Neuroendocrinology Letters Volume 45 No. 6 2024
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

Childhood trauma and dissociation in patients with panic disorder, obsessive-compulsive disorder, and borderline personality disorder

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

Krystof Kantor[1,6], Jan Prasko[1,2,3,4], Kamila Belohradova[1], Jakub Vanek[5], Frantisek Hodny[1,7], Antonin Kolek[1], Marie Ociskova[1,4]

1 Department of Psychiatry, Faculty of Medicine and Dentistry, University Palacky 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.
5 Beskydy Mental Health Centre, Frydek-Mistek Hospital, Czech Republic.
6 Department of Paediatric Psychiatry, Motol University Hospital, Czech Republic.
7 Department of Psychology, Faculty of Arts, University of Ostrava, Ostrava, Czech Republic

Correspondence to: prof. Jan Prasko, 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: 2024-09-02 Accepted: 2024-10-15 Published online: 2024-12-12

Key words: **Adverse Childhood Experiences; Panic Disorder; Obsessive-Compulsive Disorder; Borderline Personality Disorder; Dissociative Experiences; Treatment Efficacy; Cognitive-Behavioral Therapy; Prediction of Treatment Effectiveness**

Neuroendocrinol Lett 2024; **45**(6):379–392 **PMID:** 39732466 45062404

Abstract

INTRODUCTION: PAdverse Childhood Experiences (ACEs) are associated with an increased risk of mental health issues in general, but their relationship with panic disorder (PD) and obsessive-compulsive disorder (OCD) has received less attention compared to borderline personality disorder (BPD). Dissociative experiences are significant predictors of increased symptoms, reduced treatment adherence, and poor prognosis in several psychiatric conditions, including PD, OCD, and BPD; still, their impact remains underexplored. This part of the study focuses on the overall efficiency of psychotherapeutic programs on treatment-resistant patients diagnosed with PD, OCD, and BPD (or combined), as well as the relationship between ACEs, dissociation rates, and treatment results.

METHOD: The study was conducted under standard conditions in an inpatient psychotherapy unit that specialized in anxiety, affective disorders, and personality disorders. Patients were hospitalized for 6 weeks and treated with a comprehensive CBT program and pharmacotherapy. The study included patients diagnosed with PD, OCD, or BPD (or combined). Two independent psychiatrists confirmed the inclusion and exclusion criteria. Patients were assessed using the Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI-II), Clinical Global Impression

Scale – Severity (CGI-S), Dissociative Experience Scale (DES), and Childhood Trauma Questionnaire (CTQ-SF).

RESULTS: A total of 349 out of 357 patients completed the study. The average age of patients was 33.33 ± 11.59 years. After the 6 week treatment, there was a statistically significant decrease in mean scores across all assessed scales. Changes in any scale during treatment did not correlate with the total CTQ-SF score or sub-scores. The relative change in CGI-S showed a statistically significant negative correlation with the total dissociation score on the DES scale at the beginning of treatment but not with pathological dissociation assessed by the DES-T questionnaire. Statistically significant decreases in mean CGI-S scores were observed in patients with a single diagnosis of PD, OCD, and BPD. Among comorbid groups, significant changes were observed only in patients with comorbid OCD and BPD. No statistically significant change in mean BDI-II scores was observed in patients with comorbid PD and OCD or comorbid OCD and BPD.

CONCLUSIONS: Our analysis showed that treatment led to a significant decrease in the severity of depressive symptoms assessed by BDI-II and anxiety symptoms assessed by BAI in patients with PD, OCD, and BPD. This decrease was not statistically significant in patients with comorbid disorders, suggesting that the presence of multiple diagnoses may affect treatment efficacy. ACEs did not correlate to treatment results, but dissociation rates were linked with poorer treatment outcomes.

INTRODUCTION

Mental health disorders such as panic disorder (PD), obsessive-compulsive disorder (OCD), and borderline personality disorder (BPD) are major health conditions that affect millions of people worldwide (World Health Organization 2020). These disorders have a profound impact on an individual's quality of life and can lead to other complications, including an increased risk of suicide (Nock *et al.* 2008).

Adverse childhood experiences (ACEs) increase the risk of mental health problems in general. However, their relationship to PD and OCD has received relatively little attention compared to BPD. (Zhang *et al.* 2023). The importance of this study is underscored by the existing literature highlighting the role of early ACEs in the development of mental disorders. ACEs are associated with higher rates of dissociation, depression, anxiety, and self-stigma (Zhang *et al.* 2023). These experiences may also influence treatment outcomes and patient prognosis.

Dissociative experiences are a significant predictor of more pronounced symptoms, poor treatment adherence, and adverse prognosis in several psychiatric conditions, including PD, OCD, and depression (Krause-Utz *et al.* 2021). When it comes to BPD, stress-induced dissociation, in particular, is a prevalent symptom that can interfere with psychosocial functioning and treatment outcomes (Krause-Utz *et al.* 2022).

The presence of dissociation is a key factor influencing treatment outcomes in patients with depressive and anxiety disorders, including OCD and PD (Watson *et al.* 2006; Praško *et al.* 2009; Krause-Utz *et al.* 2021). Elevated levels of dissociation are associated with worse outcomes in exposure therapy in patients with panic disorder (Ball *et al.* 1997; Michelson *et al.* 1998). The degree of dissociation may be one of the reasons for treatment resistance in these patients (Ball *et al.* 1997; Segui *et al.* 2000; Gulsun *et al.* 2007). Similarly, treatment-resistant patients with OCD also report high dissociative symptoms (Belli 2014; Semiz *et al.* 2014). It has been suggested that individuals with high dissociation tend to dissociate in response to negative emotions in psychotherapy, leading to a less favourable outcome (Spitzer *et al.* 2007).

Study objectives

This study aims to compare three groups of patients with different disorders – PD, OCD, and BPD – in terms of dissociation, depression, anxiety, and early adverse experiences. The aim is to determine whether these groups have significant differences in these areas and whether these factors can predict improvement during treatment.

Hypotheses

Five key areas were identified to formulate hypotheses based on knowledge and previous experience from our studies. In each of these areas, specific hypotheses were established:

(1) Rate of improvement in overall severity of the disorder

- 1a: Patients with panic disorder show a greater rate of improvement in the overall disorder severity of the disorder compared to patients with obsessive-compulsive disorder.
- 1b: Patients with panic disorder show a greater rate of improvement in the overall disorder severity of the disorder compared to patients with borderline personality disorder.

(2) Rate of improvement in general anxiety

- 2a: Patients with panic disorder show greater improvement in general anxiety compared to patients with obsessive-compulsive disorder.
- 2b: Patients with panic disorder show greater improvement in general anxiety compared to patients with borderline personality disorder.

(3) Rate of improvement in depression symptoms

- 3a: Patients with panic disorder show a greater rate of improvement in the overall severity of depressive symptoms compared to patients with obsessive-compulsive disorder.

- 3b: Patients with panic disorder show a greater rate of improvement in the overall severity of depressive symptoms compared to patients with borderline personality disorder.
- 3c: Patients with borderline personality disorder show a greater rate of improvement in the overall severity of depressive symptoms compared to patients with obsessive-compulsive disorder.

(4) Predictor of improvement – dissociation
- 4a: Severity of dissociation is a significant predictor of improvement in overall disorder severity during treatment.
- 4b: Severity of pathological dissociation is a significant predictor of improvement in overall disorder severity during treatment.
- 4c: Severity of dissociation is a significant predictor of improvement in anxiety symptoms severity.
- 4d: Severity of pathological dissociation is a significant predictor of improvement in anxiety symptoms severity.
- 4e: Severity of dissociation is a significant predictor of improvement in depressive symptoms severity.
- 4f: Severity of pathological dissociation is a significant predictor of improvement in depressive symptoms severity.

(5) Predictor of improvement – adverse childhood experiences

Total CTQ-SF score is significantly negatively correlated with:
- 5a: relative change in overall disorder severity
- 5b: relative change in anxiety symptoms
- 5c: relative change in depressive symptoms

METHOD

The study was conducted under standard conditions in an inpatient psychotherapy department specializing in anxiety, affective, and personality disorders. Two independent psychiatrists confirmed the inclusion and exclusion criteria: the attending physician and the head of the clinic. Patients diagnosed with PD, OCD, or BPD were included in the study.

Patients

The inclusion criteria were as follows:
- Diagnosis of PD/agoraphobia, OCD, or BPD according to ICD-10 research criteria.
- Age between 18 and 70 years.
- SSRI treatment resistance is defined as failure to respond to at least 12 weeks of prior treatment with an SSRI antidepressant.

The exclusion criteria were as follows:
- Current Major depressive episode.
- High risk of suicide.
- Organic psychiatric disorder.
- Psychotic disorder, current or past.
- Current substance abuse or dependence.
- Severe somatic illness.

Assessment

Beck Anxiety Inventory (BAI)

The Beck Anxiety Inventory (BAI) is a 21-item instrument developed by Aaron T. Beck, with each item scored from 0 (not at all) to 3 (extremely limiting). Patients rate their anxiety symptoms over the past week. The instrument has high internal consistency (α = 0.92) (De Ayala *et al.*, 2005). The Czech translation was validated by Kamaradová *et al.* (2015) with a Cronbach's alpha of 0.92 and a test-retest reliability of 0.75 after 1 week.

Beck Depression Inventory (BDI-II)

The Beck Depression Inventory (BDI-II) is a 21-item instrument for assessing depressive symptoms, rated on a 4-point scale. Patients rate their symptoms over the past 14 days. The Czech version has high internal consistency and reliability (Ptáček *et al.* 2016; Ocisková *et al.* 2017).

Clinical Global Impression-Severity (CGI-S)

The Clinical Global Impression Scale - Severity (CGI-S) is a tool for the global assessment of the severity of psychopathology created by Guy (1976). Healthcare professionals and patients can use it for self-assessment. Internal consistency is satisfactory (Zaider *et al.* 2003).

Dissociative Experience Scale (DES)

The Dissociative Experience Scale (DES) contains 28 items and measures dissociative experiences, including amnesia, depersonalization, and derealization. The questionnaire includes a domain for relatively normal dissociation (e.g., daydreaming) but also discerns pathological dissociation scale DES-T (e.g., absorption and fantasy, experiences of depersonalization and derealization, amnesia, and pathological anxiety and dissociation) (Waller & Ross 1997). It has high test-retest stability (0.93), and internal consistency is satisfactory (α = 0.96) (Frischholz *et al.* 1990). Regarding reliability, validity, and factor structure, the Czech version corresponds to the original (Ptáček *et al.* 2007). The Cronbach's alpha for this method reaches a value of 0.95 in our research.

Childhood Trauma Questionnaire (CTQ-SF)

The questionnaire measures the severity of maltreatment-related ACEs and contains 28 items rated on a 5-point Likert scale. It focuses on emotional, physical, and sexual abuse and neglect. The internal consistency of the factors is high (Bernstein *et al.* 2003), and the test-retest reliability after three months is 0.80 (Adams, 2007). Both the original (Bernstein & Fink 1998) and the Czech version (Kaščáková *et al.* 2018) show a good level of psychometric properties.

Statistics

Each patient in the study completed a test battery at predetermined time intervals (whole battery at the beginning of the treatment, BAI and BDI-II every week, and whole battery at the end). The head psychiatrist recorded objective CGI weekly after consulting with the attending psychiatrist.

Data were recorded in an Excel spreadsheet and analyzed using SPSS version 24.0, G*Power 3, and Prism programs. Means and standard deviations were calculated using descriptive statistics. We verified the normality of the data with the Shapiro-Wilk W test. For comparisons of multiple groups, we used one-way ANOVA with Bonferroni post hoc test or Kruskal-Wallis test with Dunn's post hoc test. Comparisons between two groups were performed using unpaired t-tests or Mann-Whitney U tests, and comparisons for repeated measures datasets were performed using paired t-tests or Wilcoxon tests.

Correlations between variables were evaluated using Pearson or Spearman correlation coefficients. Relative change during therapy was assessed for CGI, BDI-II, BAI, DES, and DES-T (difference between baseline and end-of-stay scores divided by baseline score). The significance level was set at 0.05.

Ethics

Patients were fully informed about the nature of the research and could decide to participate voluntarily. They could withdraw at any time without giving a reason. The Ethics Committee of the University Hospital Olomouc approved the project on 14 October 2014 (decision no. 108/14).

The ethical principles were stated in the information letter for patients. Instructions for completion, ethical rules, and informed consent were part of the test battery (Ferjenčík 2000). Patients had the right to be informed at any time during the research.

RESULTS

The results of the patients who completed the treatment program are reported in the therapeutic effectiveness part of the study. Changes in symptom severity and their relationship to demographic factors, baseline scores on depression, anxiety, dissociation symptom scales, and ACEs were analyzed. The goal was to determine how these factors influence treatment effectiveness.

Results of the therapeutic effectiveness part of the study for the entire group

Characteristics of patients who completed the study

Three hundred forty-nine patients completed the study out of 357 who entered the study. The mean age of the patients was 33.33 ± 11.59 years, with a mean age of onset of 21.82 ± 11.18 years and a mean duration of the disorder of 11.13 ± 10.14 years. The following table shows the mean pre- and post-treatment values in the scales and questionnaires, which were used to assess the effectiveness of the treatment and the correlation of the baseline data with the treatment effectiveness (Table 1). The table also contains a statistical evaluation of the differences between pre-and post-treatment means. Data on ACEs (CTQ-SF) were collected only at the beginning of the treatment.

Tab. 1. Patients who completed the study – pre- and post-treatment means of the analyzed variables

Variable	Average at baseline	Average at the end	Statistics
CGI	4.37 ± 1.40	3.85 ± 1.32	WS test: W = 12170; p <0.0001
BAI	24.75 ± 13.42	21.34 ± 13.65	WS test: W = 17800; p <0.0001
BDI-II	28.20 ± 12.96	23.33 ± 15.24	paired t-test: t = 7.799 df = 347; p < 0.0001
DES	19.54 ± 17.70	18.54 ± 17.82	WS test: W = 6162; p < 0.05
DES-T	13.88 ± 16.00	13.71 ± 17.41	WS test: W = 3838; ns
Total CTQ-SF score	50.81 ± 18.58		
Emotional abuse	12.29 ± 5.67		
Physical abuse	7.97 ± 4.46		
Sexual abuse	6.62 ± 4.01		
Emotional neglect	15.21 ± 5.33		
Physical neglect	8.81 ± 3.94		
Antidepressant Index	40.5 ± 25.1 (n = 301)	38.8 ± 23.6 (n = 300)	
Antipsychotic index	2.0 ± 2.1 (n = 80)	2.0 ± 1.9 (n = 78)	
Anxiolytic index	12.3 ± 10.6 (n = 19)	13.4 ± 11.9 (n = 8)	
Antiepileptic index	145.4 ± 110.9 (n = 40)	145.6 ± 91.2 (n = 42)	

WS test = Wilcoxon signed rank test;

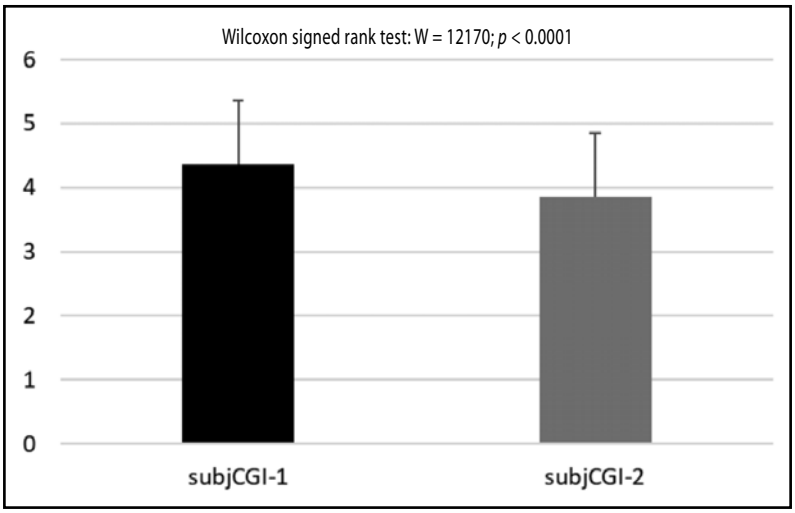

Fig. 1. Pre- and post-treatment mean CGI score in patients who completed treatment

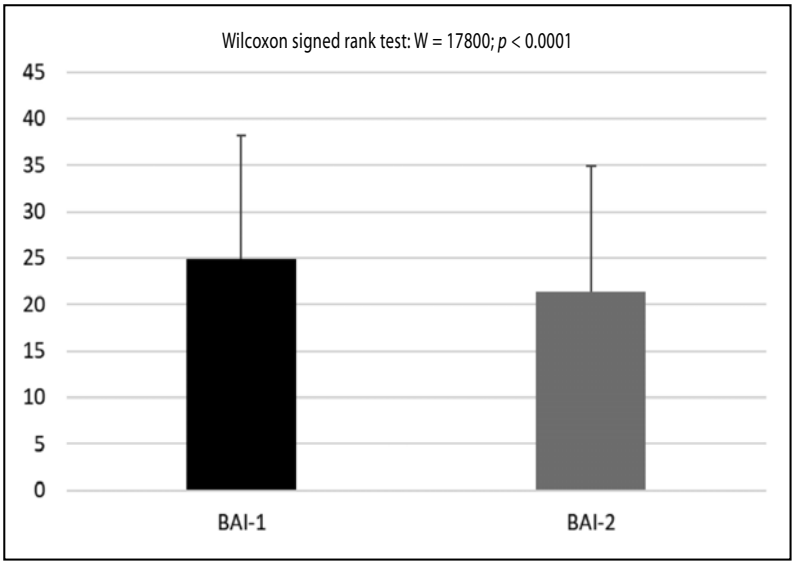

Fig. 2. Pre- and post-treatment mean BAI in patients who completed treatment

Tab. 2. Correlation coefficients of the relationship of demographic variables to the change in clinical variables during treatment

Variable	Relative change in scores throughout treatment		
	CGI	BAI	BDI-II
Age	0.03	0.04	0.04
Onset of disorder	0.06	0.02	0.07
Duration of disorder	0.01	0.09	0.11

The mean score on the CGI rating scale, which assesses the overall severity of the disorder, showed a statistically significant decrease (Table 1, Figure 1). This decrease indicates a significant reduction in the overall disorder severity.

Similarly, there was a significant decrease in mean BAI scores, which assesses anxiety symptoms severity during treatment (Table 1 and Figure 2).

A statistically significant decrease in the BDI-II questionnaire, which measures the severity of depressive symptoms, was also observed (Table 1, Figure 3).

A statistically significant decrease was also noted in the severity of dissociation (as assessed by the DES questionnaire). However, there was no significant decrease in the severity of pathological dissociation (DES-T) (Table 1).

Relationship of demographic variables to changes in clinical variables during treatment

None of the demographic variables (age, onset of disorder, duration of disorder) correlated significantly with the mean relative changes in symptom severity (as assessed by CGI, BAI, and BDI-II) (see Table 2).

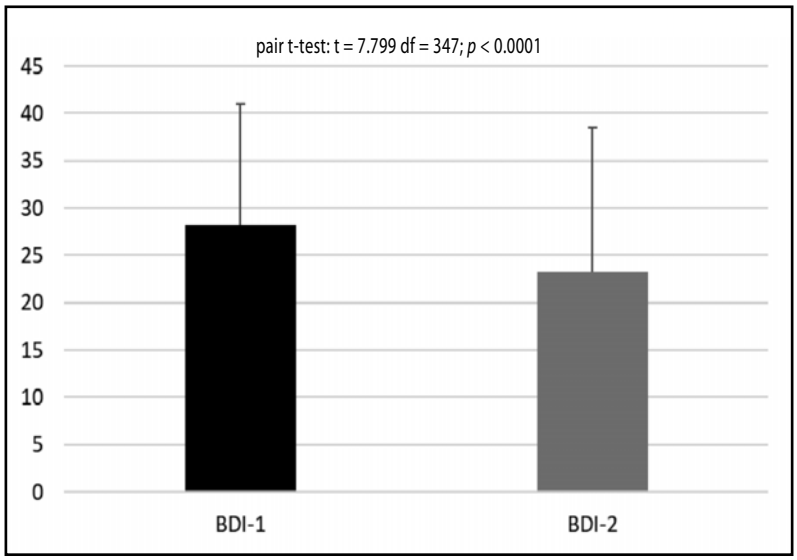

Fig. 3. Pre- and post-treatment mean BDI-II in patients who completed treatment

Tab. 3. Correlation coefficients of the relationship between baseline clinical variables and their change during treatment

Score at baseline	Relative change in scores throughout treatment		
	CGI	BAI	BDI-II
CGI	0.41 ···	0.08	-0.04
BAI	0.08	0.28 ···	-0.08
BDI-II	0.05	0.04	0.13 ·

Relationship of baseline clinical variables to their change during treatment

The relative change in rating scales during treatment showed a statistically significant positive correlation with the initial scores on the same scale (Table 3).

Relationship of ACEs to changes in clinical variables during treatment

The change in assessment scales used during treatment did not correlate with the total CTQ-SF score or individual subscores (Table 4).

Relationship of dissociation to changes in clinical variables during treatment

Relative change in clinical variables during treatment showed a statistically significant negative correlation with baseline DES scale total dissociation score but not pathologic dissociation as assessed by the DES-T subscale (Table 8). The magnitude of change in DES and DES-T during treatment was statistically significantly positively correlated with the relative change in the CGI (Table 5).

A statistically significant positive correlation was found between the relative change in anxiety (as measured by the BAI) and the relative change in the DES and DES-T scores (Table 5). A similar relationship was found with the relative change in the BDI-II, which was also significantly positively correlated with the relative change in the DES and DES-T scores (Table 5).

To test the hypotheses formulated before the study began, correlations were calculated between the baseline DES scores and the relative changes in the CGI, BAI, and BDI-II scores, with the following results:

- (4a) Baseline DES score was statistically significantly negatively correlated with the relative change in CGI during treatment (Spearman r = -0.1238; $p < 0.05$), i.e. the higher the dissociation score, the smaller the change during therapy
- (4b) Baseline pathological dissociation score (DES-T) did not correlate significantly with the relative change in CGI during treatment (Spearman r = -0.09545; ns).
- (4c) Baseline DES score did not correlate significantly with the relative change in anxiety during treatment (measured by the BAI) (Spearman r = -0.05647; ns).
- (4e) Baseline dissociation severity (measured by the DES) did not correlate significantly with the relative change in depressive symptoms (as measured by the BDI-II) (Spearman r = -0.05994; ns).
- (4d) Baseline pathological dissociation score (DES-T) did not correlate significantly with the relative change in anxiety symptoms during treatment (measured by the BAI) (Spearman r = -0.04442; ns).
- (4f) Baseline pathological dissociation score (DES-T) did not correlate significantly with the relative change in depressive symptoms (measured by the BDI-II) (Spearman r = -0.02002; ns).

Tab. 4. Correlation of early adverse events and changes in clinical variables during treatment

Variable	Relative change in scores throughout treatment		
	CGI	BAI	BDI-II
Total CTQ-SF score	-0.04	-0.01	-0.05
Emotional abuse	-0.04	-0.02	-0.02
Physical abuse	-0.03	-0.01	-0.04
Sexual abuse	0.04	-0.06	-0.09
Emotional neglect	0.04	-0.01	-0.01
Physical neglect	0.01	0.01	-0.01

Tab. 5. Correlation of dissociation and pathological dissociation with change in clinical variables during treatment

Variable	Relative change in scores throughout treatment		
	CGI	BAI	BDI-II
DES	-0.12 ·	-0.06	-0.06
DES-T	-0.10	-0.04	-0.02
Relative change DES	0.23 ···	0.31 ···	0.34 ···
Relative change DES-T	0.22 ···	0.18 ··	0.27 ···

Results of the therapeutic effectiveness part of the study when divided into diagnosis-specific subgroups

The following results were observed when the therapeutic efficacy portion was divided into diagnosis-specific subgroups.

Pre- and post-treatment mean scores in clinical scales in diagnosis-specific subgroups

The mean scores on the assessment scales, including their standard deviations at baseline and the end of treatment, divided into diagnosis-specific subgroups, are shown in Table 6. The mean scores are compared between groups using multiple comparison tests (one-way ANOVA or Kruskal-Wallis test for non-parametric distribution). Furthermore, the mean scores are compared at baseline and the end of the study within each group using paired t-tests or Wilcoxon rank sum test for non-parametric distribution.

CGI

In the assessment of the overall severity of the disorder (CGI), it was shown that the groups did not differ statistically significantly at the beginning, although it was at the margin of statistical significance (Kruskal-Wallis test: KW = 11.2; ns, $p = 0.051$). However, at the treatment's end, the groups differed statistically significantly (Kruskal-Wallis test: KW = 20.13; $p < 0.005$). Looking at the individual diagnosis-specific subgroups, a statistically significant decrease in mean CGI scores was observed in patients with PD, OCD and BPD. Of the comorbid groups, a significant change occurred only in patients with comorbid OCD/BPD (Table 6, Figure 4).

To address the hypotheses formulated before the study began, separate groups of patients were compared using relative changes in the CGI, with the following conclusions:

- (1a) When comparing the relative change in CGI scores between the individual groups of patients with OCD and PD or BPD, there was no statistically significant difference (Kruskal-Wallis test: Kruskal-Wallis statistic 3.187; ns).
- (1b) No statistically significant difference was made when comparing the relative change in CGI scores between patients with PD and patients with BPD (Mann-Whitney test: Mann-Whitney U=4348; ns).

BAI

In the assessment of the overall severity of anxiety (BAI), it was shown that the groups differed significantly in the mean score at baseline (one-way ANOVA: F = 2.326; df = 354; $p < 0.05$). Statistically significant differences were also noted at the end of the study (one-way ANOVA: F = 2.558; df = 346; $p < 0.05$). Looking at the individual diagnosis-specific subgroups, statistically significant decreases in mean scores occurred during treatment in patients with PD, OCD, and BPD. However, there was no statistically significant improvement in mean BAI scores in the comorbidity groups (Table 6, Figure 5).

To address the hypotheses that were formulated before the study began, separate groups of patients were compared using relative changes in BAI with the following conclusions:

- (2a) There was no statistically significant difference in the relative change in the general anxiety score

Tab. 6. Average scores on assessment scales when divided into diagnostic subgroups – before and after treatment

VARIABLE	PD	OCD	BPD	PD+HPO BPD	PD+OCD	OCD+BPD	STATISTIC
CGI–1	4.4 ± 1.1	4.5 ± 1.5	4.2 ± 1.4	4.4 ± 1.0	4.9 ± 1.6	5.0 ± 1.3	Kruskal-Wallis test: KW = 11.2; ns (p = 0.051)
CGI-2	3.7 ± 1.4	4.1 ± 1.4	3.7 ± 1.2	4.0 ± 1.2	4.4 ± 1.0	4.6 ± 1.0	Kruskal-Wallis test: KW = 20.13: ***p* < 0.005**
statistic	WS: W = 622: ***p* < 0.0005**	PT: t = 2.223 df = 52; ***p* < 0.05**	WS: W = 2195 ***p* < 0.0001**	WS: W = 107; ns	PT:: t = 0.8911 df = 6; ns	WS: W = 126: ***p* < 0.05**	
BAI-1	27.1 ± 13.2	21.1 ± 12.4	24.3 ± 12.4	27.3 ± 13.7	29.1 ± 16.5	28.3 ± 13.2	one-way ANOVA: F = 2.326 df = 354; ***p* < 0.05**
BAI-2	20.7 ± 12.7	17.7 ± 13.5	21.5 ± 13.9	24.6 ± 14.1	21.3 ± 6.5	27.4 ± 12.3	one-way ANOVA: F = 2.558 df = 346; ***p* < 0.05**
Statistic	PT: t = 3.697 df = 691; ***p* < 0.0005**	PT: t = 3.027 df = 51; ***p* < 0.005**	PT: t=2.805 df = 146; ***p* < 0.01**	PT: t = 1.142 df = 35; ns	PT: t = 0.9586 df = 7; ns	PT: t = 0.5188 df = 31; ns	
BDI-II-1	22.4 ± 10.8	23.1 ± 12.5	32.5 ± 11.9	29.7 ± 11.7	24.6 ± 8.5	33.2 ± 12.0	one-way ANOVA: F = 11.14 df = 354; ***p* < 0.0001**
BDI-II-2	17.4 ± 11.0	20.3 ± 15.1	26.8 ± 16.0	22.3 ± 14.3	21.9 ± 9.5	29.9 + 14.9	one-way ANOVA: F = 5.779 df = 344; ***p* < 0.0001**
statistic	PT: t = 3.627 df = 68; ***p* < 0.0005**	PT: t = 2.008 df = 53; ***p* < 0.05**	PT: t = 5.371 df = 146; ***p* < 0.0001**	PT: t = 3.897 df = 35; ***p* < 0.0005**	PT: t = 0.7086 df = 7; ns	PT: t = 1.995 df = 30; ns (*p* = 0.055)	

Abbreviations: BAI = Beck Anxiety Inventory; BDI-II = Beck Depressive Inventory, second edition; CGI = Clinical Global Impression-Severity; PT = pair t-test; KW= Kruskal-Wallis test; PT=pair t-test, df – degrees of freedom

between patients with PD and patients with OCD (unpaired t-test: t = 0.05154; df = 120; ns).
- (2b) Comparing the relative decrease in anxiety symptoms on the BAI showed no statistically significant difference between patients with PD and patients with BPD (unpaired t-test: t = 0.9282; df = 215; ns).

BDI-II

In the assessment of the overall severity of depressive symptoms using the BDI-II questionnaire, it was shown that the groups differed statistically significantly in the mean score at baseline (one-way ANOVA: F = 11.14; df = 354; $p < 0.0001$). Statistically significant differences were also noted at the end of the study (one-way ANOVA: F = 5.779; df = 344; $p < 0.0001$). Looking at the individual diagnosis-specific subgroups, statistically significant decreases in mean scores occurred during treatment in patients with PD, OCD, BPD, and comorbid PD/BPD (Table 6 and Figure 6). There was no statistically significant change in mean BDI-II scores during treatment in patients with comorbid PD/OCD nor in patients with comorbid OCD/BPD.

To address the hypotheses that were formulated before the study began, separate groups of patients were compared using relative changes in the BDI-II with the following conclusions:
- (3a) Patients with PD did not show a greater improvement in the overall severity of depressive symptoms as assessed by the relative change in the BDI-II compared to patients with OCD (unpaired t-test: t = 0.6070; df = 118; ns).
- (3b) The relative change in the severity of depressive symptoms in patients with PD did not differ significantly from the change in patients with BPD (unpaired t-test: t = 0.1846; df = 212; ns).
- (3c) Relative change in the severity of depressive symptoms in patients with BPD did not show a higher rate of improvement compared to patients with OCD (unpaired t-test: t = 0.9380; df = 198; ns).

Dissociation and therapeutic change in diagnosis-specific subgroups

The mean scores for dissociation and pathological dissociation and their standard deviations at baseline and at the end of treatment when divided into diagnosis-specific subgroups are presented in the following table (Table 7).

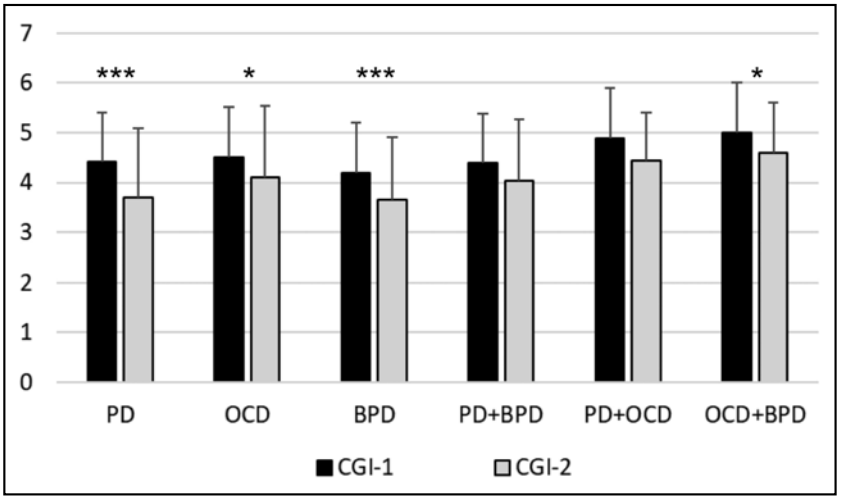

Fig. 4. Pre- and post-treatment CGI in the diagnosis-specific subgroups
Abbreviations:
* paired t-test: $p < 0.05$; *** paired t-test: $p < 0.001$

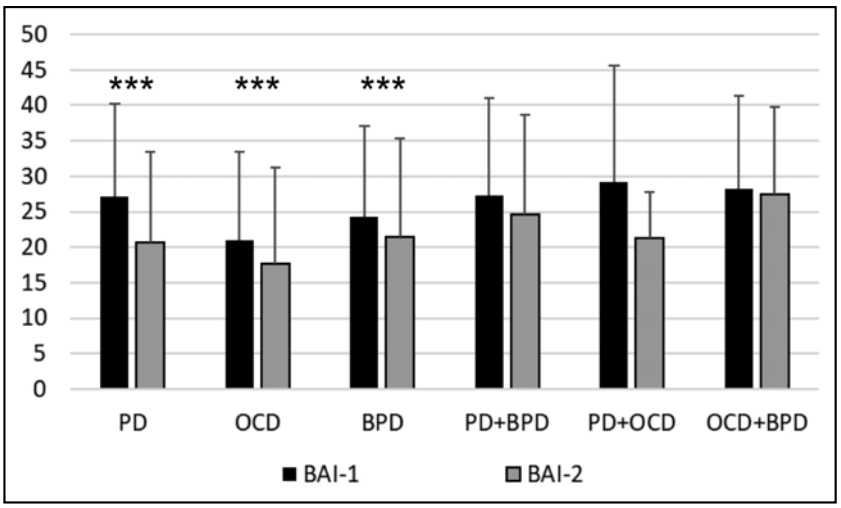

Fig. 5. Pre- and post-treatment BAI scores in the diagnosis-specific subgroups
Abbreviations:
*** paired t-test: $p < 0.001$

DES

In assessing the severity of dissociation, it was shown that the groups differed statistically significantly in the mean score at the beginning (Kruskal-Wallis test: KW = 31.2; $p < 0.0001$). Similarly, they showed statistically significant differences between themselves at the end of the study (Kruskal-Wallis test: KW = 25.95; $p < 0.0001$) (Table 7). When looking at the individual diagnosis-specific subgroups, no statistically significant change in the average scores during treatment was observed.

DES-T

In assessing the severity of pathological dissociation using the DES-T, it was shown that the groups differed statistically significantly in the mean score at the beginning (Kruskal-Wallis test: KW = 26.13; $p < 0.0001$). Similarly, they showed statistically significant differences between themselves at the end of the study (Kruskal-Wallis test: KW = 22.48; $p < 0.0005$) (Table 7). Looking at the individual diagnosis-specific subgroups, there was no statistically significant change in the mean scores during treatment.

ACEs and therapeutic change

Correlation analysis of maltreatment-related ACEs (as measured by the CTQ-SF) showed the following results:

- (5a) The total CTQ-SF score did not correlate significantly with the improvement in the overall severity of the disorder (CGI) during treatment (Spearman r = -0.04472; ns).
- (5b) The total CTQ-SF score did not correlate significantly with decreased general anxiety symptoms (BAI) (Spearman r = -0.01022; ns).
- (5c) The total CTQ-SF score did not correlate significantly with decreased depressive symptoms (BDI-II) (Spearman r = -0.05004; ns).

DISCUSSION

Our study aimed to examine how adverse childhood experiences, dissociation, and comorbidity influence the effectiveness of a six-week combined CBT and pharmacotherapy in patients with treatment-resistant PD, OCD, and BPD. The average scale scores significantly decreased across all measurements, indicating

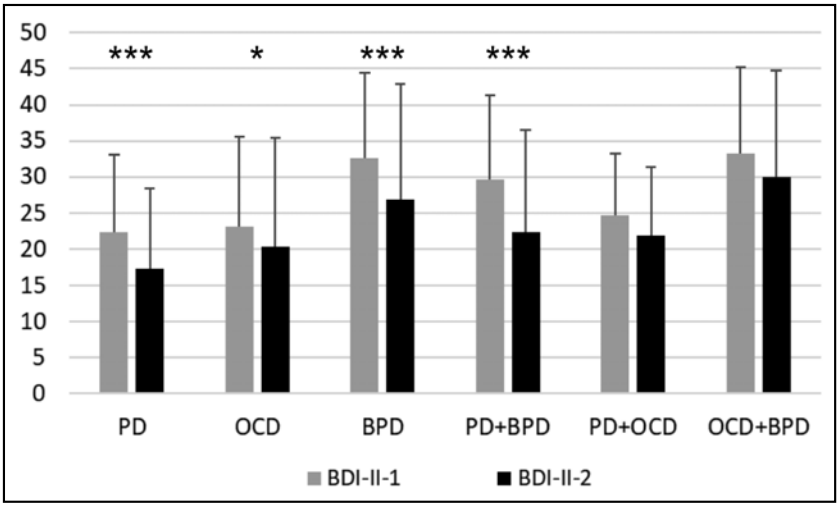

Fig. 6. Pre- and post-treatment BDI-II scores in the diagnosis-specific subgroups
Abbreviations:
* paired t-test: $p < 0.05$; *** paired t-test: $p < 0.001$

a positive treatment effect. Similar effectiveness has been demonstrated in studies by other authors focusing on PD (Otto *et al.* 1999; Heldt *et al.* 2003; Craske *et al.* 2005; Furukawa *et al.* 2006; Heldt *et al.* 2006; Roy-Byrne *et al.* 2006; Simon *et al.* 2009; Rodrigues *et al.* 2011) and in our previous research on patients with anxiety or neurotic spectrum disorders, OCD, and BPD (Prasko *et al.* 2005; Prasko *et al.* 2015; Prasko *et al.* 2016; Ociskova *et al.* 2016; Ociskova *et al.* 2018; Kolek *et al.* 2019; Hodny *et al.* 2022).

The novelty of this study lies in comparing therapeutic efficacy across diagnosis-specific subgroups of patients with PD, OCD, and BPD, as well as comparing associations between ACEs and dissociation in these disorders. Such a comparison has not been published in the available literature.

The results of our study provide valuable insights into the efficacy of treatment in patients with PD, OCD, and BPD.

Severity of depressive and anxiety symptoms

Our analysis showed that treatment led to a significant decrease in the severity of depressive symptoms and anxiety symptoms in patients with PD, OCD, and BPD. This decrease was not statistically significant in patients with comorbid disorders, suggesting that the presence of multiple diagnoses may affect treatment efficacy. This outcome is consistent with earlier studies showing that comorbidity can complicate treatment and require specific therapeutic approaches (Kolek *et al.* 2019; Hodny *et al.* 2022).

However, as for the comparison between selected conditions, patients did not significantly differ in presented depressive or anxious experiences. This may serve as a solid reminder that diagnosis itself does not define the patient as a whole, and less diagnosis-specific treatment (CBT group therapy combined with pharmacotherapy in this case) might

Tab. 7. Pre- and post-treatment mean DES and DES-T scores in the diagnosis-specific subgroups

VARIABLE	PD	OCD	BPD	PD+BPD	PD+OCD	OCD+BPD	STATISTIC
DES-1	14.6 ± 15.7	11.8 ± 11.9	21.4 ± 16.0	24.0 ± 19.9	27.6 ± 28.0	26.9 ± 23.0	Kruskal-Wallis test: KW = 31.2; **$p < 0.0001$**
DES-2	13.7 ± 14.4	11.4 ± 14.1	21.4 ± 18.4	20.6 ± 17.8	13.0 ± 6.2	26.0 ± 22.8	Kruskal-Wallis test: KW = 25.95; **$p < 0.0001$**
STATISTIC	WS: W = 151: ns	WS: W = 243: ns	WS: W = 243: ns	PT: t = 0.5544 df = 33; ns	PT: t = 1.158 df = 25; ns	PT: t = 1.536 df = 26; ns	
DES-T-1	10.8 ± 15.4	7.4 ± 10.3	15.3 ± 15.5	18.4 ± 15.6	11.6 ± 4.9	19.2 ± 20.8	Kruskal-Wallis test: KW = 26.13; **$p < 0.0001$**
DES-T-2	9.8 ± 14.8	7.7 ± 13.4	15.6 ± 17.8	17.7 ± 16.9	10.7 ± 10.7	21.7 ± 23.7	Kruskal-Wallis test: KW = 22.48; **$p < 0.0005$**
STATISTIC	WS: W = 151: ns	WS: W = 76: ns	WS: W = 235: ns	PT: t = 1.436 df = 33; ns	PT: t = 0.2720 df = 26; ns	WS: W = 17: ns	

be effective when super-specialized treatment is unavailable.

Dissociation

The results showed that the severity of dissociation differed statistically significantly between groups at baseline and at the end of treatment. However, there was no statistically significant change in mean scores across diagnosis-specific subgroups during treatment. That may suggest dissociative symptoms are less responsive to standard treatment approaches and require specialized interventions (Ociskova *et al.* 2018; Kolek *et al.* 2019). On the other hand, the relative decrease in the severity of the dissociative symptoms was strongly associated with a reduction in both general anxiety and depression symptoms as well as with the reduction of the general severity of the disorder. That corresponds with the result of our previous study (Praško *et al.* 2016). Also, higher dissociation could indeed predict poorer treatment results, as suggested in the introduction and previous findings.

Adverse childhood experiences

Correlation analysis did not determine a statistically significant association between the total score of maltreatment-related ACEs (as measured by CTQ-SF) and improvement in overall severity of disorder, anxiety symptoms or depressive symptoms during treatment. This result suggests that while ACEs may play a role in the development of psychiatric disorders, they may not directly influence short-term treatment efficacy (Hodny *et al.* 2022).

Answers to hypotheses

(1) Rate of improvement in overall severity of the disorder

Hypothesis 1a: Patients with PD show a higher rate of improvement in the overall severity of the disorder than patients with OCD.

This hypothesis was not confirmed in the study. Patients with PD and OCD did not differ significantly in the relative rate of improvement during treatment.

Hypothesis 1b: Patients with PD show a higher rate of improvement in the overall severity of the disorder than patients with BPD.

This hypothesis was not confirmed. There was no statistically significant difference between the relative change in patients with PD and patients with BPD.

Hypothesis 1c: The rate of improvement in the overall severity of the disorder does not differ between patients with BPD and patients with OCD.

This hypothesis was confirmed. The relative change in the overall severity of the disorder did not differ statistically significantly between these groups.

(2) Rate of improvement in general anxiety

Hypothesis 2a: Patients with PD show a greater improvement in general anxiety than patients with OCD.

This hypothesis was not confirmed, as there was no significant difference in the relative change in the severity of anxiety symptoms.

Hypothesis 2b: Patients with PD show a greater improvement in general anxiety than patients with BPD.

This hypothesis was not confirmed in this study, as the comparison of the relative decrease in anxiety in patients with PD and patients with BPD did not show a significant difference.

Hypothesis 2c: The improvement in general anxiety is not significantly different in patients with OCD and BPD.

This hypothesis was confirmed. The relative change in general anxiety is not statistically significantly different between the group of patients with OCD and the group with BPD.

(3) Rate of improvement in depression symptoms

Hypothesis 3a: Patients with PD show a greater rate of improvement in the overall severity of depressive symptoms than patients with OCD.

This hypothesis was not confirmed, as the relative improvement rate was not statistically significantly different between patients with PD and OCD.

Hypothesis 3b: Patients with PD show a greater rate of improvement in the overall severity of depressive symptoms than patients with BPD.

This hypothesis was not confirmed, as the relative change in the BDI-II was not statistically significantly different between the groups of patients with PD and those with BPD.

Hypothesis 3c: Patients with BPD show a greater rate of improvement in the overall severity of depressive symptoms than patients with OCD.

This hypothesis was not confirmed. The relative change in depressive symptom scores was not statistically significantly different between the BPD group and the OCD group.

(4) Predictor of improvement – dissociation

Hypothesis 4a: Severity of dissociation is a significant predictor of improvement in overall disorder severity during treatment.

This hypothesis was confirmed. In the entire group of patients, the score on the DES questionnaire at the beginning of treatment was statistically significantly negatively correlated with the relative change in CGI during treatment.

Hypothesis 4b: Severity of pathological dissociation significantly predicts improvement in overall disorder severity during treatment.

This hypothesis was not confirmed. No correlation was found between the baseline pathological dissociation score and the relative change in the overall severity of the disorder during treatment.

Hypothesis 4c: Severity of dissociation is a significant predictor of improvement in anxiety symptoms severity.

This hypothesis was not confirmed. The baseline severity of dissociation in the DES did not correlate significantly with the relative change in anxiety symptomatology.

Hypothesis 4d: Severity of pathological dissociation is a significant predictor of improvement in anxiety symptoms severity.

This hypothesis was not confirmed. The severity of pathological dissociation was not significantly correlated with the change in the severity of anxiety symptoms.

Hypothesis 4e: Severity of dissociation is a significant predictor of improvement in depressive symptoms severity.

This hypothesis was not confirmed because the severity of dissociation at the beginning of treatment was not significantly correlated with the relative change in the severity of depressive symptoms.

Hypothesis 4f: Severity of pathological dissociation is a significant predictor of improvement in depressive symptoms severity.

This hypothesis was not confirmed. The baseline pathological dissociation score was not correlated with the change in the severity of depressive symptoms.

(5) Predictor of improvement – adverse childhood experiences

Hypothesis 5a: Total CTQ-SF score is significantly negatively correlated with relative improvement in the overall disorder severity.

This hypothesis was not confirmed. The total score of maltreatment-related ACEs assessed using the CTQ-SF questionnaire did not correlate significantly with a relative improvement in the overall severity of the disorder assessed using the CGI.

Hypothesis 5b: Total CTQ-SF score is significantly negatively correlated with a relative improvement in anxiety symptoms.

This hypothesis was not confirmed. The total score of maltreatment-related ACEs assessed using the CTQ-SF did not correlate significantly with a decrease in general anxiety symptoms assessed using the BAI.

Hypothesis 5c: Total CTQ-SF score is significantly negatively correlated with relative improvement in depressive symptoms.

This hypothesis was not confirmed. The total score of maltreatment-related ACEs assessed using the CTQ-SF did not correlate significantly with a decrease in depressive symptoms in the BDI-II.

Study limitations

It is important to mention several limitations of this study. First, the sample size and its distribution into different diagnostic subgroups may have affected the statistical power of the analyses. Second, the use of self-report questionnaires may be influenced by subjective factors such as social desirability or the momentary mood of the respondents. The study also lacks a power analysis to confirm whether our sample is representative.

Future research should include larger, more diverse samples and combine self-report questionnaires with objective measures. Another point of interest is a long-term follow-up to establish whether the treatment interventions last over a longer period.

CONCLUSIONS

This study offers significant insights into the effectiveness of combined CBT and pharmacotherapy in patients with treatment-resistant PD, OCD and BPD. Our findings underscore the importance of particular factors when addressing treatment resistance in these patients, such as comorbidities and higher dissociative symptoms). The observed reductions in symptom severity suggest that even short-term intensive treatment can be beneficial in reducing anxiety and depressive symptoms across different diagnostic groups. However, the variations in therapeutic outcomes across diagnoses indicate that specific attention should be given to dissociative processes, which appear to influence treatment responses. Our results on ACEs influencing short-term treatment outcomes were not conclusive. Still, given the association between dissociation, ACEs and treatment outcomes, we suggest further research on this topic is necessary.

These results open pathways for future research to explore the underlying mechanisms that impact treatment effectiveness, especially with comorbid disorders and dissociation. Developing targeted therapeutic interventions that account for these factors could enhance treatment outcomes and provide more effective relief for patients with complex presentations.

DISCLOSURE

The authors have no conflict of interest. We have read the journal's position on ethical publications and confirm that this text is under the guidelines.

REFERENCES

1 Adams T (2007). The effects of childhood trauma on adult perception and worldview. Nova Southeastern University.
2 Ball S, Robinson A, Shekhar A, Walsh K (1997). Dissociative symptoms in panic disorder. J Nerv Ment Dis. **185**: 755–760.
3 Belli H. (2014). Dissociative symptoms and dissociative disorders comorbidity in obsessive compulsive disorder: Symptom screening, diagnostic tools and reflections on treatment. World journal of clinical cases. **2**(8): 327–331.
4 Bernstein DP, Fink L (1998). Childhood Trauma Questionnaire: A retrospective self-report: Manual. Harcourt Brace & Company.
5 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.
6 Craske MG, Golinelli D, Stein MB, Roy-Byrne P, Bystritsky A, Sherbourne C (2005). Does the addition of cognitive behavioral therapy improve panic disorder treatment outcome relative to medication alone in the primary-care setting? Psychological Medicine. **35**(11): 1645–1654.
7 De Ayala RJ, Vonderharr-Carlson DJ, Kim D (2005). Assessing the reliability of the Beck Anxiety Inventory scores. Educ Psychol Meas. **65**(5): 742–756.
8 Ferjenčík J (2000). Psychodiagnostika dospělých. Praha: Portál.
9 Frischholz EJ, Braun BG, Sachs RG, Hopkins L, Shaeffer DM, Lewis J, Leavitt F, Pasquotto MA, Schwartz DR (1990). The Dissociative Experiences Scale: further replication and validation. Dissociation. **3**(3): 151–153.
10 Furukawa TA, Watanabe N, Churchill R (2006). Psychotherapy plus antidepressant for panic disorder with or without agoraphobia: systematic review. The British Journal of Psychiatry. **188**(4): 305–312.
11 Gulsun M, Doruk A, Uzun O, Turkbay T, Ozsahin A (2007). A comparative study on dissociative experiences of patients with panic disorder and generalized anxiety disorder. Comprehensive Psychiatry. **48**(2): 158–163.
12 Guy W (1976). ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: US Department of Health, Education, and Welfare Public Health Service Alcohol, Drug Abuse, and Mental Health Administration.
13 Heldt E, Manfro GG, Kipper L, Blaya C, Isolan L, Otto MW (2006). One-year follow-up of pharmacotherapy-resistant patients with panic disorder treated with cognitive-behavior therapy: outcome and predictors of remission. Behaviour Research and Therapy. **44**(5): 657–665.
14 Heldt E, Manfro GG, Kipper L, Blaya C, Maltz S, Isolan L, ... & Otto MW (2003). Treating medication-resistant panic disorder: predictors and outcome of cognitive-behavior therapy in a Brazilian public hospital. Psychotherapy and psychosomatics. **72**(1): 43–48.
15 Hodny F, Ociskova M, Prasko J, Vanek J, Visnovsky J, Sollar T, Slepecky M, Nesnídal V, Kolek A (2022). 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. Neuro Endocrinol Lett. **43**(6): 345–358.
16 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.
17 Kaščáková N, Fürstová J, Šolcová IP, Bieščad M, Hašto J, Tavel P (2018). Psychometrická Analýza Českej Verzie Dotazníka Trauma Z Dětství (CTQ) so Sociodemografickými Rozdielmi v Traumatizácii Dospelých Obyvateľov Českej Republiky. Československa Psychologie. **62**(3): 212–230.
18 Kolek A, Prasko J, Ociskova M, Holubova M, Vanek J, Grambal A, Slepecky M (2019). Severity of panic disorder, adverse events in childhood, dissociation, self-stigma and comorbid personality disorders Part 2: Therapeutic effectiveness of a combined cognitive behavioural therapy and pharmacotherapy in treatment-resistant inpatients. Neuro Endocrinol Lett. **40**(6): 271–283.
19 Krause-Utz A, Frost R, Chatzaki E, Winter D, Schmahl C, Elzinga BM (2021). Dissociation in Borderline Personality Disorder: Recent Experimental, Neurobiological Studies, and Implications for Future Research and Treatment. Curr Psychiatry Rep. **23**(6): 37.
20 Krause-Utz A (2022). Dissociation, trauma, and borderline personality disorder. Borderline Personal Disord Emot Dysregul. **9**(1): 14.
21 Michelson L, Mavissakalian M, Marchione K (1998). Cognitive-behavioral and pharmacological treatments of social phobia: A controlled study. Arch Gen Psychiatry. **55**(12): 1133–1141.
22 Nock MK, Borges G, Bromet EJ, Alonso J, Angermeyer M, Beautrais A, Bruffaerts R, Chiu WT, de Girolamo G, Gluzman S, de Graaf R, Gureje O, Haro JM, Huang Y, Karam E, Kessler RC, Lepine JP, Levinson D, Medina-Mora ME, Ono Y, Posada-Villa J, Williams D (2008). Cross-national prevalence and risk factors for suicidal ideation, plans and attempts. Br J Psychiatry. **192**(2): 98–105.
23 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.
24 Ociskova M, Prasko J, Latalova K, Kamaradova D, Grambal A (2016). Psychological factors and treatment effectiveness in resistant anxiety disorders in highly comorbid inpatients. Neuropsychiatric Disease and Treatment. **12**: 1539–1551.
25 Ociskova M, Prasko J, Vrbova K, Kasalova P, Holubova M, Grambal A, Machu K (2018). Self-stigma and treatment effectiveness in patients with anxiety disorders - a mediation analysis. Neuropsychiatr Dis Treat. **14**: 383–392.
26 Otto MW, Pollack MH, Penava SJ, Zucker BG (1999). Group cognitive-behavior therapy for patients failing to respond to pharmacotherapy for panic disorder: a clinical case series. Behav Res Ther. **37**(8): 763–770.
27 Prasko J, Grambal A, Kasalova P, Kamaradova D, Ociskova M, Holubova M, Vrbova K, Sigmundova Z, Latalova K, Slepecky M, Zatkova M (2016). Impact of dissociation on treatment of depressive and anxiety spectrum disorders with and without personality Disorders. Neuropsychiatric Disease and Treatment. **12**: 2659–2676.
28 Prasko J, Houbova P, Novak T, Zalesky R, Espa-Cervena K, Paskova B, Vyskocilova J (2005). Influence of personality disorder on the treatment of panic disorder--comparison study. Neuro Endocrinol Lett. **26**(6): 667–674.
29 Prasko J, Kamaradova D, Cakirpaloglu S, Talova B, Diveky T, Grambal A, Jelenova D, Kovacsova A, Latalova K, Ociskova M, Sedlackova Z, Sigmundova Z, Silhan P, Vrbova K, Zapletalova J (2015). Predicting the therapeutic response to intensive psychotherapeutic programs in patients with neurotic spectrum disorders. Act Nerv Super Rediviva. **57**(1–2): 30–39.
30 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.
31 Ptacek R, Bob P, Paclt I, Pavlat J, Jasova D, Zvolsky P, Raboch J. (2007). Psychobiology of dissociation and its clinical assessment. Neuroendocrinology letters. **28**(2): 191–198.
32 Ptáček R, Raboch J, Vňuková M, Hlinka J, Anders M (2016). Beckova škála deprese (BDI-II) – standardizace a využití v praxi. Čes a slov Psychiat. **112**(6): 270–274.
33 Rodrigues H, Figueira I, Gonçalves R, Mendlowicz M, Macedo T, Ventura P (2011). CBT for pharmacotherapy non-remitters--a systematic review of a next-step strategy. J Affect Disord. **129**(1–3): 219–228.
34 Roy-Byrne PP, Craske MG, Stein MB (2006). Panic disorder. Lancet. **16**;368(9540): 1023–1032.
35 Segui J, Marquez M, Garcia L, Canet J, Salvador-Carulla L, Ortiz M (2000). Depersonalization in panic disorder: a clinical study. Compr Psychiat. **41**: 172–178.
36 Semiz UB, Inanc L, Bezgin CH (2014). Are trauma and dissociation related to treatment resistance in patients with obsessive–compulsive disorder? Social psychiatry and psychiatric epidemiology, **49**: 1287–1296.

37 Simon NM, Otto MW, Worthington JJ, Hoge EA, Thompson EH, Lebeau RT, Moshier SJ, Zalta AK, Pollack MH (2009). Next-step strategies for panic disorder refractory to initial pharmacotherapy: a 3-phase randomized clinical trial. J Clin Psychiatry. **70**(11): 1563–1570.
38 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**: 682–687.
39 Waller NG, Ross CA. (1997). The prevalence and biometric structure of pathological dissociation in the general population: Taxometric and behavior genetic findings. Journal of Abnormal Psychology. **106**(4): 499–510.
40 Watson S, Chilton R, Fairchild H, Whewell P (2006). Association between childhood trauma and dissociation among patients with borderline personality disorder. Aust N Z J Psychiatry. **40**(5): 478–481.
41 World Health Organization (2018). International classification of diseases for mortality and morbidity statistics (11th Revision). WHO.
42 Zaider TI, Heimberg RG, Fresco DM, Schneier FR, Liebowitz MR (2003). Evaluation of the clinical global impression scale among individuals with social anxiety disorder. Psychol Med. **33**(4): 611–622.
43 Zhang J, Wiecaszek P, Sami S, Meiser-Stedman R (2023). Association between panic disorder and childhood adversities: a systematic review and meta-analysis. Psychol Med. **53**(6): 2585–2595.