series, were found.

#### RESULTS

The reviewed evidence indicates that CBT is: (1) safe, *i.e.*, does not worsen psychotic symptoms; (2) well accepted, with a discontinuation rate quite similar to that reported for patients with OCD without psychosis comorbidity; (3) effective, with a symptom reduction quite similar to that reported for patients with OCD without psychosis and for SRIs treatment of OCD co-occurring with psychosis; and (4) effective in patients with OCD induced by second-generation antipsychotic as well as in patients with OCD not induced by second-generation antipsychotic. Alcohol/substance use disorder comorbidity and OCD onset preceding that of SCH/SA was predictors of poor outcome. These results are derived only by additional studies with adequate sample size.

## CONCLUSION

Our results support the use of CBT for OCD in patients with psychosis.

**Key words:** Obsessive compulsive disorder; Obsessive compulsive symptoms; Schizophrenia; Schizoaffective disorder; Cognitive behavioural therapy; Second-generation antipsychotic; Clozapine

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**Core tip:** Ten percent of patients with schizophrenia fulfill criteria for obsessive compulsive disorder (OCD) and in 1/3 of cases OCD onset is related to second-generation antipsychotic (SGA) treatment. Reviewed evidence indicates that cognitive-behavioral therapy for OCD in patients with psychosis is: (1) safe (does not worsen psychotic symptoms); (2) well accepted (discontinuation rate similar to that reported for patients with OCD without psychosis); (3) effective (symptom reduction similar to that reported for patients with OCD without psychosis); and (4) effective in patients with OCD induced by SGA as well as in patients with OCD not induced by SGA. These conclusions are preliminary.

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## INTRODUCTION

The association of schizophrenia (SCH) or schizoaffective disorder (SA) with obsessive compulsive disorder (OCD) or symptoms (OCS) is quite common. In a meta-analysis of 36 studies, including a total of 3,308 patients with SCH, the pooled prevalence rate reported for OCD was 12% and for OCS of 30%<sup>[1]</sup>. This prevalence rate is higher than that of OCD in general population (2%-3%)<sup>[2]</sup> and of SCH in patients with primary OCD (1.7%)<sup>[3]</sup>. Up to 20% of patients with OCS/OCD co-occurring with psychosis report the onset or aggravation of obsessive compulsive symptoms after beginning treatment with a second-generation antipsychotic (SGA), mainly with serotonergic antagonist antipsychotics as clozapine and, at less extend, with olanzapine<sup>[4-9]</sup>. Some authors suggested that in these cases OCS might be considered an adverse event of SGA and introduced the term "antipsychotic-induced OCS" or "secondary OCS" (s-OCS)<sup>[5,10]</sup>. Nevertheless, because sometimes OCS occur or worsen also under no treatment or treatment with first-generation antipsychotics which are not primarily 5HT<sub>2</sub>-R-antagonistic<sup>[11]</sup>, an interaction between genetic/biological predispositions, psychosocial factors and treatments could better explain the phenomenon<sup>[12]</sup>.

The presence of OCS in patients with schizophrenia

is associated with depressive symptoms, high suicide risk, cognitive impairment, poor social functioning, poor perceived quality of life, and poor prognosis<sup>[13-18]</sup>. The relationship between OCS and positive and negative symptoms is unclear<sup>[19]</sup>. Although etiological hypotheses have been put forward to explain the high OCS/OCD co-occurrence in patients with schizophrenia, the causes of this comorbidity remain unclear. As reported by Schirmbeck *et al.*<sup>[20]</sup>: (1) epidemiological data do not confirm the hypothesis of a random association between the two syndromes; (2) clinical data do not confirm the hypothesis that OCS/OCD protects against psychotic disintegration<sup>[21,22]</sup>; and (3) to date, results of neurobiological studies attempting to validate the hypothesis of a separate subtype of psychosis, a so-called "schizo-obsessive disorder"<sup>[23,24]</sup> comprising typical positive, negative and cognitive symptoms of SCH and OCS are inconsistent.

Despite the increasing awareness that OCS/OCD co-occurring with SCH-SA are common and disabling, research on treatment strategies for these complex and treatment-resistant patients is scanty. The American Psychiatric Association practice guidelines<sup>[25]</sup> suggest to stabilize first psychotic symptoms using an antipsychotic drug and subsequently to treat OCS by the augmentation with a serotonin reuptake inhibitor (SRI), *e.g.*, citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine, and clomipramine. Evidence on the efficacy and safety of this augmentation strategy is limited and controversial, and is based to our knowledge on 16 studies (132 patients), most of which are single or multiple case reports. Several studies demonstrated the beneficial effect of antipsychotic-SRI combination, while some studies showed poor response, a risk of psychosis worsening and sometimes aggressiveness (for a review see<sup>[26]</sup>). Furthermore, the antipsychotic-SRI combination produces some clinically significant pharmacokinetic drug interactions: (1) some SRIs (such as fluvoxamine, fluoxetine, paroxetine and venlafaxine) may increase the plasma concentration of particular antipsychotics (such as clozapine, olanzapine, risperidone) by inhibition of hepatic cytochrome P450 isoenzymes (*e.g.*, 1A<sub>2</sub>, 2D<sub>6</sub>) and consequently may increase the risk of adverse events; and (2) the anticholinergic properties of clomipramine limit its use in elderly patients and in those treated with low-potency typical antipsychotics or anticholinergic agents. Some authors suggested to treat OCS co-occurring with psychosis by augmenting antipsychotics with a mood stabilizer, but evidence supporting this strategy is limited to 11 patients treated with lamotrigine<sup>[27]</sup>. As regards s-OCS, several options were proposed: Waiting for spontaneous resolution, gradually reducing the antipsychotic dosage, switching to another antipsychotic, combining an antiserotonergic SGA with either a dopaminergic SGA (amisulpiride or aripiprazole) or a mood stabilizer, and augmenting SGA with a SRI<sup>[25,26]</sup>. So far, very limited evidence supports each of these options, that are generally grounded on theoretical

considerations and/or on the findings of single case reports or case series. Furthermore, the use of SRIs in patients with psychosis is not always safe, as previously discussed, and the dose reduction of clozapine or the switch from clozapine to another SGA could induce an exacerbation of psychotic symptoms.

Hence, an alternative to pharmacological approaches to primary and secondary OCS/OCD co-occurring with SCH/SA is needed.

Of the other existing treatment options for non-comorbid OCD, cognitive-behavioral therapy incorporating exposure and ritual prevention (CBT) is the psychological therapy most supported by research evidence<sup>[25]</sup>.

The aim of this study is to review available evidence on the use of CBT with or without ritual prevention for treating OCD co-occurring with SCH/SA.

## MATERIALS AND METHODS

In this paper we present a detailed and comprehensive review of the current literature focusing on CBT treatment of OCD co-occurring with SCH/SA. We identified relevant literature published between 2001 and May 2016 through MEDLINE/PubMed search using as search string ("obsessive compulsive disorders" or "obsessive compulsive symptoms") and ("schizophrenia" or "schizoaffective disorder" or "psychosis") and ("cognitive behavioural therapy"). The title and the abstract of the retrieved articles were reviewed by the two authors independently and non-pertinent papers were excluded. Of 182 papers screened, only papers including original articles which directly addressed CBT treatment for OCD co-occurring with psychosis were retained for review and inclusion in this study. Other citations of interest were further identified from references reported in the accessed articles. The search was limited to studies written in English and carried out in adult patients. A total of 9 studies, 8 case reports and 1 case series, including overall 31 patients, were found.

## RESULTS

### **Effectiveness of CBT for OCD comorbid with psychosis**

No randomized, controlled trials investigated the efficacy of CBT for OCD in patients with psychosis. However, several important suggestions can be derived from the identified case reports and case series. Table 1 shows the demographic and clinical characteristics and the response to CBT of the 10 patients included in the 8 case reports; characteristics and treatment response of the 21 patients included in the case series are reported separately<sup>[28-35]</sup>. Briefly, 8 patients were male, the mean age was 28 years (range 19-50), and the mean duration of OCD before starting CBT was 7 years (range 1-15). In 1 patient CBT did not include ERP strategies, and in 6 patients psychological treatment was supplemented with pharmacological treatment (SSRIs). One patient, despite an initial reduction of OCS after starting CBT, dropped out. Of the other 9 patients, 5 showed a full

remission and 4 a clinical relevant decrease of OCS severity. Some studies reported follow-up assessments, lasting from 6 mo to 3 years, suggesting a long-term stabilization of the improvement. Although case reports suggest a potential benefit of CBT for OCD co-occurring in psychosis, caution is needed in interpreting these results because of the small number of cases and the heterogeneity of the treatment as regards CBT duration (from "few" to 45 h) and concomitant use of SSRIs.

More homogeneous and clinically useful information can be derived from the case series reported by Tundo *et al.*<sup>[36]</sup> in a naturalistic study including 21 consecutive patients (age 18-65 years) meeting DSM-IV<sup>[37]</sup> criteria for OCD of at least moderate severity [Yale-Brown Obsessive Compulsive Scale<sup>[38,39]</sup> (Y-BOCS) total score  $\geq 16$ ] and either for SCH or SA of up to moderate psychotic severity (Positive and Negative Symptoms<sup>[40]</sup> total score < 95). Treatment included antipsychotics, in association with mood stabilizers in SA patients (50% of cases), for SCH or SA and CBT for OCD. Patients were treated in a tertiary care setting, in which treatment guidelines were personalized taking into account each patient's insight into illness, treatment adherence, Axis I comorbidity and alcohol/substance use disorder. ERP strategies were supplemented with cognitive techniques and other ad hoc interventions, when necessary. Psychotherapy was scheduled flexibly: The mean number of CBT sessions was 34 (range 23-41) in patients with SA and 31 (range 8-40) in patients with SCH. During the study, 5 patients with SCH discontinued the therapy: One refused it after the first session, 1 was hospitalized because of the worsening of psychosis and 3 said that CBT was ineffective. Patients who dropped out from the study had their last observation carried forward for statistical analysis, thus 21 patients were analyzed.

The results showed a significant OCS reduction over 12 mo (Y-BOCS total score  $30.8 \pm 6.7$  at baseline,  $22.3 \pm 8.3$  after 12 mo of treatment), as well as improvements in severity of illness, as measured by Clinical Global Impression-Severity<sup>[41]</sup> (CGI-S) ( $5.5 \pm 1.6$  at baseline,  $4.5 \pm 1.0$  after 12 mo of treatment), and functional improvement, as measured by the Global Assessment of Functioning<sup>[42]</sup> (GAF) ( $49.2 \pm 10.1$  at baseline,  $55.9 \pm 12.3$  after 12 mo of treatment). At the end of the trial, 52% patients were rated as much or very much improved, 33% as responders and 19% as remitters. The 1-year change from baseline in the YBOCS score was 8.1 (95%CI: 5.4-10.8), only slightly lower than that observed in pre-to-post treatment comparisons of ERP (mean 11.4; range 10.5-12.2), and CBT studies (mean 10.6; range 8.5-12.8) in primary OCD<sup>[43]</sup>. Furthermore, insight into illness significantly increased.

### **Effectiveness of CBT for OCD induced by SGA**

MacCabe *et al.*<sup>[28]</sup> first described the case of a man with OCS emerging one year after starting clozapine and responding to 4 mo of CBT (Y-BOCS total score decreased from 12 to 4). The result was maintained at

**Table 1** Case reports of cognitive-behavioural therapy for obsessive-compulsive disorder co-occurring with psychosis

Ref.	Demographic characteristics	OCD duration	Treatments	CBT duration	OCD response	Follow up
Ganesan <i>et al</i> <sup>[30]</sup>	Male, 33 yr	12 yr	CBT/ERP + SSRI	NA	Remitted	8 wk
	Male, 31 yr	11 yr	CBT/ERP + SSRI	NA	Improved	8 wk
	Female, 25 yr	1 yr	CBT/ERP + SSRI	NA	Improved	8 wk
MacCabe <i>et al</i> <sup>[28]</sup>	Male, 50 yr	5 yr	CBT/ERP	4 mo	Remitted	11 mo
Ekers <i>et al</i> <sup>[31]</sup>	Male, 31 yr	15 yr	CBT/ERP	20 h	Remitted	6 mo
Peasley-Miklus <i>et al</i> <sup>[29]</sup>	Male, 22 yr	12 yr	CBT/ERP	6 mo	Responded	36 mo
Rufer <i>et al</i> <sup>[32]</sup>	Female	NA	CBT/ ERP + SSRI	45 h	Improved	15 mo
Kobori <i>et al</i> <sup>[33]</sup>	Male, 26 yr	6 yr	CBT + SSRI	19 h	Remitted	24 mo
Rodriguez <i>et al</i> <sup>[34]</sup>	Male, 19 yr	< 2 yr	CBT/ERP + SSRI	Few hours	Dropped out	
Hagen <i>et al</i> <sup>[35]</sup>	Male, > 20 yr	several years	CBT/ERP	9 h	Remitted	6 mo

OCD: Obsessive compulsive disorder; CBT: Cognitive behavioural therapy; ERP: Exposure and responder prevention; SSRI: Selective serotoninergic reuptake inhibitor; NA: Not available.

follow-up, 11 mo later.

Recently, Tundo *et al*<sup>[44]</sup> reanalyzed their case series to compare the adherence to and the effectiveness of CBT in patients with SCH/SA and comorbid primary OCD (p-OCD) to those with secondary OCD (s-OCD). As suggested by Schirmbeck *et al*<sup>[45]</sup>, they used the order of three events (first psychotic manifestation, start of SGA treatment and subsequent onset of OCD) to define s-OCD. The authors reported an OCD induction in 7 out of 21 patients, related to olanzapine in 4 patients and to clozapine in 3 patients. Neither of these drugs nor their dosages were changed during the study.

During the trial the improvement of OCS did not differ significantly between s-OCD and p-OCD (Y-BOCS total score at baseline  $28.0 \pm 2.3$  and  $32.1 \pm 1.6$ , respectively; after 12 mo of treatment  $24.0 \pm 2.1$  and  $24.5 \pm 1.5$ , respectively), while global functioning, as measured by GAF, improved more rapidly in patients with p-OCD. At 12 mo drop-out rates (s-OCD 14.3% vs p-OCD 28.6%) were lower and improvement (s-OCD 57.1% vs p-OCD 50%), response (s-OCD 42.9% vs p-OCD 28.6%) and remission (s-OCD 42.9% vs p-OCD 7.1%) rates proved to be higher in patients with s-OCD, although not significantly. The findings indicate that the adherence to CBT in patients with psychosis and s-OCD did not differ from that of patients with psychosis and p-OCD and the drop-out rate is similar to that reported in the literature for CBT in patients with OCD without psychosis comorbidity<sup>[44]</sup>. Improvement, response and remission rates in s-OCD group did not differ from those of p-OCD group and are quite similar to those reported in the literature for pharmacological treatment of OCD comorbid with schizophrenia<sup>[44]</sup>.

### Predictors of response

Tundo *et al*<sup>[46]</sup> identified two outcome predictors of CBT effectiveness on co-occurring OCS: The alcohol/substance use disorder comorbidity and the temporal onset of OCD compared to that of SCH/SA.

Patients with alcohol/substance use disorder were significantly less likely to improve than those without this comorbidity (0% vs 68%, respectively;  $P = 0.012$ ).

The rate of improvement was lower in patients in which OCD onset preceded that of SCH/SA than in patients in which OCD onset occurred after that of SCH/SA or in patients in which the onset of the two disorders was simultaneous (0%, 50%, and 83.3%, respectively;  $P = 0.067$ ).

### CBT tolerability

One reason why CBT as treatment for OCS co-occurring with schizophrenia has been scarcely investigated can be related to safety and tolerability concerns<sup>[47]</sup>. In this regard, a focus group evaluating clinician's perceptions on CBT use among patients with severe mental illness reported the fear that intervention-related arousal would result in severe exacerbation of psychotic symptoms<sup>[48]</sup>.

However, the results of the studies included in this review do not support these concerns and, on the contrary, suggest that CBT not only significantly decreases OCS severity, but also ensures a stable remission of psychosis or even the improvement of psychotic symptoms.

In fact, psychotic exacerbation was reported in 2 of 31 patients reviewed. In one case the patient showed reluctance to commit to ERP so the therapist focused on different cognitive techniques<sup>[29]</sup>. In the other case CBT was discontinued because of psychotic exacerbation and subsequent hospitalization after more than 6 mo of psychotherapy<sup>[36]</sup>. The authors argued that the worsening of psychotic symptoms was related to the natural course of schizophrenia and not to the symptom intensification triggered by the involvement in ERP.

Therefore, available results, although limited by the small sample size and the lack of controlled clinical trials, provide encouraging evidence about safety and tolerability of CBT in patients with OCS/OCD co-occurring with psychosis.

## DISCUSSION

In patients with schizophrenia or schizoaffective disorder the co-occurrence of OCD or OCS is quite common (12% and 30%, respectively) and it is associated with

high impairment (great burden of disease, anxiety and depressive symptoms, suicide risk, cognitive impairment, poor social and vocational functioning, and poor prognosis). In about 1 in 4 cases the onset or aggravation of OCS took place after the beginning of SGA treatment. In clinical practice the more frequent treatment of p-OCD and s-OCD is pharmacotherapy, mainly the association of antipsychotic and SRI, while data on the efficacy and the safety of pharmacotherapy are limited and controversial.

The results of the present review support the use of CBT for treating OCS/OCD in patients with SCH/SA. The available data show that this psychological treatment is: (1) safe, *i.e.*, it does not worsen psychotic symptoms; (2) well accepted, with a drop-out rate quite similar to that reported for patients with OCD without psychosis comorbidity; (3) effective, with a symptoms reduction quite similar to that reported for patients with OCD without psychosis and for SRIs treatment of OCD co-occurring with psychosis; and (4) effective in patients with s-OCD as well as in patients with p-OCD. Only subjects with lifetime alcohol/substance use disorder pose a challenge.

Our findings should be interpreted taking into account the limitations of studies included in this review: (1) they are all case-reports; (2) they include a small number of patients; (3) their methodological quality is low; and (4) they do not include a control group or control treatments and, as a consequence, it is not possible to attribute the observed effects to CBT, to the natural course of illness or to non-specific therapeutic factors. So, randomized clinical trials and observational studies with larger samples are required to confirm the safety, the tolerability and the efficacy/effectiveness of CBT for OCS/OCD in patients with psychosis. Despite these limitations, however, the available evidence provides useful information for clinicians planning OCS treatment in patients with SCH/SA and suggests that in these patients CBT might be a viable alternative to pharmacological treatment with SRI. So, in our opinion psychiatrists should not only rely on pharmacotherapy, the most common treatment in clinical practice (for a review see<sup>[49]</sup>), but also on CBT, to select the appropriate treatment for each patient according to their clinical judgment. According to our experience, pharmacotherapy should be used in patients who either refused or did not respond to CBT and, *vice versa*, CBT should be tried in patients who did not respond to medication or are at higher risk of psychotic exacerbation. In high resistant patients further potential options could be some somatic treatments (*e.g.*, electroconvulsive therapy, repetitive transcranial magnetic stimulation, deep brain stimulation)<sup>[50-52]</sup> and psychological treatments alternative to CBT (*e.g.*, psychodynamic therapy)<sup>[53]</sup>. Further clinical trials are warranted to accrue evidence on the efficacy of CBT as well as pharmacological treatment and their combination and to provide useful information to define specific guidelines for the treatment of OCS/OCD in schizophrenia.

## COMMENTS

### Background

More than 10% of patients with schizophrenia (SCH) have comorbid obsessive compulsive disorder (OCD) and in about 20% of cases the onset or worsening of obsessive compulsive symptoms (OCS) is related to treatment with second-generation antipsychotic (SGA), typically serotonergic antagonist antipsychotics as clozapine and olanzapine. The OCS-psychosis comorbidity is associated with high suicide risk, cognitive impairment, poor social functioning and quality of life, and poor prognosis. Management of this condition is a hard challenge for physicians and the evidence on the efficacy and safety of antipsychotic-SRI combination, the most frequent treatment in clinical practice, is limited and controversial.

### Research frontiers

An alternative to pharmacological approach to OCS/OCD co-occurring with psychosis could be cognitive-behavioral therapy incorporating exposure and ritual prevention (CBT), the currently available psychological treatment for non-comorbid OCD most supported by research evidence.

### Innovation and breakthroughs

The present article aims to review available evidence on the use of CBT for treating OCD co-occurring with SCH.

### Applications

The review suggests that CBT for OCD co-occurring with psychosis is: (1) safe, *i.e.*, does not worsen psychotic symptoms; (2) well accepted, with a discontinuation rate quite similar to that reported for patients with OCD without psychosis comorbidity; (3) effective, with a symptom reduction quite similar to that reported for patients with OCD without psychosis and for SRIs treatment of OCD co-occurring with psychosis; and (4) effective in patients with OCD induced by SGA as well as in patients with OCD not induced by SGA.

### Terminology

The study does not include terms that may not be familiar to the majority of the readers.

### Peer-review

This is a comprehensive review of the literature.

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