Neuroendocrinology Letters Volume 43 No. 6 2022
ISSN: 0172-780X; ISSN-L: 0172-780X; Electronic/Online ISSN: 2354-4716
Web of Knowledge / Web of Science: Neuroendocrinol Lett
Pub Med / Medline: Neuro Endocrinol Lett

ORIGINAL ARTICLE

Early life experiences and adult attachment in obsessive-compulsive disorder

Part 2: Therapeutic effectiveness of combined cognitive behavioural therapy and pharmacotherapy in treatment-resistant inpatients

Frantisek Hodny[1], Marie Ociskova[1,4], Jan Prasko[1,2,3,4], Jakub Vanek[1], Jozef Visnovsky[1], Tomas Sollar[2], Milos Slepecky[2], Milos Slepecky[2], Vlastimil Nesnídal[1], Antonin Kolek[1]

1 Department of Psychiatry, Faculty of Medicine and Dentistry, University Palacky Olomouc, University Hospital, 77520 Olomouc, Czech Republic.
2 Department of Psychology Sciences, Faculty of Social Science and Health Care, Constantine the Philosopher University in Nitra, Slovak Republic.
3 Institute for Postgraduate Education in Health Care, Prague, Czech Republic.
4 Rehabilitation Hospital Jessenia Inc., Akeso Holding, Beroun, Czech Republic.

Correspondence to: prof. Jan Prasko, MD, PhD.
Department of Psychiatry, Faculty of Medicine and Dentistry, Palacky University in Olomouc, Hnevotinska 976/3, Olomouc, 775 15, Czech Republic
e-mail: praskojan@seznam.cz

Submitted: 2022-10-03 Accepted: 2022-11-13 Published online: 2022-11-13

Key words: **obsessive-compulsive disorder; cognitive behavioral therapy; pharmacotherapy; treatment resistance; early adverse experiences; parental styles; attachment; dissociation**

Neuroendocrinol Lett 2022; **43**(6):345–358 **PMID:** 36716392 NEL430622A12

Abstract

OBJECTIVES: Obsessive-compulsive disorder (OCD) is a chronic mental disorder that is often hard to treat with current treatment options. Therapeutic outcomes are predicted by many factors, ranging from biological to psychosocial. Early life experiences and adult attachment influence the effectiveness of the treatment. This study explores their predictive abilities in the combined treatment of adult inpatients with OCD.

METHODS: Seventy-seven patients with OCD, diagnosed according to the ICD-10 criteria, were included in the study, out of which 66 patients completed the treatment. All patients were previously unsuccessfully treated with a minimum of two antidepressants for three months each. They were evaluated with rating scales and questionnaires at the start and the end of a six-week hospitalization in a psychotherapeutic department. The treatment approach presented a combination of group cognitive-behavioural therapy and medication.

RESULTS: The average severity of OCD, anxiety and depressive symptoms significantly decreased during the inpatient treatment. The improvement in Y-BOCS negatively correlated with the age of onset. The history of emotional abuse and neglect and physical neglect predicted a lower change in anxiety evaluated by a psychologist and perceived maternal care positively correlated with a decrease in anxiety assessed with a rating scale. Adult attachment anxiety predicted a lower decrease in the anxiety measured by the clinician but not the OCD symptomatology. Dissociative symptoms did not significantly predict a change in any of the

measures. Comorbid personality disorder did not have a significant impact on therapeutic change.

CONCLUSIONS: The early onset of the disorder was the sole predictor of the treatment outcomes regarding specific OCD symptomatology. Selected early adverse experiences, maternal care, and adult attachment anxiety predicted a change in the anxiety symptoms. Future research should focus on mediation and moderation analyses that could help target specific treatment strategies to decrease the impact of these factors.

INTRODUCTION

Obsessive compulsive disorder (OCD) is a mental disorder that significantly impacts an individual's quality of life and functioning. The lifetime prevalence ranges from 1 and 3 % (Reddy *et al.* 2017). Core symptoms include obsessive thoughts and compulsive or avoidant behaviours. Obsessional thoughts are unpleasant and involuntary and cause anxiety in the patient. The patient then tries to alleviate the anxiety with compulsions or prevent it by engaging in avoidant behaviour (APA 2013). OCD typically has a chronic course, and many patients do not achieve full remission after standard treatment (Fineberg *et al.* 2013). The treatment of choice is cognitive-behavioral therapy (CBT) with exposure and response prevention (ERP) or medication (NICE 2013, Menchon *et al.* 2019, Woody *et al.* 2019). Approximately 50 % of patients with OCD show an adequate response to pharmacotherapy using SSRIs, and the likelihood of reaching full remission is lower (Hollander *et al.* 2000, Reddy *et al.* 2017). The remission rates are comparable for ERP and show significant room for improvement (Simpson *et al.* 2006). The patient's response to treatment varies; unfortunately, residual symptoms often persist (Fineberg *et al.* 2013, Kühne *et al.* 2020). Identifying predictors of treatment outcomes can help improve patient care by providing information about a likely prognosis and appropriate treatment strategies.

Demographic and clinical predictors of the treatment efficacy

The early onset of the disorder (Rosario-Campos *et al.* 2001, Tibi *et al.* 2020), its long duration (Eisen *et al.* 2013), and greater severity (Prasko *et al.* 2009) predict worse outcomes. Tibi *et al.* (2019) examined treatment completion, outcome predictors, and patient status 4 and 13 months after the treatment in a sample of 118 OCD patients treated with exposure and response prevention. OCD severity was a major moderator of the treatment outcome, leading to poorer response to the acute treatment. In the follow-up, however, it became clear that the symptoms were alleviated even in these patients. The patients with severe symptomatology experienced a larger improvement during the treatment and the follow-up than those with less severe OCD.

Adverse childhood experiences

Adverse childhood experiences (ACE) are a heterogeneous group of negative experiences, such as child neglect or abuse, bullying, the death of a parent, or domestic violence. Many authors relate the etiopathogenesis of OCD to adverse childhood experiences (Briggs & Price 2009, Benedetti *et al.* 2014, Park *et al.* 2014; Barcaccia *et al.* 2015, Bey *et al.* 2017). Adverse events in childhood can contribute to the development and severity of OCD (Park *et al.* 2014; Ivarsson *et al.* 2016). Semiz *et al.* (2014) found that treatment resistant patients with OCD have more severe OCD, anxiety, depression, and traumatic experiences than the responders. These connections also showed in the correlational analyses. More recent research also explored the influence of childhood traumatic experiences on treatment outcomes (Boger *et al.* 2020). The patients exposed to early adverse experiences in childhood showed more severe OCD symptomatology before and after the treatment and in a six-month follow-up. However, childhood trauma did not affect the treatment effectiveness. Tibi *et al.* (2020) reported the presence of childhood trauma and the early age of onset of the disorder as predictors of a worse four-year follow-up.

Parental styles

Investigations into the relationships between parental style in childhood and response to the treatment in adults with OCD have not been published. There is similarly an absence of studies on the relationship between parental styles in childhood and the treatment response in other neurotic spectrum disorders, with one notable exception in the study of Holubova *et al.* (2021). In this study, maternal care significantly positively correlated with the change in the measure of depression in patients with neurotic disorders treated with psychodynamic psychotherapy, and it was similar to paternal care. The paternal control negatively correlated with the relative change in the depressive symptoms, and the relative change of anxiety positively correlated with the paternal care and negatively with the paternal control.

Furthermore, parents of adolescents with OCD, major depressive disorder, or a combination of these disorders in childhood were more likely to fail to function as a "safe haven" and to exhibit behaviours that met their children's emotional needs (Ivarsson *et al.* 2016). Ehiobuche (1988) showed that students with a high score in compulsive phenomena more often described their parents as rejecting, overprotective, and less emotionally warm. According to Turgeon *et al.* (2002), parental overprotection was more common in families of children with OCD than in control families. Such styles of parental interaction can make children anxious and lead to intense emotions. Some parents who avoid strong emotions may over-control their children, showing increased control over their time, space, beliefs, feelings, and wishes. They may communicate

with their children: "No, you do not feel that, but you feel this. No, you do not need this, you need this." (Sunderland & Armstrong 2005). These interactions undermine the child's ability to cope independently with emotionally charged situations. So, when a child has no one to help them with emotions, obsessive rituals or controlling behaviours become their way to make the world at least a somewhat safe place (Sunderland & Armstrong 2005).

Attachment

An emotional bond - *attachment* - is formed in early childhood between the child and the primary caregiver and fundamentally influences the child's self-evaluation and perception of the world as a safe place (Bowlby 1969, 1973). An insecure attachment lowers a person's sense of self-worth and can lead to perfectionism and compulsive behaviour, which becomes a way to secure and stabilize self-worth and control surrounding events (Doron & Kyrios 2005). Of the two dimensions that define insecure attachment in adulthood (anxious and avoidant), attachment anxiety has a greater association with OCD (Ivarsson *et al.* 2016). A study by Tibi *et al.* (2019) found the anxious attachment style to be a significant moderator of the treatment outcome, leading to a poorer response to acute treatment. In another study by Tibi *et al.* (2020), a secure attachment style proved a protective factor that led to better outcomes.

Dissociation

Dissociation is a defence mechanism that protects from painful emotions, stress, or traumatic events. It may impact perception, memory, emotions, thinking, psychomotor functions, and other personality and integration qualities (Dell and O'Neil 2009, Schimmenti 2016, Evans *et al.* 2022). The presence of dissociation can be an important factor influencing the treatment results in OCD patients (Rufer *et al.* 2006, Prasko *et al.* 2009). Spitzer *et al.* (2007) indicated that dissociation directly or indirectly impacts treatment results because it triggers as a defence against negative emotions experienced intensively in psychotherapy.

Comorbid personality disorder

Spitzer *et al.* (2007) found that comorbid personality disorder, low baseline psychopathology, and high dissociation emerged as relevant predictors of non-responsive OCD patients. Ociskova *et al.* (2021) showed a small decrease in specific obsessive-compulsive symptoms during treatment in OCD patients with comorbid personality disorders, but the improvement was similar to those without personality disorders (Ociskova *et al.* 2021). However, other studies reported larger improvements in patients without this comorbidity (Thamby & Khanna 2019, Kart *et al.* 2020, Kathmann *et al.* 2022). Still, many comorbid patients significantly improve (Vyskocilova *et al.* 2016; Ociskova *et al.* 2021).

Aims of the study

The study aimed to determine if adverse childhood experiences, parental styles, adult attachment, and comorbidity with a personality disorder predict treatment outcomes in pharmacoresistant OCD patients.

Study objectives and hypotheses

The exploration of the current state of knowledge led to the following hypotheses:

(1) Earlier onset of the disorder predicts lower treatment outcomes.
(2) Higher severity of the disorder predicts lower treatment outcomes.
(3) A higher level of adverse childhood experiences predict lower treatment outcomes.
(4) A higher level of maternal care predicts higher treatment outcomes.
(5) A higher level of paternal care predicts higher treatment outcomes.
(6) A higher level of attachment anxiety predicts lower treatment outcomes.
(7) A higher level of dissociation predicts lower treatment outcomes.
(8) Patients with a comorbid personality disorder have lower treatment outcomes than patients without a comorbid personality disorder.

METHODS

Patients

Two independent raters confirmed meeting the inclusion and exclusion criteria. *The inclusion criteria* were the following:

(a) the ICD-10 research criteria for obsessive-compulsive disorder (ICD-10 1996);
(b) resistency to treatment 18–60 years;
(c) defined as a total Y-BOCS change < 25 % after at least one SSRI trial lasting three or more months (Pallanti *et al.* 2002).

The exclusion criteria were:

(a) current depressive disorder;
(b) high suicidal risk;
(c) an organic mental disorder;
(d) psychotic disorder, current or anamnestic;
(e) current substance abuse;
(f) severe somatic illness (oncologic, cardio-vascular).

Measurements

The subjects were assessed at the start and the end of the hospitalization. All measures were described in detail in the first part of the study. The measurements include the following rating scales and questionnaires:

- *MINI* – Mini International Neuropsychiatric Interview is a diagnostic tool used for basic screening for mental disorders meeting the Axis I criteria according to the Diagnostic and Statistical Manual of Mental Disorders - 4th edition and ICD-10 (Sheehan *et al.* 1998, Amorim 2000, Pinninti *et al.* 2003).

- *CGI* – Clinical Global Impression is an overall assessment of the severity of psychopathology by the physician (CGI-O) on a scale of 1–7 (Guy 1976, 2000). The second is a patient self-evaluation on a scale of 1–7 (CGI-S).
- *HAMA* is a rating scale for measuring the severity of anxiety symptoms, consisting of 14 items defined by a series of symptoms (Maier *et al.* 1988).
- *BAI* – Beck Anxiety Inventory consists of 21 self-administered items that described anxiety symptoms in the last week (Beck *et al.* 1988). The Czech version has good test-retest reliability, validity and factor structure (Kamaradova *et al.* 2015).
- *BDI-II* – Beck Depression Inventory, second edition, consists of 21 items in which patients choose how often they perceived the described depressive symptoms in the last week (Beck *et al.* 1974, 2010). The Czech version of the inventory is equivalent to the original in terms of its test-retest reliability, validity, and factor structure (Ociskova *et al.* 2017).
- *Y-BOCS-SR* is a self-rating scale used to assess the severity of OCD (Goodman *et al.* 1989a, 1989b). Previous studies showed a high correlation between the Czech version of YBOCS-SR and the Y-BOCS rated by a clinician (Prasko *et al.* 2006).
- *PBI* – Parental Bonding Instrument contains 25 statements related to the behaviour of the patient's parents during their childhood (Parker *et al.* 1979). They express their agreement with the statements and retrospectively evaluate their parents as they perceived them in their first 16 years of life. Cikosova & Preiss (2011) published an analysis of the Czech version and reported good internal consistency (α = 0.79–0.85).
- *ECR-R* – Experiences in Close Relationships–Revised consists of two subscales with 18 items each – the first represents attachment anxiety, and the second is attachment avoidance (Fraley *et al.* 2000). The items are rated on a seven-point Likert-type scale (from 1 – strongly disagree to 7 – strongly agree). The ECR-R scale is a revised version of the original scale, with some items replaced to achieve better psychometric properties of the method. The Czech translation has not yet undergone standardisation. The Slovak version we used during this research reached good internal consistency (α = 0.82) (Rozvadsky-Gugova *et al.* 2014). The Cronbach's alpha of the scale was similar in this research (α = 0.80).
- *DES* – Dissociative Experiences Scale is a self-administered 28-item inventory with dissociative symptoms (Carlson *et al.* 1991). The Czech version of the scale is equivalent to the original text in terms of its test-retest reliability, validity and factor structure (Ptacek *et al.* 2007). Pathological DES (DES-T) includes more severe dissociative symptoms (Waller *et al.* 1996). The method had high internal consistency in the presented study (Cronbach's alpha = 0.95).
- *CTQ* – The Childhood Trauma Questionnaire-Short Form (CTQ-SF) is a self-report retrospective questionnaire with 28 items evaluating five childhood adverse experiences: physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect (Bernstein & Fink 1998, Scher *et al.* 2001, Bernstein *et al.* 2003, Thombs *et al.* 2009). Each subscale has five items, with the score's severity of the subscales ranging from 5 to 25. The total score is calculated using all 25 items and measures the overall childhood maltreatment severity (Scher *et al.* 2001). The Czech questionnaire version is equivalent to the original version regarding its test-retest reliability, validity, and factor structure (Kascakova *et al.* 2018). The method showed good internal consistency in this study (Cronbach's alpha = 0.92).
- *Demographic data*, including sex, age, the onset of the disorder, duration of the disorder, the number of psychiatric hospitalisations, heredity, employment status, relationship status, pension income, education, and current medication, were obtained in an interview and using a demographic questionnaire.

The primary outcome criteria of the therapeutic change were defined as follows:

- The relative change in Y-BOCS-SR;

The secondary outcome criteria of the therapeutic change were defined as follows:

- The relative change in CGI-S
- The relative change in HAMA

Treatment approach

Patients were treated with a combination of group cognitive behavioural therapy (CBT) and medication with standard dosages. The structured CBT program contained twenty-four CBT group sessions, each lasting 1.5 hours. The main topics include education about obsessive-compulsive disorder and its treatment, a vicious circle of obsessive-compulsive symptoms, cognitive restructuring, exposure in vivo with response prevention, imagery exposure, training in communication skills and problem-solving, and working with cognitive schemas and self-stigma. Each patient had an additional weekly individual session with a CBT therapist. Supplementary programs consisted of ergo-therapy, daily relaxation, and physical exercise. The pharmacotherapy was heterogeneous and not controlled by the researchers. The changes in the medication were minimal; the average dosages of antidepressants, antipsychotics, and anxiolytics did not significantly differ at the start and the end of the hospitalization (Table 1). The mean dosage of antidepressants was 48.8 ± 25.9 mg of paroxetine equivalent at the beginning (n=58) and 49.6 ± 22.5 mg at the end of the program (n=60). The average dosage of antipsychotics was 1.8 ± 1.5 mg of risperidone equivalent at the beginning (n=32) and 2.0 ± 1.7 mg at the end of the program (n=29). The mean dosage of anxiolytics was 12.2 ± 9.0 mg of diazepam equivalent at the beginning (n=17) and 11.1 ± 9.3 mg at the end of the program (n=12).

Tab. 1. Included patients and completers

Variable / Sample	Patients entering the study (n=77)	Completers: Treatment start (n=66)	Completers: Treatment end	Statistic: Difference between the 1st and 2nd assessment of completers
Age	34.2 ± 11.7	35.0 ± 11.6		
Sex: male / female	38 / 39	34 / 32		
Age of onset of the disorder	17.0 ± 8.6	17.0 ± 8.9		
Duration of the disorder	16.5 ± 10.7	17.7 ± 10.0		
Number of hospitalizations	3.0 ± 5.7	3.1 ± 6.1		
Heredity: no / other disorder / OCD	29 / 21 / 27	26 / 18 / 22		
Education: basic / vocational / secondary / university	14 / 13 / 28 / 22	11 / 9 / 26 / 20		
Employment: student / (self-) employed / unemployed or pensioned	15 / 24 / 38	12 / 22 / 32		
Marital status: single / married / divorced	57 / 13 / 7	48 / 12 / 6		
Partner: no / yes	45 / 32	36 / 30		
Another anxiety disorder: no/ yes	64 / 13	56 / 10		
Personality disorder: no/yes	58 / 19	49 / 17		
CGI-S	4.6 ± 0.7	4.5 ± 0.7	3.7 ± 0.8	dependent t-test: t=5.821 df=65 ; $p<0.0001$
Y-BOCS-SR – total	23.9 ± 7.3	23.6 ± 7.2	20.8 ± 8.0	dependent t-test: t=4.627 df=56; $p<0.0001$
HAMA	23.0 ± 10.1	22.9 ± 9.9	16.3 + 12.1	dependent t-test: t=7.481 df=64; $p<0.0001$
BAI	23.1 ± 13.5	22.8 ± 12.9	19.9 ± 13.9	dependent t-test: t=2.739 df=64; $p<0.01$
BDI-II	25.0 ± 13.3	25.2 ± 13.5	22.1 ± 15.1	dependent t-test: t=2.401 df=64; $p<0.05$
ECR-R – Fear	4.0 ± 1.5	3.9 ± 1.5		
ECR-R – Avoidance	3.4 ± 0.9	3.4 ± 0.9		
DES	13.4 ± 14.9	13.2 ± 14.4	12.4 ± 15.6	dependent t-test: t=1.468 df=59 ; ns
DES-T	9.0 ± 13.9	9.1 ± 13.9	8.7 ± 15.2	dependent t-test: t=0.9848 df=59 ; ns
PBI – Maternal care	23.4 ± 10.5	23.6 ± 10.2		
PBI – Maternal control	15.0 ± 7.9	15.0 ± 8.0		
PBI – Paternal care	19.4 ± 9.7	19.5 ± 9.5		
PBI – Paternal control	12.7 ± 7.6	13.0 ± 7.8		
CTQ-SF Total	45.7 ± 20.0	45.4 ± 19.9		
Emotional abuse	11.4 ± 6.2	11.4 ± 6.3		
Psychical abuse	7.0 ± 4.3	7.1 ± 4.2		
Sexual abuse	6.0 ± 3.6	6.0 ± 3.7		
Emotional neglect	14.1 ± 5.8	13.9 ± 5.7		
Physical neglect	7.6 + 4.0	7.3 ± 3.7		
Antidepressant index	49.4 ± 25.0 (n=69)	48.8 ± 25.9 (n=58)	49.6 ± 22.5 (n=60)	dependent t-test: t=0.7178 df=66; ns
Anxiolytic index	12.2 ± 9.0 (n=17)	12.2 ± 9.0 (n=17)	11.1 ± 9.3 (n=12)	dependent t-test: t=1.799 df=10; ns
Antipsychotic index	1.9 ± 1.5 (n=37)	1.8 ± 1.5 (n=32)	2.0 ± 1.7 (n=29)	dependent t-test: t=0.09286 df=30; ns

CGI-S = the Clinical Global Impression – Severity; Y-BOCS-SR = Yale-Brown Obsessive Compulsive Scale – Self-Report; HAMA = Hamilton Anxiety Rating Scale Measurement; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory, Second version; ECR-R Experiences in Close Relationships – Revised; DES = Dissociative Experience Scale; DES-T = Dissociative Experience Scale, pathologic dissociation score; PBI = Parental Bonding Instrument; CTQ-SF = Childhood Trauma Questionnaire – Short Form

Tab. 2. Correlations of initial measurements, OCD onset, and therapeutic change

Factors / Relative change	CGI-S change	Y-BOCS-SR change	HAMA change
Disorder onset	0.10	**0.31** P*	**0.32** P*
Disorder length	-0.08	**-0.29** P (p=0.05)	-0.17
Number of hospitalizations	0.17	-0.13	**-0.34** S**
CGI-S	**0.56** S***	-0.01	0.16
Y-BOCS-SR-total	-0.08	**0.25** P(p=0.06)	-0.12
Obsessions	-0.06	0.16	-0.11
Compulsions	-0.12	-0.13	-0.11
HAMA	-0.13	-0.15	**-0.35** P**
BAI	-0.08	**-0.24** P(p=0.06)	**-0.36** P**
BDI-II	-0.14	-0,06	**-0,38** P**
ECR-R – anxiety	0.11	0.12	**-0.46** P**
ECR-R – avoidance	-0.18	-0.13	-0.20
DES	-0.09	-0.20	-0.15
DES-T	-0.14	-0.15	-0.18
PBI – maternal care	0.22	0.10	**0.32**P*
PBI – maternal control	-0.18	-0.04	-0.16
PBI – paternal care	0.06	0.20	0.21
PBI – paternal control	-0.04	-0.13	**-0.26** P*
CTQ-Total	-0.07	-0.02	**-0.39** P**
Emotional abuse	-0.03	-0.06	**-0.28** P*
Physical abuse	-0.05	0.10	-0.22
Sexual abuse	-0.09	0.05	-0.02
Emotional neglect	-0.14	-0.19	**-0.41** P**
Physical neglect	-0.17	-0.11	**-0.39** S**
Antidepressant index	-0.22	-0.03	-0.02
Antipsychotic index	0.23	0.13	0.11

Notes: objCGI = objective Clinical Global Impression scale; Y-BOCS-SR = Yale-Brown Obsessive Compulsive Scale – Self-Report; HAMA = Hamilton Anxiety Rating Scale Measurement; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory, Second version; ECR-R Experiences in Close Relationships – Revised; DES = Dissociative Experience Scale; DES-T = Dissociative Experience Scale, pathologic dissociation score; PBI = Parental Bonding Instrument; CTQ-SF = Childhood Trauma Questionnaire – Short Form

Statistical procedure

Sample size calculations were calculated with G*Power (Faul *et al.* 2007). The results estimated that a minimum of 64 patients were required to achieve 80% power for correlation tests (one-tailed) and paired t-tests. We expected that the treatment changes would range from small (for anxiety) to medium (for depressive symptoms) and large (for the overall psychopathology and the OCD symptoms), as found by Ociskova *et al.* (2021).

Patients' demographical, clinical, and psychological data were examined using column statistics. All data are presented as the mean and standard deviation. Normal distributions of the variables were analyzed using the Shapiro-Wilk W test. Parametric or nonparametric independent and dependent t-tests calculated changes among the scores at the start and end of the treatment and for differences according to sex, education, employment, and relationship status. The chi-square tests were used for the categorical variables. Spearman Rank Correlation coefficients or Pearson correlation coefficients were obtained to examine relationships between questionnaires and rating scales. Correlations analysis found relationships between treatment outcome and other factors. The level of significance was set at $p<0.05$. All analyses were conducted using STATISTICA 24.0 software and Prism 8.

Ethics

The study was carried out in agreement with the latest version of the Declaration of Helsinki and ICH-GCP guidelines (International Conference on Harmonization, Good Clinical Practice) (EMEA

2002/2009). All participants signed the informed consent before the enrolment and after the nature of the procedures had been fully explained. The Ethics Committee approved the research project of the University Hospital and the Faculty of Medicine of Palacky University on October 14, 2019, with decision number 118/19.

RESULTS

Demographic variables

Seventy-seven patients with obsessive-compulsive disorder were admitted for a six-week complex inpatient treatment program from October 2019 to August 2022. The mean age was 34.2 ± 11.7 years. Thirty-eight patients were men, and 39 were women. The mean age of disorder onset was 17.0 ± 8.6 years, with a mean duration of 16.5 ± 10.7 years. Ten other patients admitted to the department were not included in the study because they did not complete more than half of the routinely administered questionnaires. Eleven patients (14.3 %) dropped out of the treatment. Data from the completers were subsequently statistically analyzed (Table 1).

Results of the treatment

The sample showed significant decreases in the average severity of the OCD symptoms (Y-BOCS-SR), anxiety (BAI, HAMA), depressive symptoms (BDI-II), and the overall severity of psychopathology (CGI-S). The dissociative symptoms did not significantly change (Table 1, Figures 1-3).

A total of 27.3 % of the patients improved moderately or more in the overall severity of psychopathology (a decrease by 2+ points in CGI-S), and 40.9 % improved by at least 25% on this scale. A minority of the participants (28.8%) showed significant improvement in the severity of their OCD symptomatology, defined as 25% and a larger decrease in the total score of Y-BOCS-SR. The improvement was larger in the general anxiety; 57.6 % of the patients showed at least a 25 % decrease in the HAMA scores.

Initial severity of psychopathology, psychosocial measures and therapeutic change

Relative change in the severity of the subjectively rated overall psychopathology (CGI-S) significantly positively correlated only with the initial symptomatology measured by the same scale (Table 2). These outcomes did not significantly connect with ACEs, adult attachment, or parental styles (Table 2).

The relative change of the OCD symptoms (Y-BOCS-SR) significantly correlated solely with the onset of the OCD and trended towards a negative correlation with the OCD duration. This outcome parameter was also trending towards significance in the correlations with the initial anxiety (BAI) and OCD symptomatology (Y-BOCS-SR) (Table 2).

The relative change in the severity of anxiety (HAMA) was significantly positively correlated with the onset age of the disorder and negatively with the number of previous hospitalizations (Table 2). Furthermore, it negatively connected with the initial anxiety (HAMA, BAI) and several psychosocial factors – the history of emotional abuse and neglect and physical neglect, the overall severity of the ACEs (CTQ-SF), the adult attachment anxiety (ECR-R), and paternal control (PBI). On the other hand, maternal care (PBI) was associated with larger improvements in anxiety measured by HAMA (Table 2). The initial dissociative symptoms' severity did not predict either of the treatment outcomes.

Comorbid personality disorder and treatment effectiveness

Seventeen patients had a comorbid personality disorder: mostly borderline personality disorder (n = 11), followed by mixed personality disorder (n = 3), anankastic personality disorder (n = 2), and dependent personality disorder (n = 1). The comorbid

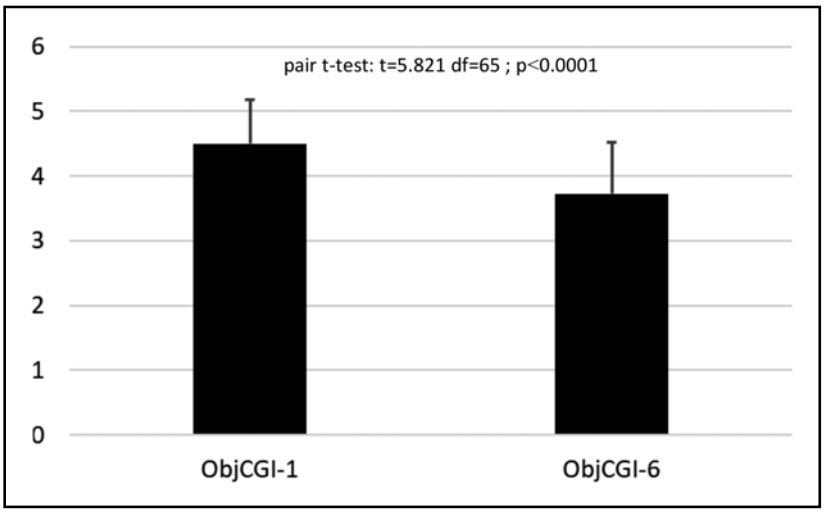

Fig. 1. Clinical Global Impression – Severity before and after the treatment

Tab. 3. Comparison of the OCD patients with and without comorbid personality disorder at the beginning and the end of the program

Variable / Comorbidity	COMORBID PERSONALITY DISORDER		
	Without personality disorder (n=49)	With personality disorder (n=17)	Statistics
Age of onset of the OCD	17.8 ± 9.8	14.6 ± 4.7	Independent t test: t=1.225 df=59; ns
Duration of OCD	18.4 ± 10.2	14.2 ± 8.7	Independent t test: t=1.243 df=50; ns
Number of hospitalizations	2.3 ± 1.6	5.4 ± 11.7	Mann Whitney test: MW U=365,5; ns
CGI-S severity-1	4.5 ± 0.7	4.5 ± 0.7	Mann Whitney test: MW U=411,5; ns
CGI-S severity-6	3.6 ± 0.7	4.0 ± 0.9	Mann Whitney test: MW U=316,5; ns
Dependent t-test	t=6.063 df=48; $p<0.001$	t=1.577 df=16; ns	
CGI-S-relative change	0.18 ± 0.22	0.08 ± 0.28	Independent t test: t=1.412 df=64; ns
Y-BOCS-SR-total-1	23.5 ± 7.1	23.8 ± 7.9	Independent t test: t=0.1186 df=62; ns
Y-BOCS-SR-total-6	20.6 ± 8.1	21.4 ± 7.9	Independent t test: t=0.3255 df=57; ns
Dependent t-test	t=3.677 df=42; $p<0.001$	t=3.383 df=13; $p<0.01$	
Y-BOCS-SR-relative change	0.13 ± 0.24	0.15 ± 0.16	Independent t test: t=0.2635 df=57; ns
HAMA-1	22.4 ± 9.9	24.7 ± 10.1	Independent t test: t=0.8203 df=64; ns
HAMA-6	15.2 ± 11.6	19.5 ± 13.4	Mann Whitney test: MW U=320; ns
Dependent t-test	t=7.031 df=47; $p<0.001$	t=5.830 df=16; $p<0.001$	
HAMA relative change	0.36 ± 0.28	0.24 ± 0.31	Independent t test: t=1.420 df=63; ns
BAI-1	22.3 ± 13.1	24.1 ± 12.6	Independent t test: t=0.4968 df=64; ns
BAI-6	18.2 ± 13.8	25.4 ± 13.2	Independent t test: t=1.828 df=63; ns
Dependent t-test	t=3.519 df=48; $p<0.001$	t=0.4506 df=15; ns	
BAI-relative change	0.16 ± 0.39	-0.12 ± 0.41	Independent t-test: t=2.459 df=63; $p<0.05$
BDI-II-1	24.5 ± 13.0	27.5 ± 15.1	Independent t test: t=0.7886 df=64; ns
BDI-II-6	21.1 ± 15.1	25.2 ± 14.9	Independent t test: t=0.9410 df=63; ns
Dependent t-test	t=2.309 df=48; $p<0.05$	t=0.7078 df=15; ns	
BDI-II-relative change	0.10 ± 0.52	0.01 ± 0.46	Independent t test: t=0.6906 df=63; ns
DES-1	11.8 ± 12.2	17.5 ± 19.2	Independent t test: t=1.382 df=61; ns
DES-6	11.2 ± 14.2	16.1 ± 19.5	Mann Whitney test: MW U=289; ns
Dependent t-test	t=0.8624 df=44; ns	t=1.820 df=14; ns	
DES-relative change	-0.12 ± 1.37	0.13 ± 0.58	Mann Whitney test: MW U= 341; ns
DES-T-1	7.5 ± 10.6	13.8 ± 20.8	Mann Whitney test: MW U=318,5; ns
DES-T-6	7.6 ± 13.4	11.9 ± 19.8	Mann Whitney test: MW U=272; ns
Dependent t-test	t=0.2733 df=44; ns	t=2.139 df=14; ns ($p=0.0505$)	
DES-T-relative change	-0.05 ± 1.25	0.18 ± 0.68	Mann Whitney test: MW U= 266; ns

and non-comorbid groups did not significantly differ in demographic, clinical, or psychosocial data at the start of the treatment (Table 3). The non-comorbid group significantly improved in most parameters – the overall severity of psychopathology (CGI-S), OCD symptoms (Y-BOCS-SR), anxiety (BAI, HAMA), and depressive symptoms (BDI-II) – but not in the severity of the dissociative symptoms. The comorbid group showed significant improvements in fewer areas, namely in the OCD symptoms and the anxiety evaluated by HAMA. Their decrease in pathological dissociation was trending towards significance. The relative anxiety change (BAI) was larger in the non-comorbid group. While the non-comorbid group improved in this area, the comorbid group was more anxious at the end of the hospitalization than at the start (Table 3).

DISCUSSION

The study intended to explore the connection between selected demographic and psychosocial factors and the effectiveness of combined CBT and pharmacotherapy

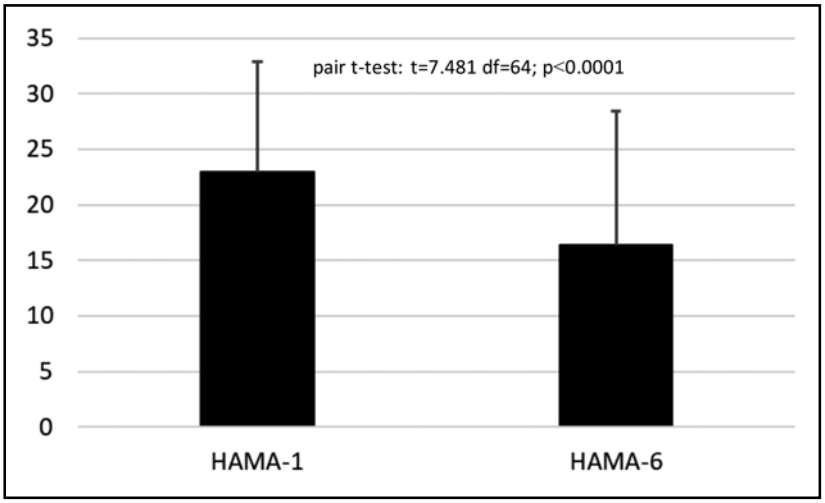

Fig. 2. HAMA before and after the treatment

in patients with treatment-resistant obsessive-compulsive disorder. The study design was naturalistic, carried out under typical conditions at the psychotherapeutic department for inpatients with neurotic, mood, and personality disorders. The 6-week combined treatment of pharmacoresistant patients with obsessive-compulsive disorder was efficient, and the mean scales' scores significantly declined in all measurements. The treatment change, measured by relative changes in CGI-S, Y-BOCS-SR, and HAMA, were comparable studies focusing on inpatients who previously did not respond to antidepressants (Mishra *et al.* 2007, Prasko *et al.* 2009, Reddy *et al.* 2010, Vyskocilova *et al.* 2016, Sijercic *et al.* 2020, Ociskova *et al.* 2021).

Responses to the hypotheses

(1) Earlier onset of the disorder predicts lower treatment outcomes.

This hypothesis was confirmed for the OCD-specific symptoms and the overall decrease in anxiety with moderate effect sizes. These results correspond to the study of Tibi *et al.* (2020), who concluded that the presence of the early age of onset predicted a worse four-year course of the disorder. However, they did not describe which type of treatment (if any) the participants received. Regarding pharmacotherapy, Rosario-Campos *et al.* (2001) found that the early-onset group responded less to clomipramine and selective serotonin reuptake inhibitors. On the other hand, based on the data analysis of 36 OCD patients who did not respond to SRI treatment, Reddy *et al.* (2010) consider a later age of onset as one of the predictors of poor pharmacotherapy outcomes.

Fontenelle *et al.* (2003) reported that early-onset OCD is connected to increased severity of obsessive-compulsive symptoms at baseline and the greater number of required therapeutic trials during the follow-up. In addition, it takes longer for patients with early-onset OCD to receive appropriate diagnosis and professional help (Ziegler *et al.* 2021). This leads to a longer duration of the disorder at the therapy initiation, considered one factor that negatively influences treatment outcomes (Bicakci *et al.* 2019). Contrary to our results, Lomax *et al.* (2009) found no difference

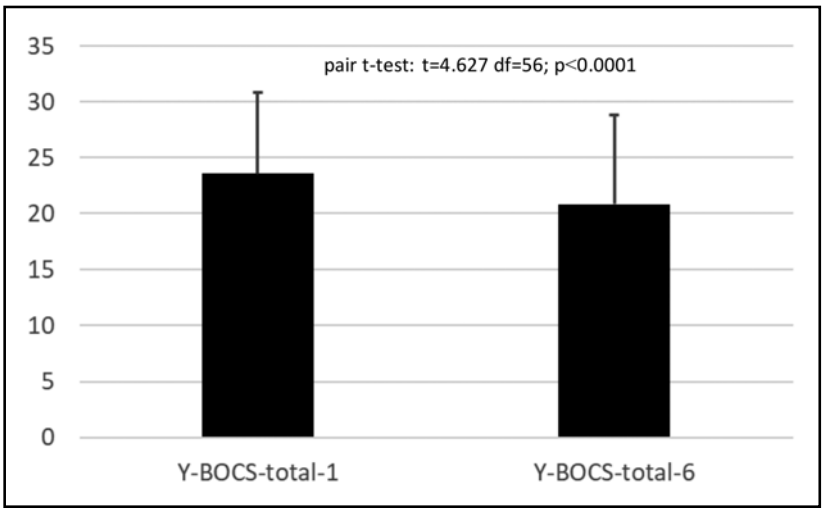

Fig. 3. Y-BOCS-SR before and after the treatment

in response to CBT between early and late-onset groups, but the research population was small (n = 45). Neither the results from another systematic review made by Olatunji *et al.* (2013) did support the age of onset as one of the predictors of the treatment outcome of CBT in OCD patients.

(2) Higher severity of the disorder predicts lower treatment outcomes.

This hypothesis was not confirmed for the clinician's assessment of the overall severity of psychopathology with a large effect size. The same was true for the specific OCD symptomatology, but only with borderline significance and small effect size. Tibi *et al.* (2019) showed similar results showing that patients with severe OCD had a more rapid symptom reduction during treatment and follow-up. Højgaard *et al.* (2020) stated low pretreatment OCD severity predicted lower OCD severity following treatment but did not predict treatment response. Their research group was also resistant to treatment, but unlike our patients, their sample comprised adolescents.

Contrary to our findings, Olatunji *et al.* (2013) found that higher pretreatment severity of OCD was significantly associated with a decrease in CBT treatment, and Kathmann *et al.* (2022) associated the initial symptom severity with poor CBT outcomes. According to Kyrios *et al.* (2015), lower pretreatment levels of OCD symptoms predicted OCD severity outcomes at post-treatment and recovery status in 79 OCD patients who received CBT. None of these studies was made on patients with pharmacoresistant OCD. However, this group has also described the correlation between a high Y-BOCS baseline and a worse CBT effectiveness (Prasko *et al.* 2009, Vyskocilova *et al.* 2016).

(3) Higher level of childhood events predict lower treatment outcomes.

The severity of ACEs did not predict a change in our sample's overall severity of the psychopathology or the specific OCD symptomatology. However, it significantly negatively predicted the change in the anxiety evaluated by a clinician, the overall severity of the adverse events, emotional abuse and neglect, and physical neglect.

Semiz *et al.* (2014) did not consider traumatic experiences a relevant predictor of the treatment outcome. Two other studies with OCD inpatients reported similar results – both of them reported that ACE was more frequent in OCD patients, and the severity of ACE was associated with the severity of OCD symptoms but did not mediate improvement during treatment (Fricke *et al.* 2007, Boger *et al.* 2020). This corresponds with the review of Fontenelle *et al.* (2011) focused on the role of traumatic and stressful life events in OCD. The authors concluded that it was not clear if OCD patients with a traumatic experience or comorbid PTSD react differently to SSRI and CBT treatment.

Comparing pharmacoresistant OCD patients (n = 30) with treatment responders (n = 30), Bicakci *et al.* (2019) identified that sexual abuse was higher in the treatment resistant group. In our research population, sexual abuse was rarely reported; the study's small population could cause the difference. Tibi *et al.* (2020) did not report the connection between ACEs and the remission rate after the treatment. On the other hand, they found that childhood trauma predicted a worse four-year disorder course. Therefore, adjusting CBT with ACE-oriented methods could still be a method for the benefit of some OCD patients.

(4) A higher level of maternal care predicts higher treatment outcomes.

Maternal care positively predicted a decrease in the general anxiety assessed by a clinician with a small effect size but not with a change in the specific OC symptomatology or the overall severity of the psychopathology.

No research has focused on the relationships between parental styles in childhood and the treatment response in adults with OCD. There is only one study by our colleagues in neurotic spectrum disorders where this association was examined (Holubova *et al.* 2021). In the case of maternal care, our results differ as the mentioned research was only related to the relative change of depression symptoms measured by BDI-II. However, it is needless to say that neither the research groups nor the tools used for measuring the anxiety were the same (the significant relationship between maternal care and anxiety symptoms was significant using HAMA in our study, whereas they used BAI).

On the other hand, much research tries to shed light on the relationship between parenting styles and OCD (but not on treatment outcomes). Some studies did not find a connection between parental styles and OCD (Mancini *et al.* 2000, Brander *et al.* 2016). Contrary to this, Turgeon *et al.* (2002) suggest that child-rearing practices such as overprotection may be a risk factor for developing anxiety disorders. Kamali *et al.* (2014) concluded that patients who had experienced authoritarian, permissive, and neglectful parenting styles were more likely to develop OCD, similar to Timpano *et al.* (2010), who found that the authoritarian parenting style was significantly associated with both the OC symptoms and OC beliefs. Yoshida *et al.* (2005) point out that paternal controlling and interfering rearing attitudes are linked to the development of OCD and depression with obsessive traits and are not linked to the development of depression itself. OCD patients also reported more parental rejection and control, and less parental warmth, according to the results of another study (Lennertz *et al.* 2010). So it seems that parental styles and OCD could be connected, but their influence on the treatment effectiveness is yet to be thoroughly examined.

(5) A higher level of paternal care predicts higher treatment outcomes.

This hypothesis was not confirmed. The paternal care was not significantly related to any assessed change in psychopathology. However, paternal control is weakly negatively correlated with a decrease in anxiety. The more the father controlled a child in childhood, the less their anxiety decreased during the treatment in adulthood. We did not expect this finding in the hypotheses and cannot rule out that it is a random finding. More research is needed on this topic, preferably with a schema-driven or similar approach.

(6) A higher level of attachment anxiety predicts lower treatment outcomes.

This hypothesis was confirmed only for the decrease in anxiety measured by HAMA with moderate effect size, not for the change in the specific OC symptomatology or the overall severity of the psychopathology Leeuwen *et al.* (2020) of medium to a large association between OCD and attachment anxiety and a medium association between OCD and attachment avoidance. Research on the relationship between attachment styles and the OCD treatment outcome is scarce. However, a meta-analysis of 36 studies (3158 patients with a wide range of psychiatric diagnoses) suggests that secure pretreatment attachment shows better psychotherapy outcomes than insecurely attached patients (Levy *et al.* 2018).

Tibi *et al.* (2019) assessed 118 patients treated by ERP and found that the fearful attachment style emerged as the main moderator of treatment outcome – these patients were more likely to drop out and improved less throughout treatment and follow-up than non-fearful clients. Our results are not in line with this research, but it could be caused partially by different research groups (outpatients vs pharmacoresistant inpatients) and partially by using different terminology. The fearful attachment style is defined by high anxiety and high avoidance, whereas our hypothesis only considered attachment anxiety. In addition, Levy *et al.* (2018) showed that (1) patients who experience low pretreatment attachment security might improve more in the therapy that integrates a focus on interpersonal interactions and close relationships and (2) improvements in attachment security during therapy might coincide with better treatment outcomes. Therefore, if the treatment positively influences patients' attachment security, it could potentially explain the better treatment outcome for patients with high baseline attachment anxiety.

(7) A higher level of dissociation predicts lower treatment outcomes.

Dissociation did not predict a change in any of the parameters we assessed. In the review focused on the context of dissociative symptoms in OCD, Belli (2014) concludes that patients not responding to treatment had high dissociative symptoms. It is well described that dissociation is associated with worse CBT outcomes of OCD (Rufer *et al.* 2006, Prasko *et al.* 2009, Prasko *et al.* 2016a, Vyskocilova *et al.* 2016). There is a theory that individuals dissociate as a response to negative emotions arising in psychotherapy, leading to a less favourable outcome (Spitzer *et al.* 2007). Based on the research with 120 OCD patients, Semiz *et al.* (2014) consider high dissociation one of the relevant predictors for treatment results in general (not only CBT). Looking at the effect sizes of the connections between dissociation and the treatment outcomes, the difference between our results and other studies is likely by the small size of our sample.

(8) Patients with a comorbid personality disorder have lower treatment outcomes than patients without a comorbid personality disorder.

This hypothesis was not confirmed. However, the non-comorbid group significantly improved in several parameters (CGI-S, BAI, BDI-II), while the comorbid group did not. Despite that, both groups only significantly differed in the relative change of subjective anxiety – a measure that was not a part of the hypothesis. This result is surprising since Kathmann *et al.* (2022) identify comorbid personality disorder as one of the factors associated with worse CBT outcomes in patients with OCD.

Speaking about specific PDs, in the study of 55 OCD patients, Baer *et al.* (1992) marked paranoid, schizoid, and schizotypal personality disorders as a predictor of poor OCD treatment by clomipramine. On the other hand, in the study of 92 OCD patients, those with comorbid OCPD demonstrated greater treatment gains during CBT in terms of OCD severity (Gordon *et al.* 2015). The latter result is contrary to Thamby & Kanna (2019), who associate OCPD and schizotypal disorder with the poor course and treatment response of OCD. Thiel *et al.* (2013) consider schizotypal and narcissistic personality disorders to have this effect in their systematic review. Most of the authors agreed that having two or more comorbid personality disorders leads to worse outcomes in OCD treatment (Baer *et al.* 1992, Thiel *et al.* 2013, Thamby & Khanna 2019). All these studies are not inconsistent with our results because our sample mostly suffered from borderline personality disorder. It seems that comorbid personality disorders could play a significant role in the treatment outcome of OCD patients, but it highly depends on the respective type of PD.

Limitations of the study

The presented study has several limitations. Self-report questionnaires were used to assess the symptoms, childhood adverse events, parental care, and attachment. We used only two objective instruments. Future research should corroborate these questionnaires with more clinician-rated instruments. Another limitation is the small sample size. The naturalistic design and the combined treatment prevented an analysis of the effectiveness of a clearly defined therapeutic approach.

Furthermore, the CTQ-SF measures only some of the ACEs and does not cover the entire range of childhood trauma or adverse events (e.g., bullying, loss of social network due to moving to another city, serious illness or injury etc.).

The comparison between the group with comorbid personality disorder and without comorbid personality disorder suffers from the lack of patients with personality disorder, so it was impossible to compare the two groups using two-way ANOVA. The fact that there were no more significant differences between the groups may be due to insufficient numbers of patients.

CONCLUSION

Hospitalized pharmacoresistant patients with obsessive-compulsive disorder significantly improved during the 6-week inpatient intensive CBT program in the severity of the OCD psychopathology, anxiety, and depressive symptoms. The early onset of the disorder was associated with worse treatment outcomes regarding specific OCD symptomatology. Adverse childhood experiences were only connected to the relative change of anxiety.

ACKNOWLEDGMENTS

The authors report no conflicts of interest in this work.

REFERENCES

1 American Psychiatric Association (2013). DSM-5 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington.
2 Amorim P (2000). Mini International Neuropsychiatric Interview (MINI): brief interview validation for diagnosing mental disorders. Rev Bras Psiquiatr. **22**(3): 106–115.
3 Baer L, Jenike MA, Black DW, Treece C, Rosenfeld R, Greist J (1992). Effect of Axis II diagnoses on treatment outcome with clomipramine in 55 patients with obsessive-compulsive disorder. Arch Gen Psych. **49**(11): 862–866.
4 Barcaccia B, Tenore K, Mancini F (2015). Early childhood experiences shaping vulnerability to obsessive-compulsive disorder. Clin Neuropsych. **12**(6): 141–147.
5 Beck AT, Beamesderfer A (1974). Assessment of depression: the depression inventory. Mod Probl Pharmacopsychiatry. **7**: 151–169.
6 Beck AT, Epstein N, Brown G, Steer RA (1988). An Inventory for Measuring Clinical Anxiety: Psychometric Properties. J Consult Clin Psychol. **56**(6): 893–897.
7 Beck AT, Steer RA, Ball R, Ranieri W (2010). Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. J Pers Assess. **67**(3): 588–597.
8 Belli H (2014). Dissociative symptoms and dissociative disorders comorbidity in obsessive compulsive disorder: Symptom screening, diagnostic tools and reflections on treatment. World J Clin Cases. **2**(8): 327–331.
9 Benedetti F, Poletti S, Radaelli D, Pozzi E, Giacosa C, Smeraldi E (2014). Adverse childhood experiences and gender influence treatment-seeking behaviors in obsessive-compulsive disorder. Comprehensive Psychiatry. **55**(2): 298–301.
10 Bernstein DP, Fink L (1998). Childhood Trauma Questionnaire: A retrospective self-report manual. San Antonio, TX: Harcourt Brace & Company.
11 Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, Stokes J, Handelsman L, Medrano M, Desmond D, Zule W (2003). Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl. **27**(2): 169–190.
12 Bey K, Lennertz L, Riesel A, Klawohn J, Kaufmann C, Heinzel S, Grützmann R, Kathmann N, Wagner M (2017). Harm avoidance and childhood adversities in patients with obsessive-compulsive disorder and their unaffected first-degree relatives. Acta Psychiatr Scand. **135**(4): 328–338.
13 Bicakci EU, Guz HO, Sahin AR, Boke O, Sarisoi G, Karabekiroglu A, Kahve AC (2019). Predictors of drug treatment resistance in obsessive compulsive disorder. Anadolu Psikiyatri Derg. **20**(6): 565–572.
14 Boger S, Ehring T, Berberich G, Werner GG (2020). Impact of childhood maltreatment on obsessive-compulsive disorder symptom severity and treatment outcome. Eur J Psychotraumatol. **11**(1):1753942.
15 Bowlby J (1969). Attachment and Loss: Attachment. New York, NY: Basic Books.
16 Bowlby J (1973). Attachment and Loss. Separation: Anxiety and Anger. New York, NY: Basic Books.
17 Brander G, Pérez-Vigil A, Larsson H, Mataix-Cols D (2016). Systematic review of environmental risk factors for obsessive-compulsive disorder: A proposed roadmap from association to causation. Neurosci Biobehav Rev. **65**: 36–62.
18 Briggs ES, Price IR (2009). The relationship between adverse childhood experience and obsessive-compulsive symptoms and beliefs: the role of anxiety, depression, and experiential avoidance. J Anxiety Disord. **23**(8): 1037–1046.
19 Carlson EB, Putnam FW, Ross CA, Anderson GG, Clark P, Torem Coons P, Bowman E, Chu JA, Dill D, Loewenstein RJ, Braun BG (1991). Factor analysis of the Dissociative Experiences Scale: A multicentre study. In BG Braun & EB Carlson (Eds.). Proceedings of the Eighth International Conference on Multiple Personality and Dissociative States. Chicago: Rush.
20 Cikosova E, Preiss M (2011). Parental Bonding Instrument. Otrokovice: Propsycho, s.r.o.
21 Dell PF, O'Neil JA (2009). Dissociation and Dissociative Disorders: DSM-V and Beyond. New York: Routledge.
22 Doron G, Kyrios M (2005). Obsessive compulsive disorder: A review of possible specific internal representations within a broader cognitive theory. Clin Psychol Rev. **25**: 415–432.
23 Ehiobuche I (1988). Obsessive-compulsive neurosis in relation to parental child-rearing patterns among the Greek, Italian, and Anglo-Australian subjects. Acta Psychiatr Scand. **78**: 115–20.
24 Eisen JL, Sibrava NJ, Boisseau CL, Mancebo MC, Stout RL, Pinto A, Rasmussen SA (2013). Five-year course of obsessive-compulsive disorder: predictors of remission and relapse. J Clin Psychiatry. **74**(3): 233–239.
25 EMEA (2002). Available from: http://www.ema.europa.eu/docs/en_GB/ document_library/Scientific_guideline/2009/09/WC500002874.pdf. Accessed March 20, 2009.
26 Evans TC, Alonso MR, Jagger-Rickels A, Rothlein D, Zuberer A, Bernstein J, Fortier CB, Fonda JR, Villalon A, Jorge R, Milberg W, McGlinchey R, DeGutis J, Esterman M (2022). PTSD symptomatology is selectively associated with impaired sustained attention ability and dorsal attention network synchronization. Neuroimage Clin. **36**: 103146.
27 Faul F, Erdfelder E, Lang AG, Buchner A (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Res Methods. **39**: 175–191.
28 Fineberg NA, Hengartner MP, Bergbaum C, Gale T, Rössler W, Angst J (2013). Remission of obsessive-compulsive disorders and syndromes: evidence from a prospective community cohort study over 30 years. Int J Psychiatry Clin Pract. **17**(3): 179–187.
29 Fontenelle LF, Cocchi L, Harrison BJ, Miguel EC, Torres AR (2011). Role of stressful and traumatic life events in obsessive-compulsive disorder. Neuropsychiatry. **1**(1): 61–69.
30 Fontenelle LF, Mendlowicz MV, Marques C, Versiani M (2003). Early- and late-onset obsessive-compulsive disorder in adult patients: an exploratory clinical and therapeutic study. J Psych Res. **37**(2): 127–133.
31 Fraley RC, Waller NG, Brennan KA (2000). An item-response theory analysis of self-report measures of adult attachment. J Pers Soc-Psychol. **78**(2): 350–365.
32 Fricke S, Kohler S, Moritz S, Schafer I (2007). Early traumatic experience in obsessive-compulsive disorders: a pilot study. [Frühe interpersonale traumatisierungen bei zwangserkrankungen: eine pilotstudie]. Verhaltenstherapie. **17**(4): 243–250.

33 Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, Charney DS (1989b). The Yale-Brown Obsessive Compulsive Scale. II. Validity. Arch Gen Psychiatry. **46**:1012–1016.

34 Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, Heninger GR, Charney DS (1989a). The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Arch Gen Psychiatry. **46**: 1006–1011

35 Gordon OM, Salkovskis PM, Bream V (2016). The Impact of Obsessive-Compulsive Personality Disorder on Cognitive Behaviour Therapy for Obsessive Compulsive Disorder. Behav Cogn Psychother. **44**(4): 444–59.

36 Guy W (1976). Clinical Global Impressions. ECDEU Assessment Manual for Psychopharmacology—Revised. Rockville, MD: U.S. Department of Health, Education, and Welfare; Public Health Service, Alcohol; Drug Abuse, and Mental Health Administration; National Institute of Mental Health; Psychopharmacology Research Branch; Division of Extramural Research Programs. 218–222.

37 Guy W (2000). Clinical Global Impressions (CGI) Scale, Modified. In Rush JA: Task Force for the Handbook of Psychiatric Measures (eds.). Handbook of Psychiatric Measures (1st ed.). Washington, DC: American Psychiatric Association.

38 Højgaard DRMA, Schneider SC, La Buissonnière-Ariza V, Kay B, Riemann BC, Jacobi D, Eken S, Lake P, Nadeau J, Goodman WK, McIngvale E, Storch EA (2020). Predictors of treatment outcome for youth receiving intensive residential treatment for obsessive-compulsive disorder (OCD). Cogn Behav Ther. **49**(4): 294–306.

39 Hollander E, Kaplan A, Allen A, Cartwright C (2000). Pharmacotherapy for Obsessive-Compulsive Disorder. Psychiatric Clinics of North America. **23**(3): 643–656.

40 Holubova M, Prasko J, Hodny F, Vanek J, Slepecky M, Nesnidal V (2021). Self-stigma, severity of psychopathology, dissociation, parental style and comorbid personality disorder in patient with neurotic spectrum disorders Part 2: Therapeutic efficacy of intensive psychotherapeutic inpatients program. Neuro Endocrinol Lett. **42**(3): 185–199.

41 International Classification of Disorders (1996). Mental and behavioural disorders: Research diagnostic criteria, 10th revision (Czech translation). Prague: Prague Psychiatric Centre.

42 Ivarsson T, Saavedra F, Granqvist P, Broberg AG (2016). Traumatic and adverse attachment childhood experiences are not characteristic of OCD but of depression in adolescents. Child Psychiatry Hum Dev. **47**(2): 270–280.

43 Kamali K, Looyeh MY, Rashid R (2014). EPA-0640 – The influence of parenting styles on the development and maintenance obsessive-compulsive disorder. Eur Psychiatry. **29**(1): Page1.

44 Kamaradova D, Prasko J, Latalova K, Panackova L, Svancara J, Grambal A, Sigmundova Z, Ociskova M, Bares V, Cakirpaloglu S, Jelenova D, Kasalova P, Kovacsova A, Vrbova K (2015). Psychometric properties of the Czech version of the Beck Anxiety Inventory –comparison between diagnostic groups. Neuro Endocrinol Lett. **36**(7): 706–712.

45 Kart A, Yucens B (2020). Personality Beliefs in Obsessive-Compulsive Disorder: How Are They Related to Symptom Severity? Psychiatry Investig. **17**(8): 822–828.

46 Kascakova N, Furstova J, Solcova I, Biescad M, Hasto J, Tavel P (2018). Psychometrická analýza českej verzie dotazníka Trauma z dětství (CTQ) so sociodemografickými rozdielmi v traumatizácii dospelých obyvateľov Českej republiky [(Psychometric analysis of the Czech version of the questionnaire Trauma from Childhood (CTQ) with socio-demographic differences in adult traumatized inhabitants of the Czech Republic) (In Czech)]. Ceskoslovenská psychologie. **62**: 212–230.

47 Kathmann N, Jacobi T, Elsner B, Reuter B (2022). Effectiveness of individual cognitive-behavioural therapy and predictors of outcome in adult patients with obsessive-compulsive disorder. Psychother Psychosom. **91**(2): 123–135.

48 Kühne F, Ay DS, Marschner L, Weck F (2020). The heterogeneous course of OCD – A scoping review on the variety of definitions. Psychiatry Res. **285**: 112821.

49 Kyrios M, Hordern C, Fassnacht DB (2015). Predictors of response to cognitive behaviour therapy for obsessive-compulsive disorder. Int J Clin Health Psychol. **15**(3): 181–190.

50 Leeuwen WA, Wingen GA, Luyten P, Denys D, Marle HJF (2020). Attachment in OCD: A meta-analysis. J Anxiety Disord. **70**: 102187.

51 Lennertz L, Grabe HJ, Ruhrmann S, Rampacher F, Vogeley A, Schulze-Rauschenbach S, Ettelt S, Meyer K, Kraft S, Reck C, Pukrop R, John U, Freyberger HJ, Klosterkötter J, Maier W, Falkai P, Wagner M (2010). Perceived parental rearing in subjects with obsessive-compulsive disorder and their siblings. Acta Psychiatr Scand. **121**(4): 280–8.

52 Levy KN, Kivity Y, Johnson BN, Gooch CV (2018). Adult attachment as a predictor and moderator of psychotherapy outcome: A meta-analysis. J Clin Psychol. **74**(11): 1996–2013.

53 Lomax CL, Oldfield VB, Salkovskis PM (2009). Clinical and treatment comparisons between adults with early- and late-onset obsessive-compulsive disorder. Behav Res Ther. **47**(2): 99–104.

54 Maier W, Buller R, Philipp M, Heuser I (1988). The Hamilton Anxiety Scale: reliability, validity and sensitivity to change in anxiety and depressive disorders. J Affect Disord. **14**(1): 61–8.

55 Mancini F, D´Olimpio F, Prunetti E, Didonna F, Genio MD (2000). Parental bonding: can obsessive symptoms and general distress be predicted by perceived rearing practices? Clinical Psychol Psychother. **7**(3): 201–208.

56 Menchon JM, Bobes J, Alamo C, Alonso P, García-Portilla MP, Ibáñez Á, Real E, Bousoño M, Saiz-Gonzalez MD, Saiz-Ruiz J (2019). Pharmacological treatment of obsessive-compulsive disorder in adults: A clinical practice guideline based on the ADAPTE methodology. Rev Psiquiatr Salud Ment. **12**(2): 77–91.

57 Mishra B, Sahoo S, Mishra B (2007). Management of treatment-resistant obsessive-compulsive disorder: An update on therapeutic strategies. Ann Indian Acad Neurol. **10**(3): 145–153.

58 NICE (2013). Obsessive-compulsive disorder: Evidence Update September 2013: A summary of selected new evidence relevant to NICE clinical guideline 31 'Obsessive-compulsive disorder: core interventions in the treatment of obsessive-compulsive disorder and body dysmorphic disorder (2005) [Internet]. London: National Institute for Health and Care Excellence (UK).

59 Ociskova M, Prasko J, Kupka M, Marackova M, Latalova K, Cinculova A, Grambal A, Kasalova P, Krnacova B, Kubinek R, Sigmundova Z, Tichackova A, Vrbova K (2017). Psychometric evaluation of the Czech Beck Depression Inventory-II in a sample of depressed patients and healthy controls. Neuro Endocrinol Lett. **38**(2): 98–106.

60 Ociskova M, Prasko J, Vanek J, Holubova M, Hodny F, Latalova K, Kantor K, Nesnidal V (2021). Self-Stigma and treatment effectiveness in patients with SSRI non-responsive obsessive-compulsive disorder. Psychol Res Behav Manag. **14**: 85–97.

61 Olatunji BO, Davis ML, Powers MB, Smits JAJ (2013). Cognitive-behavioural therapy for obsessive-compulsive disorder: A meta-analysis of treatment outcome and moderators. J Psychiatric Res. **47**(1): 33–41.

62 Pallanti S, Hollander E, Bienstock C, Koran L, Leckman J, Marazziti D, Pato M, Stein D, Zohar J, International Treatment Refractory OCD Consortium (2002). Treatment non-response in OCD: methodological issues and operational definitions. Int J Neuropsychopharmacol. **5**(2): 181–191.

63 Park S, Hong JP, Bae JN, Cho SJ, Lee DW, Lee JY, Chang SM, Jeon H J, Hahm BJ, Lee YM, Seong S, Cho MJ (2014). Impact of childhood exposure to psychological trauma on the risk of psychiatric disorders and somatic discomfort: single vs multiple types of psychological trauma. Psychiatry Res. **219**(3): 443–449.

64 Parker G, Tupling H, Brown LB (1979). A Parental Bonding Instrument. British Journal of Medical Psychology. **52**: 1–10.

65 Pinninti NR, Madison H, Musser E, Rissmiller D (2003). MINI International Neuropsychiatric Schedule: clinical utility and patient acceptance. Eur Psychiatry. **18**: 361–364.

66 Prasko J, Grambal A, Kasalova P, Kamaradova D, Ociskova M, Holubova M, Vrbova K, Sigmundova Z, Latalova K, Slepecky M, Zatkova M (2016a). Impact of dissociation on treatment of depressive and anxiety spectrum disorders with and without personality disorders. Neuropsychiatr Dis Treat. **12**: 2659–2676.

67 Prasko J, Paskova B, Zalesky R, Novak T, Kopecek M, Bares M, Horacek J (2006). The effect of repetitive transcranial magnetic stimulation (rTMS) on symptoms in obsessive compulsive disorder. A randomised, double-blind, sham-controlled study. Neuro Endocrinol Lett. **27**: 327–332.

68 Prasko J, Raszka M, Adamcova K, Grambal A, Koprivova J, Kudrnovská H, Latalova K, Vyskocilová J (2009). Predicting the therapeutic response to cognitive behavioural therapy in patients with pharmacoresistant obsessive-compulsive disorder. Neuro Endocrinol Lett. **30**(5): 615–623.

69 Ptacek R, Bob P, Paclt I, Pavlat J, Jasova D, Zvolsky P, Raboch J (2007). Psychobiology of dissociation and its clinical assessment. Neuro Endocrinol Lett. **28**(2): 191–198.

70 Reddy YC, Alur AM, Manjunath S, Kandavel T, Math SB (2010). Long-term follow-up study of patients with serotonin reuptake inhibitor-nonresponsive obsessive-compulsive disorder. J Clin Psychopharmacol. **30**: 267–72.

71 Reddy YCJ, Sundar AS, Narayanaswamy JC, Math SB (2017). Clinical practice guidelines for obsessive-compulsive disorder. Indian J Psychiatry. **59**(5): 74–90.

72 Rosario-Campos MC, Leckman JF, Mercadante MT, Shavitt RG, Prado HS, Sada P, Zamignani D, Miguel EC (2001). Adults With Early-Onset Obsessive-Compulsive Disorder. Am J Psychiatry. **158**(11): 1899–903.

73 Rozvadsky-Gugova G, Heretik A, Hajduk M (2014). Psychometric properties of the Slovak version of Experience in Close Relationships-Revised (ECR-R) on general adult sample. Studia Psychologica. **56**(1): 37–52. doi:10.21909/sp.2014.01.649

74 Rufer M, Fricke S, Held D, Cremer J, Hand I (2006). Dissociation and symptom dimensions of obsessive-compulsive disorder: a replication study. Eur Arch Psychiatry Clin Neurosci. **256**: 146–150.

75 Scher CD, Stein MB, Asmundson GJ, McCreary DR, Forde DR (2001). The childhood trauma questionnaire in a community sample: psychometric properties and normative data. J Trauma Stress. **14**(4): 843–857.

76 Schimmenti A (2016). Dissociative experiences and dissociative minds: exploring a nomological network of dissociative functioning. J Trauma Dissoc. **17**: 338–361.

77 Semiz UB, Inanc L, Bezgin CH (2014). Are trauma and dissociation related to treatment resistance in patients with obsessive-compulsive disorder? Soc Psychiatry Psychiatr Epidemiol. **49**(8): 1287–1296.

78 Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC (1998). The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry. **59**(20): 22–33.

79 Sijercic I, Whitfield KM, Cassin SE, Antony MM (2020). A systematic review of cognitive-behavioral therapy for pharmacotherapy treatment-resistant obsessive-compulsive disorder. J Obsessive Compuls Relat Disord. **26**: 100532.

80 Simpson HB, Huppert JD, Petkova E, Foa EB, Liebowitz MR (2006). Response versus remission in obsessive compulsive disorder. J Clin Psychiatry. **67**(2): 269–276.

81 Spitzer C, Barnow S, Freyberger HJ, Grabe HJ (2007). Dissociation predicts symptom-related treatment outcome in short-term inpatient psychotherapy. Aust N Z J Psychiatry. **41**(8): 682–687.

82 Sunderland M & Armstrong N (2005). Helping children who are anxious or obsessional. UK: Speechmark.

83 Thamby A, Khanna S (2019). The role of personality disorders in obsessive-compulsive disorder. Indian J Psychiatry. **6**(1): 114–118.

84 Thiel N, Hertenstein E, Nissen C, Herbst N, Kulz AK, Voderholzer U (2013). The Effect of Personality Disorders on Treatment Outcomes in Patients With Obsessive-Compulsive Disorders. J Pers Disord. **27**(6): 697–715.

85 Thombs BD, Bernstein DP, Lobbestael J, Arntz A (2009). A validation study of the Dutch Childhood Trauma Questionnaire-Short Form: Factor structure, reliability, and known-groups validity. Child Abuse & Neglect. **33**(8): 518–523.

86 Tibi L, van Oppen P, van Balkom AJLM, Eikelenboom M, Emmelkamp PMG, Anholt GE (2019). Predictors of treatment outcome in OCD: An interpersonal perspective. J Anxiety Disord. **68**: 102153.

87 Tibi L, van Oppen P, van Balkom AJLM, Eikelenboom M, Hendriks GJ, Anholt GE (2020). Childhood trauma and attachment style predict the four-year course of obsessive-compulsive disorder: Findings from the Netherlands obsessive compulsive disorder study. J Affect Disord. **264**: 206–214.

88 Timpano KR, Keough ME, Mahaffey BL, Schmidt NB, Abramowitz J (2010). Parenting and obsessive compulsive symptoms: implications of authoritarian parenting. J Cognitive Psychother. **24**(3): 151–164.

89 Turgeon L, O'Connor KP, Marchand A, Freeston MH (2002). Recollections of parent-child relationships in patients with obsessive-compulsive disorder and panic disorder with agoraphobia. Acta Psychiatr Scand. **105**: 310–316.

90 Vyskocilova J, Prasko J, Sipek J (2016). Cognitive behavioral therapy in pharmacoresistant obsessive-compulsive disorder. Neuropsychiatr Dis Treat. **12**: 625–639.

91 Waller NG, Putnam FW, Carlson EB (1996). Types of dissociation and dissociative types: A taxonometric analysis of dissociative experiences. Psychological Methods. **1**(3): 300–321.

92 Woody EZ, Hoffman KL, Szechtman H (2019). Obsessive compulsive disorder (OCD): Current treatments and a framework for neurotherapeutic research. Adv Pharmacol. **86**: 237–271.

93 Yoshida T, Taga C, Matsumoto Y, Fukui K (2005). Paternal overprotection in obsessive-compulsive disorder and depression with obsessive traits. Psychiatry Clin Neurosci. **59**(5): 533–538.

94 Ziegler S, Bednasch K, Baldofski S, Rummel-Kluge C (2021). Long durations from symptom onset to diagnosis and from diagnosis to treatment in obsessive-compulsive disorder: A retrospective self-report study. PLoS ONE. **16**(12): e0261169.