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Albert U.; Aguglia A.; Bogetto F.; Cieri L.; Marinella D.; Maina G.; Necci R.; Parena A.; Salvati L.; Tundo A.. Effectiveness of cognitive-behavioural therapy addition to pharmacotherapy in resistant obsessive-compulsive disorder: a multicenter study.. PSYCHOTHERAPY AND PSYCHOSOMATICS. 81 (6) pp: 383-385.
DOI: 10.1159/000336873

Effectiveness of Cognitive-Behavioral Therapy Addition to Pharmacotherapy in Resistant Obsessive-Compulsive Disorder: A Multicenter Study

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Available treatments for adult patients with obsessive-compulsive disorder (OCD) [1] are cognitive-behavioral therapy (CBT) and serotonin reuptake inhibitors (SRIs). Partial response to these treatments, however, is very frequent; the extant literature indicates that, when the response to SRIs is partial, augmentation with antipsychotics [2,3,4,5,6,7] may provide additional benefit. Antipsychotics' side effects, mainly the metabolic ones [8], however, limit this option. The second strategy consists of sequentially adding CBT; the efficacy of this strategy is suggested by open-label reports [9,10,11,12,13,14] and a single randomized, controlled trial [15]. Randomized, controlled studies have strong internal validity, but the generalizability of their findings to the real word could be limited by several factors [16,17]. In the study by Simpson et al. [15], for example, comorbid diagnoses were allowed only if secondary; mania, psychosis, suicidal ideation, and substance abuse/dependence in the previous 6 months were exclusion criteria. Moreover, ERP protocol consisted of 17 twice-weekly sessions (90–120 min each), daily homework assignments, and between-session phone calls and included ≥2 sessions in the patients' home. One might ask if patients in the real world can follow this intensive CBT format. So, it could be useful for clinicians to know if the results of Simpson et al. [15] have been confirmed in large multicenter effectiveness studies.

The aim of this prospective, multicenter study was to investigate the effectiveness of routinely delivered CBT as an adjunct to medication in real-world OCD patients with incomplete response to medication.

Patients were recruited from the Department of Neuroscience, University of Turin, and the Istituto di Psicopatologia in Rome, Italy. Eligible participants were outpatients, aged ≥18 years, with a primary DSM-IV (SCID-I) diagnosis of OCD, a Y-BOCS total score ≥16, and incomplete response to ≥1 adequate, prospective SRI trial. We included patients with partial but incomplete response (Y-BOCS reduction <25%) to at least 12 weeks of: ≥40 mg/day of citalopram, fluoxetine, and paroxetine, ≥100 mg/day of clomipramine, ≥20 mg/day of escitalopram, ≥200 mg/day of fluvoxamine and sertraline, and ≥250 mg/day of venlafaxine. Exclusion criteria were a lifetime diagnosis of schizophrenia or other psychotic disorders, mental retardation, or an organic brain syndrome. All patients gave written informed consent, and a local ethical committee approved the research project.

Patients maintained the same drug and dosage while CBT was added (exposure and response prevention; cognitive therapy and other ad hoc interventions were used when necessary). Patients were treated in a naturalistic setting in the sense that manualized guidelines [18] were

adapted to each patient by taking due account of the insight level into the senselessness of OCD symptoms, treatment adherence, and the presence of Axis I disorders. The therapist and the patient scheduled therapy sessions flexibly and jointly. CBT duration was not fixed in advance.
The primary outcome was Y-BOCS change from the beginning of CBT to the endpoint. CGI-S and GAF scores (although poorly validated) were also used. Response was defined as a Y-BOCS decrease ≥25% and remission as a Y-BOCS decrease ≥25% and Y-BOCS <16 posttreatment [19]. Predictors of the percentage of Y-BOCS reduction at T2 were examined with independent t tests for dichotomous variables and Pearson's correlations for continuous variables. Significant variables were then entered into a stepwise multiple linear regression analysis.
One hundred nineteen patients were enrolled; 68.1% of them had ≥1 lifetime comorbid disorder, and 28.6% bipolar disorder. All patients were currently taking ≥1 SRI; 19.3% were taking two SRIs, and 34.5% were taking SRI plus atypical antipsychotic. The mean duration of the current treatment was 7.13 months, and most patients (82.4%) received an adequate SRI dose for more than the required minimum time of 12 weeks. The number of lifetime ineffective trials, including the current one, was 2.78. Nineteen patients dropped out before T1, and 22 dropped out between T1 and T2; the cumulative proportion of dropouts was 34.5%. Table 1 shows the variation of mean Y-BOCS, CGI-S, and GAF scores across time. The mean reduction in Y-BOCS score was 17.9% at T1 and 29.3% at T2. Responder rates were 32.8% at T1 and 58% at T2; remitter rates were 15.1 and 31.1%, respectively. A higher baseline GCI-S score, having had a previous hospitalization for OCD, and a longer duration on the current ineffective treatment independently predicted in the final regression analysis a lower reduction in the Y-BOCS total score.
Our multicenter, prospective, naturalistic study indicates that the positive results of the controlled study concerning the efficacy of CBT addition to medication in partial responder OCD patients [15] can be generalized, although to a lesser degree, to routine clinical practice. The demonstration of the effectiveness of CBT addition in this clinical population is of high clinical relevance.
Our results are consistent with findings of previous open studies, with smaller samples [9,10,12,13]. Our response rates are lower than those of the controlled study (58% at 12 months and 74% at 8 weeks, respectively) [15]. This difference could be explained by differences in the considered samples: we enrolled more severe patients than those participating in the controlled study in terms of the Y-BOCS total score (28.5 and 25.4, respectively), alcohol or substance use/dependence comorbidity (10.1 and 0%, respectively), the number of previous ineffective treatments (2.78 and 1.5, respectively), and current use of combination/augmentation pharmacotherapy (53.8 and 8%, respectively). Moreover, we cannot exclude that the lower response rate in our study may also be due to differences in treatment. CBT in our study was practiced in a naturalistic setting: manual procedures were adapted to each patient's needs, sessions were scheduled flexibly, treatment duration was not prefixed, and ERP exercise intensity was

lower than in the controlled study. According to the typical use of CBT in the clinical setting, these changes in protocol were needed to enhance adherence to treatment and to test whether CBT addition was as effective in real-world patients as it was in the controlled trial.
Some caveats to our findings must be considered; there was no control group, participants were self-selected for inclusion, and there was no randomization across interventions. These design factors reflect the real-world nature of mental health services and represent, in our opinion, a major strength of our study as they give clinicians an idea of the exact amount of improvement to be expected in clinical practice.

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Table 1

Outcome measures for the intent-to-treat sample (n = 119)

Variable	Baseline (T0) (mean ± SD)	6 months (T1) (mean ± SD)	12 months (T2) (mean ± SD)	Repeated measures ANOVA		Post hoc with Bonferroni correction					
						T0 versus T1		T0 versus T2		T1 versus T2	
				F	p	mean difference	p	mean difference	p	mean difference	p
YBOCS total score	28.50 ± 5.83	23.63 ± 7.41	20.54 ± 8.90	138.87	<0.001	4.866	<0.001	7.958	<0.001	3.092	<0.001
YBOCS obsessions	14.64 ± 3.04	12.26 ± 3.79	10.67 ± 4.49	119.46	<0.001	2.378	<0.001	3.966	<0.001	1.588	<0.001
YBOCS compulsions	13.86 ± 3.74	11.45 ± 4.19	9.87 ± 4.86	115.95	<0.001	2.403	<0.001	3.992	<0.001	1.588	<0.001
YBOCS insight	1.84 ± 1.38	1.46 ± 1.32	1.22 ± 1.27	46.50	<0.001	0.378	<0.001	0.622	<0.001	0.244	<0.001
CGI-S	4.97 ± 1.03	4.29 ± 1.37	3.82 ± 1.59	92.20	<0.001	0.681	<0.001	1.143	<0.001	0.462	<0.001
GAF	49.93 ± 8.38	57.13 ± 10.92	61.26 ± 13.37	158.32	<0.001	−7.202	<0.001	−11.328	<0.001	−4.126	<0.001

Y-BOCS = Yale-Brown obsessive compulsive scale; CGI-S = clinical global impression-severity of illness scale; GAF = global assessment of functioning.