

Effectiveness and outcome predictors of cognitive-behavioural therapy for obsessive-compulsive disorder co-occurring with psychosis

Efficacia e predittori di risposta alla terapia cognitiva nel disturbo ossessivo compulsivo in comorbidità con disturbi psicotici

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Summary

Objectives

The co-occurrence of obsessive-compulsive disorder (OCD) in patients with schizophrenia (SCH) or schizoaffective disorder (SA) is frequent (7.8%-25%) and is associated with a high risk of suicide, severe impairment of social behaviour, poor quality of life and poor prognosis. Data on the effectiveness of serotonin reuptake inhibitors in patients with SCH/SA OCD comorbidities are limited and controversial, and to date no study exploring the effectiveness of CBT for patients with this comorbid condition has been carried out. The aims of this investigation are to examine the effectiveness of CBT for OCD in patients with stabilized SCH/SA and to analyze the relationship of alcohol/substance use disorder and temporal onset of OCD compared to that of SCH/SA and type of OCD (primary/secondary to second generation antipsychotics) with CBT outcomes in a naturalistic clinical setting.

Methods

Twenty-one consecutive patients with SCH/SA OCD comorbidity were enrolled. Inclusion criteria were: age 18-65 years; meeting DSM-IV criteria for OCD and either schizophrenia or schizoaffective disorder; OCD of at least moderate severity (Yale-Brown Obsessive Compulsive Scale [Y-BOCS] total score ≥ 16); 4) stabilized SCH or SA, even if symptoms were not entirely absent (Positive and Negative Symptoms Scale [PANSS] total score ≤ 75). Primary outcomes were: adherence rate, defined as the percentage of patients who did not drop out during the trial and the OCD remission rate, defined as a Y-BOCS total score < 16 . Secondary outcomes were OCD response, defined as a $\geq 25\%$ decrease in the total Y-BOCS score from baseline to 1 year, and a Clinical Global Impression-Improvement (CGI-I)

score of ≤ 2 ("much" or "very much" improved). An intent-to-treat analysis was performed.

Results

One patient (4.7%) discontinued CBT after 1 session, and 4 patients (19%) dropped out of the study. The mean scores of Y-BOCS, CGI-S and Global Assessment of Functioning (GAF) scales showed statistically significant improvements at 6 months; from 6 to 12 months improvement continued, albeit at a slower rate. From baseline to 12 months, the mean total score reduction on the Y-BOCS was 8.5 points; on the Y-BOCS insight subscale it was 1 point, and on the CGI-S it was 1 point. General functioning also improved, as shown by a 6.7 point increase in GAF scores. At one year, 52% (11/21) of patients were rated as much/very much improved; 33% (7/21) were responders and 19% (4/21) were remitters. Compared with patients without alcohol/substance use, those with alcohol/substance use were significantly less likely to improve (68% vs. 0% $p = 0.012$). The percentage improved varied from 0% in patients in which the onset of OCD preceded that of SCH/SA to 50% in patients in which the OCD onset occurred after that of SCH/SA up to 83.3% in patients in which the onset of two disorders was simultaneous. No significant differences in outcome between patients with primary/secondary to second generation antipsychotics use OCD were found.

Conclusions

Our findings suggest that CBT is a helpful treatment for OCD in these difficult-to-treat patients, with a challenge posed by patients with lifetime alcohol/substance abuse disorder.

Key words

Obsessive-compulsive disorder • Schizophrenia • Schizoaffective disorder • Cognitive-behavioral therapy

Introduction

The co-occurrence of obsessive-compulsive disorder (OCD) and schizophrenia (SCH) or schizoaffective disorder (SA) is quite common. Recent studies have shown that 7.8% to 25% of patients with SCH or SA have comorbid

OCD¹⁻⁴. This suggests that the prevalence of OCD in patients with psychosis is considerably higher than in the general population (1.6%). Some authors have reported that obsessive-compulsive symptoms in patients with schizophrenia are associated with severe psychosis, high risk of suicide, poor neurological testing performance,

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severe impairment of social behaviour, poor quality of life and poor prognosis⁵⁻⁸. Despite growing recognition of the high prevalence and the deeply disabling effects of OCD-SCH/SA comorbidity, few studies have investigated treatment strategies for this difficult-to-treat condition. In particular, no controlled trials to guide treatment planning for OCD in these cases, to the best of our knowledge, have been carried out.

The best current available treatments for non-comorbid OCD are serotonin reuptake inhibitors (SRIs), e.g. citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine, and clomipramine, and cognitive-behavioural therapy incorporating exposure and ritual prevention (CBT)⁹. American Psychiatric Association practice guidelines⁹ suggest treating OCD co-occurring with SCH by combining either typical or atypical antipsychotics with SRIs. Yet, data on the efficacy and safety of this therapeutic strategy are limited and inconclusive. A small placebo-controlled study and a number of case reports have demonstrated the beneficial effect of this anti-psychotic-SRI combination¹⁰⁻¹². Conversely, other studies examining this treatment strategy have shown a lack of therapeutic effects¹³⁻¹⁵, potential psychosis exacerbation and, occasionally, the occurrence of aggressiveness¹⁶⁻¹⁸. Hence, alternative therapeutic approaches to SRIs for OCD co-occurring with SCH/SA are needed.

Among the currently available therapies for non-comorbid OCD, one possible option is CBT. To the best of our knowledge, Tundo et al.¹⁹ were the first to investigate the effectiveness of CBT for OCD-SCH/SA comorbidity. The aims of this paper are to extend data on effectiveness of CBT for OCD in patients with stabilized comorbid SCH/SA and to analyze the relationship between CBT outcomes and substance use disorder, and temporal onset of OCD compared to that of SCH/SA and type of OCD (primary or secondary i.e. induced by use of second generation antipsychotics). Based on our clinical experience, we hypothesized that patients with lifetime substance use disorder, with OCD secondary to second generation antipsychotics use, and with OCD onset subsequent to SCH/SA would exhibit poorer adherence to CBT and poorer outcomes.

Materials and methods

Patients

Consecutive patients seen between 1/1/2003-1/1/2008 at the Istituto di Psicopatologia in Rome (Italy) – an outpatient clinic specialized in mood and anxiety disorders – were screened for eligibility. Inclusion criteria were: 1) age 18-65 years; 2) DSM-IV criteria for OCD and either schizophrenia or schizoaffective disorder as assessed by the Structured Clinical Interview for DSM-IV (SCID-I)²⁰; 3) OCD of at least moderate severity (Yale-Brown Obses-

sive Compulsive Scale^{21,22} [Y-BOCS] total score ≥ 16); 4) stabilized SCH or SA, even if symptoms were not entirely absent (Positive and Negative Symptoms Scale²³ [PANSS] total score ≤ 75).

The exclusion criteria was the presence of neurological conditions inducing OCD, i.e. neurodegenerative disease, brain trauma, stroke, encephalitis, temporal lobe epilepsy, Prader-Willi syndrome, Sydenham's chorea and carbon monoxide or manganese poisoning. All patients gave written informed consent for the anonymous use of their clinical records, and a local ethical committee approved the research project.

Treatments

Table I shows pharmacological treatments for schizophrenia or schizoaffective disorder at T0, T1 and T2. Treatments were chosen by the first author (A.T.) based on each patient's clinical conditions and follow-up visits were scheduled as required, with frequencies ranging from weekly to every few months. CBT was conducted by 4 cognitive-behavioural psychologists (L.S., D.D.S, L.C., A.P.), all of whom have at least 5 years of experience in treating OCD. CBT consisted of imaginal and *in vivo* exposure, ritual-prevention and/or delay, cognitive therapy and other *ad hoc* interventions used to supplement exposure and ritual-prevention strategies. Patients were treated in a naturalistic setting, in the sense that manualized guidelines²⁴ were adapted to each patient after careful consideration of their level of insight, treatment adherence and the presence of another comorbid Axis I disorder. Therapy sessions were scheduled flexibly and jointly by the therapist and patient. Patients received an average of 4 sessions per month during the first 4 months and then continued therapy with 1 to 4 sessions per month. CBT duration was not determined in advance, in line with the real world practice of ending treatment when patients report either feeling better or that therapy is no longer beneficial to them. We did not use any specific CBT protocol for psychosis and alcohol/substance use disorder²⁵.

Procedure

Obsessive-compulsive symptoms were assessed using the Y-BOCS, clinical severity of illness using the Clinical Global Impressions-Severity of illness (CGI-S) scale²⁶; and the overall level of functioning using the Global Assessment of Functioning (GAF) scale²⁷. The scales were administered at baseline (T0) and after 6 (T1) and 12 months (T2) of CBT. The Clinical Global Impressions-Improvement of illness (CGI-I) scale²⁶ was used to evaluate patient improvement at T1 and T2. Schizophrenic and schizoaffective symptoms at T0 were assessed using the PANSS²³. All assessments were made by the first author, who was not involved in CBT.

TABLE I.
Pharmacological treatments*. *Trattamenti farmacologici*.

Drug	n = 21 (%)	T0	n = 19 (%)	T1	n = 16 (%)	T2
		Mean dose (range)		Mean dose (range)		Mean dose (range)
Lithium	9 (42.8)	0.7 (0.55-0.90) [†]	9 (47.3)	0.7 (0.57-0.90) [†]	8 (50)	0.7 (0.51-0.93) [†]
Antiepileptics	11 (52.3)		11 (57.8)		7 (43.7)	
valproate	9 (42.8)	733 (500-1500) [‡]	10 (52.6)	820 (500-1500) [‡]	4 (25)	750 (600-900) [‡]
carbamazepine	2 (9.5)	700 (400-1000) [‡]	1 (5.2)	400 [‡]	2 (12.5)	400 [‡]
gabapentin	1 (4.7)	1800 [‡]			1 (6.25)	150 [‡]
topiramate						
Atypical antipsychotics	19 (90.4)		19 (100)		15 (93.7)	
olanzapine	9 (42.8)	15 (5-20) [‡]	6 (31.5)	16.6 (5-20) [‡]	6 (40)	16 (5-20) [‡]
clozapine	7 (33.3)	257 (200-400) [‡]	7 (36.8)	278 (150-400) [‡]	5 (33.3)	290 (200-400) [‡]
quetiapine	3 (14.2)	133 (100-200) [‡]	4 (21.0)	300 (100-600) [‡]	2 (13.3)	450 (100-800) [‡]
risperidone	2 (9.5)	5.5 (5-6) [‡]	2 (10.5)	3.5 (1-6) [‡]	2 (13.3)	3.5 (1-6) [‡]
Typical antipsychotics	10 (47.6)		7 (36.8)		4 (25)	
haloperidol	9 (42.8)	2.2 (1-6) [‡]	7 (36.8)	2.1 (1-5) [‡]	4 (25)	3.2 (1-7) [‡]
pipamperone	1 (4.7)	200 [‡]				
Benzodiazepines	10 (47.6)	5.2 (2-7) ^{‡§}	10 (52.6)	5.2 (2-7) ^{‡§}	8 (50)	4.6 (2-5) ^{‡§}

* Percent totals do not equal 100, as participants could be on more than one medication; [†] mEq/l; [‡] mg/die; [§] diazepam-equivalent dose.

Outcome measures

The primary outcomes were the adherence rate, defined as the percentage of patients who completed the trial, and the remission rate, defined as a Y-BOCS total score < 16. Secondary outcomes were treatment response, defined as a decrease of Y-BOCS total score from baseline to T2 ≥ 25%, and a CGI-I score of ≤ 2 (denoting “much” or “very much” improved OCD).

Statistical analysis

We conducted an intent-to-treat analysis, with the last observation carried forward for patients who dropped out from the study. Repeated-measures analysis of variance (ANOVA) or Friedman test (non-parametric ANOVA, with a χ^2 approximation to test statistics) were used as appropriate to analyze changes in scores over time. Following significant ANOVA, post-hoc paired-sample tests (t-test or Wilcoxon test) were performed. Outcomes (proportion of completers, responders, remitters and improved) were compared among groups using exact tests and logistic regression. Bootstrap procedures were carried out to estimate the regression coefficient and its standard error²⁸. The significance level (for two-tailed tests) was set at 0.05. Data were analyzed using SPSS, version 20.

Results

Twenty-one patients (13 M, 8 F) were enrolled; 9 (43%) had SCH and 12 (57%) SA. Four patients met criteria for other Axis-I lifetime disorders, i.e. panic disorder (n = 2), social anxiety (n = 2), generalized anxiety disorder (n = 1) and eating disorder (n = 1). The onset of OCD was subsequent to that of SCH/SA in 12 patients (6 SCH, 6 SA), anterior in 3 patients (3 SA), and simultaneous in 6 patients (3 SCH, 3 SA). In 7 of 21 (33%) patients, OCD onset was secondary to second-generation antipsychotics, mostly clozapine, olanzapine and risperidone. Other demographic and clinical characteristics are shown in Table II. Patients with SA received on average 34.3 CBT hours (range 23-41) and patients with SCH received on average 31.1 CBT hours (range 8-40), excluding one patient who participated in a single session and then withdrew from the study.

One patient with SCH refused CBT after 1 session (4.7%); 4 patients (19%) dropped out of the study – 1 with SCH before T1, 1 with SCH and 2 with SA before T2. Of these, 3 reported that CBT was ineffective, and 1 was hospitalized for an episode of psychotic exacerbation. The remaining 16 patients were still receiving CBT at T2. Regarding the psychotic state, following Leucht et al.²⁹ criteria, at baseline 6 patients were “mildly ill”, 3 patients

TABLE II.

Baseline demographic and clinical characteristics of the sample ($n = 21$). *Caratteristiche demografiche e cliniche del campione ($n = 21$).*

Variable	
Age, mean (SD), y	29.3 (5.4)
Men, N (%)	13 (61.9)
Married, N (%)	2 (9.5)
Education, mean (SD), y	14.4 (2.8)
Employed, N (%)	9 (42.8)
Student/housewife, N (%)	4 (19)
Age at SCH/SA onset, mean (SD), y	20.1 (5.5)
Duration of SCH/SA, mean (SD), y	8.8 (5.5)
Age at OCD onset, mean (SD), y	22.3 (7.6)
Duration of OCD, mean (SD), y	6.8 (5.2)
Baseline Y-BOCS total score, mean (SD)	30.8 (6.7)
Baseline Y-BOCS insight item score, mean (SD)	3.1 (0.9)
Baseline PANSS total score, mean (SD)	55.9 (15.5)
Baseline CGI-S score, mean (SD)	5.5 (0.8)
Baseline GAF score, mean (SD)	49.2 (10.1)
Alcohol or substance use/dependence, N (%)	5 (23.8)
Lifetime comorbid Axis I disorder, N (%)	4 (19.0)

SCH: Schizophrenia; SA: Schizoaffective disorder; OCD: obsessive compulsive disorder; Y-BOCS: Yale-Brown Obsessive Compulsive Scale; PANSS: Positive and Negative Symptom Scale; CGI-S: Clinical Global Impressions-Severity of Illness Scale; GAF: Global Assessment of Functioning Scale.

were “moderately ill” and the rest of the sample was borderline mentally ill or not ill.

Table III shows the mean obsession, compulsion, insight and total Y-BOCS scores at baseline, 6 and 12 months in the overall sample. All measures showed statistically significant improvements at 6 months; from 6 to 12 months improvement continued but at a slower rate. General functioning also improved, as shown by a 3.8 point increase in GAF scores from T0 to T1 (49.2 ± 10.1 vs. 53.0 ± 12.1 , $t = -5.3$, $df = 20$, $p < 0.001$) and by a 6.7 point increase in GAF from T1 to T2 (53.0 ± 12.1 vs. 55.9 ± 12.3 , $t = -2.1$, $df = 20$, $p < 0.05$). Clinical severity of illness, measured by the CGI-S, decreased from T0 to T1 (5.5 ± 0.8 vs. 5.0 ± 1.6 , $t = 2.8$, $df = 20$, $p < 0.01$) and from T1 to T2 (5.0 ± 1.6 vs. 4.5 ± 1.0 , $t = 2.0$, $df = 20$, $p < 0.05$). At T2, 52% (11/21) of patients were rated as “much/very much” improved (CGI-I); 33% (7/21) were responders and 19% (4/21) were remitters.

Outcomes of patients with different clinical characteristics are shown in Table IV. Compared with patients without alcohol/substance use disorder, those with alcohol/substance use disorder were significantly less likely to improve. The percentage improved varied from 0% in patients in which the onset of OCD preceded that of SCH/SA to 50% in patients in which the OCD onset occurred after that of SCH/SA up to 83.3% in patients in which the onset of two disorders was simultaneous. The percentage of remitters increased from 7.1% in patients with primary OCD to 42.9% in patients with secondary OCD. No significant differences were found considering adherence or

TABLE III.

Outcome measures for the intent-to-treat sample ($n = 21$). *Variazioni di punteggi della Y-BOCS durante il trattamento (intent-to-treat analysis) ($n = 21$).*

Scale	Time point			ANOVA or Friedman test	post-hoc tests	p	T0-T1 t, df, p	T1-T2 t, df, p
	T0 mean (SD)	T1 mean (SD)	T2 mean (SD)					
Y-BOCS score								
Total	30.8 (6.7)	26.8 (8.0)	22.3 (8.3)	20.02	2.19	< 0.001	5.55, 20, < 0.001	2.63, 20, < 0.05
Obsession	16.9 (3.0)	13.7 (4.3)	11.4 (4.3)	12.22	2.19	< 0.001	4.12, 20, < 0.001	2.79, 20, < 0.05
Compulsion	14.7 (4.3)	13.0 (4.2)	10.8 (4.5)	13.04	2.19	< 0.001	3.95, 20, < 0.001	2.14, 20, < 0.05
Insight	3.1 (0.9)	2.5 (1.1)	2.1 (1.3)	11.04	2.19	< 0.001	4.24, 20, < 0.001	1.25, 20, .225

T1: 6 months; T2: 12 months; Y-BOCS: Yale-Brown Obsessive Compulsive Scale.

TABLE IV. Treatment outcomes as a function of substance use disorder, temporal onset and type of OCD. Relazione tra risposta al trattamento e uso di sostanze, sequenza di esordio e DOC primario/secondario.

	Dropout						Improved*						Response*						Remission*							
	no		yes		p†	p‡	no		yes		p†	p‡	no		yes		p†	p‡	no		yes		p†	p‡		
	n	%	n	%			n	%	n	%			n	%	n	%			n	%	n	%			n	%
ASUD	no	12	75.0%	4	25.0%	1.000	0.158	5	31.3%	11	68.8%	0.012	0.012	0.012	6	62.5%	6	37.5%	0.624	0.205	13	81.3%	3	18.8%	1.000	0.033
	yes	4	80.0%	1	20.0%		5	100.0%	0	0.0%				4	80.0%	1	20.0%		4	80.0%	1	20.0%				
OCD type	primary	10	71.4%	4	28.6%	0.624	0.599	7	50.0%	7	50.0%	1.000	0.484	10	71.4%	4	28.6%	0.638	0.355	13	92.9%	1	7.1%	0.088	0.594	
	secondary	6	85.7%	1	14.3%			3	42.9%	4	57.1%			4	57.1%	3	42.9%		4	57.1%	3	42.9%				
Temporal onset	OCD before SCH/SA	3	100.0%	0	0.0%	0.278	0.013	3	100.0%	0	0.0%	0.067	0.127	2	66.7%	1	33.3%	1.000	0.327	2	66.7%	1	33.3%	0.416	0.167	
	OCD after SCH/SA	10	83.3%	2	16.7%		0.072	6	50.0%	6	50.0%		0.007	8	66.7%	4	33.3%		0.474	9	75.0%	3	25.0%		0.307	
	same time	3	50.0%	3	50.0%			1	16.7%	5	83.3%			4	66.7%	2	33.3%			6	100.0%	0	0.0%			

* For improved, response and remission definition see text ("outcomes measures"); † exact test; ‡ adjusted for PANSS baseline score. OCD: obsessive compulsive disorder; ASUD: alcohol/substance use disorder; SCH: schizophrenia; SA: schizoaffective disorder.

response between clinical subgroups.

When outcome comparisons were adjusted for the PANSS score at baseline in logistic regression models using bootstrap estimates, it was confirmed that patients with alcohol/substance use disorders had lower improvement rates and in addition they proved to have significantly lower remission rates. Patients in which OCD preceded SCH/SA had higher adherence rates than those with a simultaneous onset of the two disorders (the reference group). In contrast, patients with OCD occurring after SCH/SA were more likely to improve compared to the reference group. No relationship was found between primary/secondary OCD and outcomes.

Conclusions

Our results indicate a good adherence to CBT in patients with OCD and SCH/SA comorbidity. Our dropout rate (24%) is consistent with those reported in the literature for patients with OCD and without SCH/SA comorbidity (13-36%)³⁰⁻³⁴.

Secondly, CBT proved to be a helpful strategy for treating OCD in patients with stabilized SCH/SA. All outcome measures in our sample showed gradual, but continuous and significant improvement from baseline to 6 months, and to a lesser extent from 6 months to 12 months of treatment. The most promising results were the reduction of OCD symptoms and the improved insight into illness. At 12 months, 52% (11/21) of patients were improved, 33% (7/21) were responders and 19% (4/21) remitters. These findings are quite similar to the results of clinical trials on the efficacy of adjunctive fluvoxamine to antipsychotics in patients with OCD and schizophrenia^{11 18}. The advantage of using CBT vs. fluvoxamine, and vs. SRIs in general, is the absence of the potential risks of either psychotic exacerbation or increased aggressiveness. To determine if improvement was stable over time, we planned a follow-up evaluation after end of CBT.

Our results show the acceptability and feasibility of CBT in this difficult-to-treat population, with a challenge posed by patients with lifetime alcohol/substance use disorder: none of the patients with alcohol or substance abuse improved. The proportion of patients with OCD secondary to second-generation antipsychotics in our sample (33%) is consistent with the one reported in the literature (20%-70%)³⁵. Contrary to our expectation, patients with secondary OCD did not show poorer adherence to CBT and poorer outcomes than those of patients with primary OCD. To our knowledge, this is the first evidence that a psychological treatment is effective for secondary OCD. The relationship between the sequence of onset of OCD and SCH/SA and outcomes was complex and requires further investigation in larger samples.

Our results should be interpreted keeping in mind some

important limitations. First, this clinical study presents the methodological limitations that are inherent to a naturalistic study, i.e. the study is neither double-blind nor placebo-controlled. In the absence of a control group not receiving CBT, we cannot rule out the possibility that the observed improvement in obsessive-compulsive symptoms was at least partially spontaneous.

Type I error might be inflated because of the small sample size and the large number of comparisons, although the use of bootstrapping techniques partially weakens this limitation. Despite these limitations, however, the present study provides useful information for clinicians planning OCD treatment in patients with SCH/SA. Our results suggest that psychiatrists can rely not only on SRIs, but also on CBT. Thus, according to their clinical judgment, they can select the right treatment for each patient. In our opinion, SRI may be used in patients who either refused or did not respond to CBT and, *vice versa*, CBT may be attempted in patients who did not respond to medication or who are at higher risk of psychotic exacerbation.

Randomized clinical trials and observational studies with larger samples are required to confirm the efficacy, effectiveness and outcome predictors of CBT in patients with SCH/SA OCD comorbidity.

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