Predicting the therapeutic response to cognitive behavioural therapy in patients with pharmacoresistant obsessive-compulsive disorder

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Submitted: 2009-09-01 Accepted: 2009-09-25 Published online: 2009-11-11

Key words: **obsessive-compulsive disorder; prediction of therapeutic response; SSRI; CBT; insight; resistance; dissociation**

Neuroendocrinol Lett 2009; **30**(5):615–623 **PMID:** 20035255 NEL300509A14

Abstract

OBJECTIVE: The aim of our study was to establish the efficacy of CBT on the sample of non-selected medication-resistant patients with OCD and to search for predictors of therapeutic response in such a group.

METHODS: The treatment was carried out under usual conditions at the department for anxiety disorders. Systematic CBT steps were tailored to the needs of each patient. Pharmacology treatment remained grossly unchanged during the trial period. We used the following outcome measures in the study: Yale-Brown Obsessive Compulsive Scale, subjective version (S-Y-BOCS), the Clinical Global Impression – Severity of Illness scale (CGI-S), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Somatoform Dissociation Questionnaire (SDQ-20) and Dissociative Experience Scale (DES). The primary outcome measure was a decrease by 35% in Y-BOCS rating. Remission was defined as a 12 point score or lower in Y-BOCS and 1 or 2 points in CGI-S.

RESULTS: 47 patients completed the study (19 male and 28 female). One female patient refused to participate. All patients completed at least 5 weeks of intensive CBT programme and showed significant improvement on Y-BOCS, CGI-S, and BDI scales. At the end of the treatment 40.4% of the patients achieved clinical remission according to the CGI-S scale. The main characteristics present at the beginning of the trial increasing probability of achieving improvement or remission during the treatment were a Y-BOCS score lower than 22, good insight, higher resistance to symptoms, low level of dissociation, and aggressive obsessions.

CONCLUSION: As negative predictors we identified higher scores in Y-BOCS, poorer insight, low resistance to symptoms, high level of dissociation, obsessions focused on control/symmetry and obsessive slowness/ambivalence as associated with poor improvement.

ORIGINAL ARTICLE

INTRODUCTION

Clear predictors of successful therapeutic intervention in obsessive-compulsive disorder have not been known yet (Mataix-Cols *et al*., 1999). Among characteristics associated with resistance to treatment we may find a number of demographic parameters such as age at onset of disorder, duration of a disorder, sex, education, positive family history, influence of dissociation, and cognitive deficit. Comorbid disorders are also important, mostly depression and personality disorders. More severe OCD symptoms were proven in patients with a higher degree of dissociation (Goff *et al*., 1992). There are some studies investigating the relationship between dissociation, specific obsessions/compulsions, and CBT treatment effect (Rufer *et al*., 2005). Cognitive dysfunction may have an influence on the severity of symptoms as well (Nakao *et al*., 2005). Patients with longer duration of illness had more compulsions and also performed worse in cognitive tests (Stroop test and WMS-R). Therapeutic response is significantly worse in patients having more severe cognitive dysfunction. Better prognosis is usually associated with higher socioeconomic status, episodic course of the illness, and presence of precipitating events (Karno *et al*., 1991). Mataix-Cols *et al*. (1999) used factor analysis of Y-BOCS scale in 354 patients and concluded that 5% of factors explain 65.5% of variance in results: symmetry/order, contamination/washing, aggression/controlling and sexual/religious obsessions. Most frequent predictors of poor therapeutic outcome are higher frequency and intensity of symptoms, presence of cleaning and hoarding rituals (Saxena *et al*., 2002), positive family history, mental disorder on axis II (mostly personality disorders), comorbid body dysmorphic disorder, earlier age of onset, longer duration and chronicity, more admissions to psychiatric hospitals and comorbid tic disorder (Pigott and Seay, 1997). Leonard *et al*. (1993) conducted a study on negative predictors in children suffering from OCD. They examined 54 children treated with clomipramine after 2 to 7 years again. Only 6% of the children achieved full remission, 70% were on long-term medication, 43% still met criteria for OCD, and 19% remained unimproved or even deteriorated. A worse course of OCD was predicted by more severe OCD symptoms after 5 weeks on clomipramine treatment, tic disorder, and a parent suffering from mental disorder. Ravizza *et al*. (1995) tried to identify predictors of successful treatment in 53 patients taking clomipramine or fluoxetine for 6 months. Therapeutic response (defined as 40% decrease in Y-BOCS) was achieved in 58.5% of the patients. Patients who did not respond adequately exhibited a higher frequency of compulsions, washing rituals, chronic course of illness, early age at onset, longer duration of illness, concomittant schizotypal disorder, and had been admitted to the hospital previously. Alonso *et al*. (2001) tried to predict the long-term outcome of a combined treatment with SSRI and behavioural therapy. Altogether 36.7% of patients did not respond sufficiently to the treatment. Of all Y-BOCS items, only obsessions with sexual or religious content were associated with poor long-term therapeutic outcome of SSRI treatment as well as behavioural therapy. Hantouche *et al*. (2000) carried out a naturalistic one-year study with 155 patients with OCD. Mainly poor insight was a predictor of inadequate therapeutic response to SSRI and behavioural treatment. A higher level of impulsivity predicted better therapeutic response after 6 months, while severe slowness was associated with a delay of treatment response (between month 6 and 12). Geller *et al*. (2003) in their study with children with OCD explored whether therapeutic response to treatment with paroxetine is influenced by comorbidity with other mental disorder. Despite overall response to paroxetine being high in children with OCD (71%), in the case of comorbidity with ADHD, tic disorder or oppositional defiant disorder, response was significantly lower (56%, 53%, and 39%) than in patients with only OCD (75%). After switching to a placebo in a double-blind follow-up study, children suffering from comorbidity had significantly more relapses (46% with one or more comorbidities and 56% with two or more comorbidities vs 32% without any comorbidity). Their two-year study with 122 patients with OCD on SRIs treatment Shetti *et al*. (2005) revealed that inadequate therapeutic response is related to comorbid depressive disorder, poor insight, presence of sexual obsessions, washing, and miscellaneous compulsions. Early age at onset showed a trend toward prediction of a nonresponse. Predictors of a treatment response are rarely confirmed repeatedly. Saxena *et al*. (2007) found out that patients with hoarding rituals respond to treatment with paroxetine equally as patients with other rituals. Analogously, another study revealed that the presence of body dysmorphic disorder does not impair therapeutic efficacy (Steward *et al*., 2008). Denys *et al*. (2007) were interested in whether the treatment effect of venlafaxine or paroxetine is related to genetic dispositions. The study showed that venlafaxin efficacy is associated with S/L genotype for 5-HTTLPR serotonin transporter polymorphism and paroxetine efficacy with G/G genotype of 5-HT2A polymorphism.

AIM OF THE STUDY AND HYPOTHESES

This study aims to identify predictors of therapeutic response to a complex and systematic CBT programme in patients resistant to previous antidepressant treatment in an outpatient setting.

Hypotheses:

Clinical improvement (defined as at least a 35% decrease in S-Y-BOCS score) and clinical remission (defined as S-Y-BOCS score of 12 points and less, CGI-S score of 1 or 2) will be significant in patients with following characteristics:

Demographics

Later age at onset (15 years old and more), shorter duration of disorder (less than 15 years)

Symptoms

Lower global S-Y-BOCS scores at the baseline (less than 22), better insight, lower BDI scores (less than 16), no comorbidity with other anxiety or depressive disorder, no comorbid personality disorder, no sexual, religious, magical, or hoarding obsessions and compulsions, lower dissociation score in DES (less than 12), and SDQ-20 (less than 22).

METHODS

Antidepressant treatment-resistant patients suffering from OCD, referred to Prague Psychiatric Centre or to the Department of psychiatry University Hospital Olomouc for an intensive daily programme, were enrolled in the study.

Assessment

Diagnosis of OCD according to ICD-10 criteria (1996) was confirmed by two independent psychiatrists before the treatment was started. To confirm the same diagnosis according to DSM-IV-TR and to diagnose axis I comorbidity, a MINI structured interview was administered (Lecrubier *et al*., 1997). Only patients meeting the following criteria were included in the study: on adequate dose of recommended antidepressants in the last year, in an outpatient setting, last antidepressant administered for at least 3 months and due to treatment resistance, a referral to the specialised treatment programme. For study inclusion criteria see Table 1.

Severity of obsessions and compulsions was assessed once a week by a subjective version of Y-BOCS (Yale-Brown Obsessive Compulsive Scale; Goodman *et al*., 1986). General psychopathology was assessed by CGI (Clinical Global Impression; Guy, 1976) in the beginning and at the end of the treatment. Subjective scales measuring depression and anxiety, BDI (Beck Depression inventory) and BAI (Beck Anxiety Inventory; Beck and Emery 1985) were administered once a week during the trial. Rating scales measuring dissociation were employed as well: DES (Dissociative Experience Scale; Bernstein and Putman, 1986) and SDQ-20 (Somatoform Dissociation Questionaire; Nijenhuis *et al*., 1996). For the time schedule of rating scales administration see Table 2.

Results were processed using the STATISTICA 7.0 software. Demographic data and average global scores were processed using descriptive statistics: means, standard deviations, and data distribution. As there was normal distribution found in all rating scales, one-way ANOVA with correction for multiple comparisons (Bonferroni correction) was employed to compare means of particular rating scales from week 0 to 5 and its trends. Pair t-tests were used for comparison of baseline and endpoint scores (LOCF-last observation carried forward). To calculate the relationship between alternative variables (sex, yes/no, duration of illness up to and over 15 years, baseline S-Y-BOCS score less than 22, DES score less than 12, presence of particular obsessions and compulsions, etc.) and reaching improvement or remission, the Fisher test was employed. It was agreed that a 5% level of statistical significance would be accepted in all tests. The study was approved by the local ethical committee.

Treatment

Patients were treated using usual doses of antidepressants, same as they were on when referred; there were no substantial changes in pharmacotherapy. Medication doses were chanted minimally (exceptionally there

Tab. 1. Study inclusion criteria.

INCLUDING CRITERIA	EXCLUDING CRITERIA
■ ICD-10 research criteria for OCD, diagnosis must be confirmed using MINI structured interview (Lecrubier et al. 1997) ■ Age 18-65 years ■ Both sexes ■ Previous treatment with an adequate dose of serotonergic antidepressants for at least one year ■ Last treatment with one serotonergic antidepressant at an adequate dosage for at least 3 months ■ Signed Informed Consent	■ Depressive disorder ■ Higher risk of suicide ■ Organic mental disorder ■ Psychotic disorder in history ■ Alcohol or other substance dependency ■ Severe physical illness ■ Patients taking unprescribed medication ■ Epilepsy or pathological EEG ■ Noncompliant patient ■ Antisocial personality disorder ■ Eating disorder

Tab. 2. Time schedule of administration of diagnostic and assessment scales and questionnaire.

ASSESSMENT SCALE	WEEK 0	WEEK 1–5	END OF TREATMENT
ICD-10	X		
MINI	X		
CGI	X		X
S-Y-BOCS	X	X	X
BDI	X	X	X
BAI	X	X	X
DES	X		
SDQ-20	X		

ICD-10 = The International Classification of Disorders 10th revision, MINI = Mini-International Neuropsychiatric Interview; CGI = Clinical Global Impression, S-Y-BOCS = Subjective-Yale-Brown Obsessive Compulsive Scale; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; DES = Dissociative Experience Scale ; SDQ-20 = Somatoform Dissociation Questionnaire

was an increase in dose towards the upper limit and lowering or tapering benzodiazepines off). The mean antidepressant dose was 38.68 ± 30.52 mg of paroxetine equivalent at the beginning and 39.57 ± 30.8 mg of paroxetine equivalent at the end of the treatment. 17 patients had a combination of antidepressant with second generation antipsychotic, and 3 patients with anticonvulsant. 2 patients had a combination of two serotonergic antidepressants. Four patients previously not responding to antidepressants refused to take them and were treated only with CBT and no medication.

All patients participated in an open group structured CBT programme lasting 5 to 8 weeks. This programme consists of standard steps covering psychoeducation, elaboration of list of obsessions and compulsions, cognitive restructuring, exposure therapy with response prevention according to the hierarchy of obsession/compulsion severity, working with conditional and core beliefs, and problem solving. Each patient had an opportunity to have a autobiographical group session focused on cognitive schemes and mapping of life problems and most of patients participated. The programme was complemented by communication skills practice, ergo therapy, and sports.

Tab. 3. Demographic and clinical data at the beginning of treatment.

Age	32.2 ± 9.3 years
Sex	19 men a 28 women
Length of education	14.0 ± 3.1 years
Onset of disorder (years)	15.3 ± 7.7 years
Duration of disorder (years)	16.8 ± 9.7 years
Treatment postponed	10.5 ± 7.3 years
S-Y-BOCS	
Global	22.97 ± 6.83
Obsessions	11.15 ± 3.04
Compulsions	10.95 ± 4.32
SDQ-20	23.67 ± 4.86
DES score	
Global	12.86 ± 11.15
Depersonalization	43.33 ± 63.66
Dissociative amnesia	50.50 ± 65.55
Imaginative preoccupation	158.3 ± 140.4
CGI	4.43 ± 1.06
BAI	20.81 ± 12.14
BDI	18.00 ± 9.61
Antidepressant doses (paroxetine equivalent)	39.57 ± 30.80
Adjuvant medication (number of patients): antipsychotics anticonvulsants without medication	17 (36.2%) 3 (6.4%) 4 (8.5%)
Axis I comorbidity (current disorders)	20 (42.6%)
Axis II comorbidity (personality)	30 (62.8%)

RESULTS

In this paper we present results of the study with patients enrolled to intensive CBT programme for OCD during the period from January 2007 until June 2008. All patients signed an informed consent statement and cooperated, except for one female patient suffering from severe OCD and borderline personality disorder. There were 47 patients included in the study, 19 males and 28 females. The mean age was 32.17 ± 9.28 years. The onset of symptoms was at the age of 15.34 ± 7.73 years and duration of symptoms was 16.83 ± 9.68 years. The time of the first psychiatric treatment was on average 10.45 ± 7.339 years from the onset of symptoms. The mean scores of S-Y-BOCS 21.97 ± 6.83 prior to the study correspond to the severe form of OCD. Demographic and clinical data are shown in the Table 3.

There were significant decreases in rating scale scores during the treatment. S-Y-BOCS scores were retrieved from 39 patients. The mean score decreased from the baseline 21.97 ± 6.83 points to the endpoint score (LOCF) 14.59 ± 7.87 (pair t-test: $p<0.0001$, t=8.82, df=38; one-way ANOVA for week 0 to 5, $p<0.0001$, F=7.353, df=171). There was significant improvement between the beginning of treatment and weeks 4 and 5 in the Bonferroni multiple comparison tests applied to all weeks among each other. A number of patients were discharged after 5 weeks of treatment and therefore we did not perform further assessments. For results overview see Table 4 and Figure 1.

Clinical Global Impression – CGI – was assigned by a psychiatrist to all 47 patients at the beginning and the end of treatment (LOCF). There was a significant decrease in global score from 4.43 ± 1.06 to 2.83 ± 1.19 (pair t-test: $p<0.0001$, t=12.48, df=46), 40.4% of patients achieved the rating of 1 and 2, which was considered to be an equivalent of clinical remission.

Subjective rating scale for depression – BDI scores – were collected from all 47 patients. Mean scores decreased in time from the initial 18.00 ± 9.61, which corresponds to mild depression, to 11.47 ± 7.28 (LOCF), which corresponds to remission of depression (pair t-test: $p<0.0001$, t=4.896, df=46; one-way ANOVA between week 0 and 5: $p<0.05$, F=2.546, df=271). There was a significant change between the beginning of treatment and week 5 in the Bonferroni multiple comparison test evaluating particular weeks between each other.

Mean scores of BAI inventory were collected from all 47 patients. These scores significantly dropped during treatment from the initial score of 20.81 ± 12.14, corresponding with severe anxiety disorder, to 12.77 ± 8.186 (LOCF), corresponding to mild anxiety disorder (pair t-test: $p < 0.0001$, t=5.62, df=46; one-way ANOVA between weeks 0 and 5: n.s. F=1.646, df=271).

The best indicator of therapeutic response is the percentage of patients clinically improved or who reached remission. Our results indicate that the CBT programme led to improvement by 35% in S-Y-BOCS score

in 51.3% of the patients. When a criterion for remission of up to 12 points in Y-BOCS score is applied, 50% of the patients are in remission. According to the Clinical Global Impression Scale (reflecting wider clinical evaluation) 40.4% of patients scored 1 and 2 at the end of treatment (Figure 2). Taking into account that these patients were pharmacoresistant in previous outpatient treatment, our results are encouraging.

Analysis of results according to demographic variables

Sex

There was no significant sex difference found in comparison of patients improved by 35% in S-Y-BOCS scale and patients scoring 12 points or less on the same scale (remitting), although in some parameters the difference approached the 5% level of significance (mean decrease in S-Y-BOCS in male was 9.118 ± 1.311 and in female 6.045 ± 1.020; unpaired t-test: p=0.068; CGI 1or 2 was achieved by 11 out of 19 males and only 8 out of 28 females, Fisher's exact test: p=0.069). Thus we may conclude males profited from CBT treatment slightly more than females, though the difference was not significant.

Age at the onset of disorder

When we compare patients improved or in remission according to their age at onset (24 patients were 15 years old or younger and 25 patients older than 15 years). There was no significant difference in thus divided patient groups in terms of the number successfully treated (35% improvement or score of 12 and less in S-Y-BOCS was achieved by 10 out of 24 patients with OCD onset before the age of 15 and 10 or 8 out of 15 patients with later onset of OCD: Fisher's exact test ns.). Similarly, in the group with earlier onset, 9 out of 28 patients were given CGI-S scores of 1 or 2, in the group with later onset, 10 out of 19 achieved the same score (Fisher's exact test: ns.). Interestingly, there was a significant difference between groups in the initial S-Y-BOCS score: there was a score of 24.42 ± 1.537 with earlier onset and 19.57 ± 1.029 with later onset (unpaired t-test p<0.05, t=2.600, df=45). However, groups did not differ in the change of Y-BOCS score (7.125 ± 0.9749 vs 7.609 ± 1.088, unpaired t-test: n.s.). We may conclude that if OCD occurred before the age of 15, it had an effect on the initial level of symptomatology. Age at onset had no influence on treatment effect though.

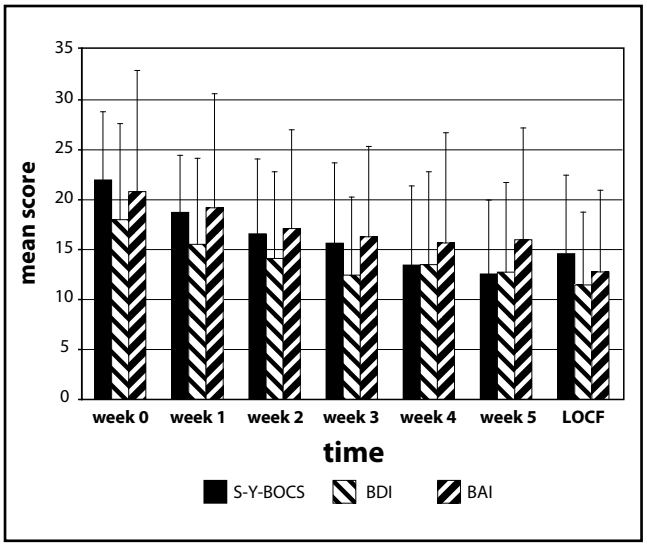

Fig. 1. Clinical rating scales – changes in mean score during treatment.
Y-BOCS: ANOVA week 0–5: p<0.0001; t-test week 0 and LOCF: p<0.0001
BDI: ANOVA week 0–5: p<0.05; t-test week 0 and LOCF: p<0.0001
BAI: ANOVA week 0–5: ns; t-test week 0 and LOCF: p<0.0001

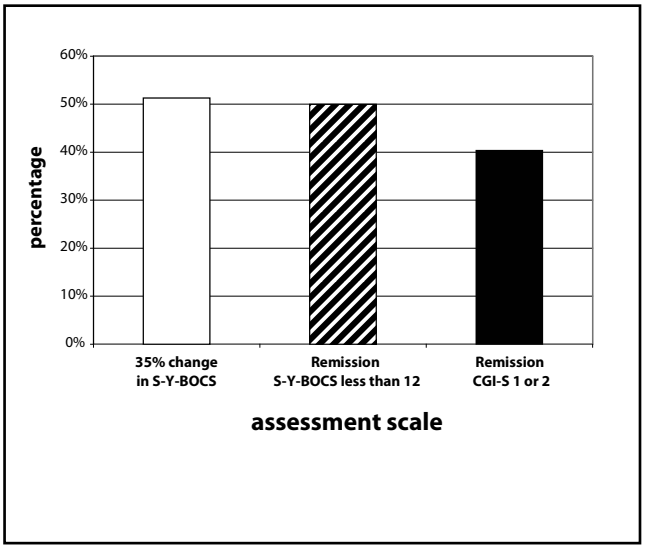

Fig. 2. Achieving improvement and remission – percentage of patients according to various criteria.

Tab. 4. Mean scores and standard deviations during the treatment.

SCALE	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6	Last assessment (LOCF)
Y-BOCS	21.97 ± 6.83	18.73 ± 5.72	16.58 ± 7.50	15.64 ± 8.06	13.46 ± 7.91	12.56 ± 7.42	16.63 ± 7.06	14.59± 7.87
CGI	4.43 ± 1.06							2.83 ± 1.19
BDI	18.00 ± 9.61	15.53 ± 8.62	14.11 ± 8.69	12.44 ± 7.82	13.51 ± 9.29	12.74 ± 8.98	13.02 ± 8.98	11.47 ± 7.28
BAI	20.81 ± 12.14	19.19 ± 11.42	17.11 ± 9.89	16.29 ± 9.05	15.67 ± 11.04	16.00 ± 11.19	15.34 ± 10.37	12.77 ± 8.19

Duration of disorder

Patients with a history of OCD shorter than 15 years (n=29) showed a significantly greater decrease of general anxiety during treatment than patients with longer histories (n=21). The mean BAI scores decreased by 10.31 ± 1.870 versus 4.762 ± 1.939 (unpaired t-test $p<0.05$, t=2.043, df=45), even though baseline scores were not significantly different (23.15 ± 2.739 versus 17.90 ± 1.939, unpaired t-test: ns.). Patients with shorter illness duration had higher mean scores for depression at the beginning (BDI 20.77 ± 2.16 versus 14.57 ± 1.36; unpaired t-test: $p<0.05$, t=2.298, df=45). There was significantly greater reduction in scores (10.31 ± 1.804 versus 2.048 ± 1.530; unpaired t-test: $p<0.005$; t=3.393, df=45), and antidepressant doses were significantly lower (mean paroxetine equivalent 31.54 ± 4.737 versus 49.52 ±7.761; unpaired t-test: $p < 0.05$, t=2.059, df=45). Significantly fewer patients with shorter histories were given augmenting medication with antipsychotics (5 out of 26 versus 12 out of 21; Fisher's exact test: $p<0.05$). Groups were not significantly different when measuring treatment effect with variables of improvement and remission (Fisher's exact test: n.s. in all variables – see Table 5). It appears that duration of illness has an influence more likely on intensity of accompanying depressive symptoms and its decrease during treatment than on intensity and a decrease in specific OCD symptoms. Patients with shorter illness duration have a higher degree of depressive symptoms than patients suffering longer. These depressive symptoms, similarly as accompanying anxiety, respond better to treatment in patients with shorter illness duration than a lower degree of depression and the same level of anxiety in chronic patients. In other demographic variables (age, education, family history of OCD, other mental disorder in the family, employment, a relationship with a partner) no significant relationship to the treatment outcome was found (Fisher tests, all ns.).

Results analysis in accordance with the degree of psychopathology

S-Y-BOCS scores

Patients with mean global scores higher than 22 at the beginning of treatment achieved remission significantly less frequently (13 out of 20) than patients with lower initial scores (5 out of 19) (Fisher's exact

Tab. 5. Treatment effect differences, groups divided according to particular putative predictors.

Entry parameters	Response to treatment Change of global Y-BOCS ≥ 35%	Remission final S-Y-BOCS ≤ 12	Remission final CGI-S ≤ 2
Onset of disorder: Under 15 years Over 15 years, incl.	Fisher exact test ns	Fisher exact test ns	Fisher exact test ns
Duration of disorders: Up to 15 years Over 15 years, incl.	Fisher exact test ns	Fisher exact test ns	Fisher exact test ns
Insight: Full (score 1 or 2) Partial (3 or 4)	Fisher exact test $p<0.001$	Fisher exact test $p<0.05$	Fisher exact test $p<0.005$
Initial Y-BOCS: Higher than 22 Lower than 22, incl.	Fisher exact test ns	Fisher exact test $p<0.05$	Fisher exact test $p<0.001$
Initial BDI: Higher than 16, incl. Lower than 16	Fisher exact test ns	Fisher exact test ns	Fisher exact test ns
Personality disorder: With Without	Fisher exact test ns	Fisher exact test ns	Fisher exact test ns
Axis I comorbidity: With Without	Fisher exact test ns	Fisher exact test ns	Fisher exact test ns
Type of obsessions: Sex/relig/mag/hoard without	Fisher exact test ns	Fisher exact test ns	Fisher exact test ns
Resisatnce lower (1,2) versus higher (3,4)	Fisher exact test $p<0.005$	Fisher exact test ns (p=0.0537)	Fisher exact test $p<0.005$
Dissociation in DES: Higher than 12 Lower than 12	Fisher exact test ns	Fisher exact test ns	Fisher exact test $p<0.05$
Dissociation in SDQ-20 Higher than 22, incl. Lower than 22	Fisher exact test ns	Fisher exact test ns	Fisher exact test ns

test, $p<0.05$). Similarly, a CGI-S rating score of 1 or 2 was attributed to significantly fewer patients with higher S-Y-BOCS scores at the beginning (n=5 out of 27 assessed) than with lower initial scores (n=14 out of 20 patients) (Fisher's exact test, $p<0.001$). It appears, then, that the more intense initial OCD symptomatology, the less likely that improvement or remission will be achieved. For patients with initial S-Y-BOCS scores higher than 22, improvement and remission are much harder to achieve than for patients with lower initial scores.

Illness insight

Insight into symptomatology was assessed on a scale of 1 to 4 (Y-BOCS assessment), where 1 represents full insight (patients is aware his obsessions and compulsions are unreasonable), higher numbers represent poorer insight and number 4, no insight (patient fully believes his obsessions and is convinced neutralising by a compulsion is necessary). Distribution of a degree of insight was as follows: (1) – 17 patients, (2) – 14 patients, (3) – 16 patients, (4) – 0 patients. Patients with better insight achieved improvement by 35% and remission (χ^2: $p<0.05$) according to S-Y-BOCS (χ^2: $p<0.001$) as well as CGI ratings of 1 and 2 (χ^2: $p<0.005$) significantly more often than patients with poorer insight. There was no significant difference found in these variables between groups of patients with good (1) and mildly poor (2) insight. A similar finding was between groups with mildly poor (2) and very poor (3) insight. There was a significant difference between groups with different insight though, comparing changes in S-Y-BOCS scores. The group with good insight improved on average by 9.6 ± 4.7 points, and the group with poor insight by 4.6 + 6.8 points (unpaired t-test: t=3.208, df=38; $p<0.05$). Interestingly, impairment of insight is related to a higher degree of dissociation in DES (correlation: r= 0.4689; $p<0.01$). As we may assume from these results, good insight into obsessions, as displayed by 36.2% of patients, is related to good therapeutic response, while poor insight, as present in 34.1% of patients, is associated with resistance to therapy.

Resistance to symptoms

Resistance was rated similarly as insight, on a scale of 1 to 4, where 1 and 3 represent maximum and minimum resistance and 4 represents total submission to urges. We divided patients into two groups: with resistance 1 and 2 versus 3 and 4. The number of patients with 35% improvement during treatment is significantly higher in the group with resistance 1 and 2 than in the other group (Fisher's exact test; $p<0.005$). The difference between groups of patients in remission only approaches a statistically significant level, but does not reach it (Fisher's exact test; ns, $p=0.0537$). From our results, we may suggest that resistance to obsessions and compulsions is an important factor related to successful treatment – the higher the resistance the higher prospects of getting better.

BDI scores

When we allocated patients into groups without any considerable signs of depression (BDI<16, n=25) and with depressive symptoms (BDI>16, n=22), we could not differentiate between patients responding to treatment or achieving remission (Fisher's exact test ns). Patients scoring lower on the depression scale suffered significantly less from axis I comorbid disorder (n=7 versus n=13; Fisher's exact test; $p<0.05$). These patients also scored significantly lower on the S-Y-BOCS scale at the beginning of treatment (mean 19.47 ± 1.56 versus 24.35 ± 1.36; unpaired t-test; $p<0.05$). It seems that a higher degree of depression does not affect successful treatment of OCD, even though these patients exhibit more severe OCD symptoms.

Presence of comorbidity

Comorbidity of personality disorder was not related to the proportion of patients responding to treatment or achieving remission (Fisher's exact test was not significant for all 3 variables assessed). Accordingly, comorbidity of another anxiety disorder did not affect the number of patients responding to treatment or reaching remission (Fisher's exact test was not significant for all 3 variables assessed).

Type of OCD

When we divided patients into groups according to their specific obsessions, patients with aggressive obsessions were given CGI-S scores of 1 or 2 and met remission criteria according to S-Y-BOCS significantly more often than patients without aggressive obsessions (8 out of 10 versus 11 out of 37 and 8 out of 9 versus 10 out of 29 respectively; both Fisher's exact test: $p<0.05$). Patients with obsessions of symmetry/control had CGI-S scores 1 or 2 less frequently than patients with no such obsessions (10 out of 34 versus 9 out of 13, Fisher's exact test: $p<0.05$). Out of 4 patients suffering from obsessive slowness/ambivalence, none reached 35% improvement in S-Y-BOCS, whereas in patients having no such obsession, 20 out of 35 reached this outcome measure (Fisher's exact test: $p<0.05$). Further allocating of patients according to their type of symptoms or their combination had no effect on improvement and remission whatsoever.

Degree of somatopsychic dissociation

The number of improved or remitting patients with SDQ scores lower than 22 does not significantly differ from those with higher scores of somatopsychic dissociation (Fisher's exact test in all parameters: ns). Therefore it seems that we cannot predict the therapeutic effect from the intensity of somatopsychic dissociation.

Psychic dissociation scores (according to DES)

After dividing the patients into groups with scores lower and higher than 12, a CGI-S score of 1 and 2 (10 out of 18 patients) is significantly more frequent in the group with lower DES than in the group with higher scores (2 out of 14) (Fisher's exact test $p<0.05$). Conversely, no statistical significance has been found in terms of improvement or remission according to Y-BOCS (Fisher's exact test: ns).

DISCUSSION

The aim of our study was to identify predictors of therapeutic response to a complex CBT programme in pharmacoresistant patients with OCD. Our preliminary hypotheses have been confirmed only partially. In the first hypothesis we postulated that the onset of disorder after the age of 15 years and its duration shorter than 15 years will be related to lesser resistance to CBT treatment and vice versa. Our data have not confirmed this hypothesis. Nevertheless, patients with later onset and shorter duration had lower S-Y-BOCS scores. Our result is opposite to findings of Pigott and Sean (1997) and Saxena *et al*. (2002), who found a relationship between poor therapeutic response and onset of OCD at younger ages, longer duration, and chronicity of symptoms. One of the plausible explanations could be that all these studies, including ours, had a small number of patients enrolled and the sample did not adequately reflect representative population. Another explanation could be that patients referred to our centre are mostly those repeatedly not responding to outpatient treatment with antidepressants. Thus our sample represents a selection, while in above-mentioned studies this was not the case.

Conversely, our second hypothesis has been partially confirmed. Lower global S-Y-BOCS scores and higher resistance to symptoms were related to greater treatment effect and vice versa. Our results correspond to findings of Hantouche *et al*. (2000) and Shetti *et al*. (2005), where poor insight was identified as a predictor of poor response to treatment. The hypothesis about initial symptom intensity effect on therapeutic response has been confirmed as well. Patients with baseline S-Y-BOCS scores lower than 22 points improve or achieve remission more often than patients with higher baseline scores. The influence of higher frequency and intensity of symptoms on the therapeutic response was described by Saxena *et al*. (2002). Unlike these authors, we have not demonstrated poor treatment response in patients with cleaning and hoarding rituals, positive family history, personality disorder, earlier onset, and longer duration of OCD. This contrast can be explained by the different patient population. In our selection, there were few patients with hoarding rituals (only 4.3%) but a relatively high proportion of patients with personality disorder (62.8%).

Contradictory to our assumption, the level of depressive symptomatology had no effect on therapeutic response, which is inconsistent with the findings of Shetti *et al*. (2005), where comorbid depressive disorder influenced the therapeutic response. As far as this study is concerned, there was a two-year follow-up of outpatients, whereas in our study, we evaluated only acute intensive treatment and so far without long-term follow up. We may question if we would obtain the same results using long term follow-up design. Similarly, we found no impact of comorbid disorders, including personality disorder. Again, our results are surprising and in conflict with study of Pigott and Sean (1997). As mentioned above, there was a high proportion of treatment-resistant patients and an unlikely high rate of personality disorders in our sample. An additional explanation might be the difference in the treatment: while the aforementioned authors referred to pharmacotherapy, we studied the treatment effect of CBT.

The expected relationship between sexual, religious, magical, and hoarding obsessions and compulsions and efficacy of CBT has not been confirmed. Less successful treatment was associated with obsessive slowness and ambivalence, a higher proportion of obsessions and compulsions of control, need of symmetry, and ordering. On the other hand, aggressive obsessions were associated with better therapeutic response. In the study of Alonso *et al*. (2001), obsessions with sexual/religious content were related to poorer treatment outcome. As we mentioned above, our sample of patients as well as cultural differences may explain the difference. There were very few religious patients in our study population, such as there are in Czech Republic, whereas in the Spanish population one may assume a different proportion of religious patients.

Lower or higher levels of somatopsychic dissociation according to SDQ had no influence on the treatment response. However, allocation of patients in accordance with the degree of psychic dissociation as indicated on DES, proved to be meaningful. Patients with lower scores had significantly lower scores on CGI-S as well. The results support the study of Rufer *et al*. (2005), who found poorer CBT efficacy in patients with higher levels of dissociation. Results draw attention to the necessity of exploring new therapeutic strategies in OCD patients with higher level of dissociation.

CONCLUSION

To identify predictors of therapeutic response in OCD patients, further studies with larger numbers of patients and their long-term follow-up are needed. That could contribute to the selection of an optimal therapeutic strategy for each patient according to his baseline characteristics. With regards to the fact that current treatment options are not able to help all the patients, and a number of them remain treatment-resistant, it is necessary to further explore alternative therapeutic approaches. This applies especially to patients with poor insight, poor resistance to symptoms, and higher levels of dissociation.

ACKNOWLEDGEMENT

This paper was supported by the research grants IGA MZ ČR No. 9323-3

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