Neuroendocrinology Letters Volume 36 No. 4 2015
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

Psychosocial aspects of resistance in complex treatment of depressive disorder

Zuzana Sedlackova [1], Jan Prasko [2], Klara Latalova [2], Dana Kamaradova [2], Marie Ociskova [1], Ales Grambal [2], Zuzana Sigmundova [2], Petra Kasalova [2], Snezana Cakirpaloglu [2]

1 Department of Psychology, Faculty of Arts, Palacky University Olomouc, Czech Republic
2 Department of Psychiatry, Faculty of Medicine and Dentistry, Palacky University Olomouc, University Hospital Olomouc, Olomouc, Czech Republic

Correspondence to: Zuzana Sedlackova
Department of Psychology, Faculty of Arts
Palacky University Olomouc, Czech Republic.
e-mail: sedlackovaa.zuzana@gmail.com

Submitted: 2015-02-20 *Accepted: 2015-03-18* *Published online: 2015-09-28*

Key words: **depressive disorder; therapy; resistance; psychosocial factors**

Neuroendocrinol Lett 2015; **36**(4):354–362 **PMID:** 26454491 NEL360415A08

Abstract

OBJECTIVE: Treatment of major depressive disorder can be affected by a broad range of factors. In our study, we focused on the relationships of demographic, psychological, clinical and social factors to the course of treatment of depression.
METHOD: The study included 151 patients (finally 140 patients were evaluated) hospitalized for major depressive disorder. They were assessed for demographic characteristics, the rates of depression and anxiety, quality of life, the rates of dissociation and insomnia, and subjective and objective disease severity at different times during treatment. Patients were treated with standard doses of antidepressants or other psychiatric medication. They also completed a 6-week long daily cognitive-behavioural therapy. Data were statistically analyzed.
RESULTS: There were significant decreases in the overall severity of the disorder, anxiety level and depression rate during treatment. Improvement measured by objective Clinical Global Impression (oCGI-I) at the end of treatment was not significantly correlated with any of the measured parameters (age of patient, onset of illness, duration of disease, doses of medication etc.). It only significantly positively correlated with the initial evaluation of the patient by oCGI. However, the improvement in subjective assessment (using sCGI-I) correlated with many parameters (increased age, later onset of the disease, greater disease severity at baseline in both overall and subjective evaluation of the severity, anxiety and depressive symptomatology). Furthermore, it was negatively correlated with most quality of life parameters, such as H (Home), F (Feelings), L (Leisure), Sr (Social relations) and G (General).
CONCLUSIONS: The results suggest that individual variables, such as the degree of psychopathology, particularly depression and anxiety, most quality of life parameters, higher patient age and age of disorder onset may be associated with poorer subjective response to complex treatment of patients with major depressive disorder.

INTRODUCTION

Every disease needs to be perceived multifactorial, i.e., in the biological, social and psychological ways (Engel 1977). Risk factors contributing to the resistance to the treatment of depressive disorder can be divided into several categories: clinical (e.g. psychotic features, comorbid panic disorder) biological (e.g genetic polymorphisms for Brain Derived Neurotrophic Factor (BDNF) and psychosocial (e.g. weak social support). Ppossible psychosocial causes of resistance are often neglected. In connection with depression, we can mention a number of psychosocial factors that may contribute to the onset of depressive disorder or worsen its course. Several psychosocial risk factors have been related to a poor response to antidepressant treatment (i.e. decrease of social support, poor social adjustment, adverse life events, substance abuse) (Bennabi *et al.* 2015). Higher rate of depressive symptoms might occur in women (Low & Hubley 2007), in populations over 65 years in comparison with general population (Honzak 1999), in individuals with lower education, with subjective feeling of poverty etc. (Rodkjaer *et al.* 2009). Personality dysfunction is associated with impaired short-term response to antidepressant treatment in major depression. Depressive individuals with comorbid personality disorder, for example, commit more suicidal attempts or have a worse reaction to antidepressants treatment in comparison with individuals with depression alone (Sato *et al.* 1994).

The apparent detrimental effect of prior depression episodes on treatment response may be accounted for by pre-existing personality dysfunction (Gorwood *et al.* 2010). Higher rates of neuroticism, harm avoidance, or lower levels of self-directedness and extraversion are associated with a worse course of depressive disorder (Celikel *et al.* 2009; Grace & O´Brien 2003). Treatment-resistant patients with unipolar depression demonstrated low scores for reward dependence and cooperativeness, using the Temperament and Character Inventory (TCI) (Takahashi *et al.* 2013).

The development of depressive disorder may be partly induced by the occurrence of a traumatic event, especially if there are multiple events (Dulin & Passmore 2010). Higher occurrence of depressive symptoms is evident in certain psychiatric disorders, such as post-traumatic stress disorder or schizophrenia, panic disorder, social phobia and agoraphobia spectrum disorders (Bousoño *et al.* 2011; Goenjian *et al.* 2011). However, it is mainly the high rate of comorbid personality disorders (Corruble *et al.* 1996) which may significantly affect the overall course of depression.

Tab. 1. Criteria for participation in the study.

Inclusion criteria	Exclusion criteria
ICD-10 diagnostic criteria for depressive disorder confirmed by two independent specialists	Organic mental disorder
Age 18–75 years	Psychotic disorder – actual/in anamnesis
Signed informed consent	Substance abuse
	Dissocial personality disorder

AIM

The aim of our study was to identify whether certain demographic, social, clinical or psychological factors are associated with the effectiveness of overall psychotherapeutic and pharmacological treatment of pharmaco-resistant patients with depressive disorder. We assumed that both the greater change in depressive symptoms (decrease of depressive scores) and the likelihood of achieving clinical remission in the overall assessment of the patient will be connected with:

- *Demographic factors*: younger patient age, shorter duration of illness, its later onset.
- *Clinical factors:* lower disease severity, lower rates of depression and anxiety, better sleep quality, lower rate of dissociation at start of treatment, absence of certain comorbidities (psychiatric, esp. personality disorder, somatic).
- *Social factors*: higher quality of life especially in the family, but also within the other social relations and in employment, marital status, higher education, employment and no pension.

METHODS

Selection of patients for the study

All patients included in our study were examined by a psychiatrist at the start of their hospitalization, and were diagnosed with major depressive disorder by criteria of International Classification of Disorders – 10 Revision (ICD-10) (1996). Severity of depression was evaluated by the Clinical Global Impression (CGI) scale. The diagnosis of depression by ICD-10 was confirmed by other two psychiatrists. All the criteria for inclusion in the study are shown in Table 1. At the beginning of therapy patients completed the following self-evaluation scales: Beck Depression Inventory – (BDI), Beck Anxiety Inventory – (BAI), demographic characteristics, Quality of Life Enjoyment and Satisfaction – (Q-LES-Q), Dissociative Experiences Scale – (DES), and Sleep Questionaire. During treatment, every week the patients filled self-assessment questionnaires measuring depression (BDI) and anxiety (BAI). At the end of treatment, depression (BDI), anxiety (BAI) and depression severity (CGI) were evaluated.

Brief description of assessment methods

BAI (Beck *et al.* 1988) scale consists of 21 items with a four-point Likert scale, in which an individual evaluates symptoms of anxiety he had suffered in the last week, and the extent of discomfort associated with them.

BDI (Beck *et al.* 1996) scale consists of 21 items, in which an individual identifies one of the four options that the best describes his/her depressive symptoms. This scale was standardized in the Czech Republic by Preiss and Vacíř (1999). Changes in BDI scores between the start and the end of treatment were the second major method for evaluation of the condition of patients.

CGI (Guy 1976) is a useful diagnostic tool to measure the severity of psychopathology. Objective CGI is an assessment of the state of the patient by a psychiatrist. It was used as the principal method for the assessment of change in patient's condition at the end of treatment. The scores 1 or 2 were the criteria for remission at the end of treatment. The subjective version of CGI is assessed by the patient using the scale 1–7. Each degree of the scale represents a particular level of severity of illness.

Sleep Questionnaire (Morin 2003**)** is used for the evaluation of seven major sleep problems with a five-point Likert scale (1=strongly disagree, 2=disagree, 3=neutral, 4=agree and 5=strongly agree). Total score of the patient reflects the severity of sleep disorder. The questionnaire was translated and edited, but it had not been yet standardized in Czech Republic (Prasko *et al.* 2004; Machalkova & Miksova 2013).

Q-LES-Q (Endicott *et al.* 1993) – questionnaires completed by patient alone or psychiatrist can assist him/her. It consists of 93 questions organized into eight domains with five point Likert answer scale. Domains focused on physical health/activities, feelings, leisure time activities, social relations and overall level of satisfaction in life are completed by every patient. Domains about work, household duties, and school/course work are filled just by patients who deal with these topics (Mülerová *et al.* 2001).

DES (Bernstein & Putman 1986) – scale describes 28 experiences and the patient marks how often he/she had such an experience, on a 10 cm long segment. It evaluates also the degree of pathological dissociation using the Dissociative Experience Scale Taxon (DES-T), which is the result of only 8 of the 28 questionnaire items(questions 3, 5, 7, 8, 12, 13, 22 and 27). DES-T assesses depersonalization, derealization, identity alteration and anamnestic quality of pathological dissociation (Waller & Ross 1996).The questionnaire was translated into Czech by Ptacek *et al.* (2007).

Statistics and ethics

The results of diagnostic methods were statistically evaluated using statistical programs Prism (GraphPad PRISM version 5.0; http://www.graphpad.com/prism/prism.htm), SPSS 17.0 (2008), and G * Power 3.1 (Faul *et al.* 2003). Averages, standard deviations and types of distributions of quantitative demographic and clinical data were calculated. Repeated measures analysis of variance (ANOVA) and correction for repeated measurements (Bonferroni correction) were used as appropriate. Paired t-tests were used for statistical comparison of changes in mean values using initial and last assessments (LOCF-last observation carried forward). Fisher exact test or chi-square test was used for evaluation of the relationship between alternative variables (gender, employment, marital status, comorbidity with other disorders including personality disorders). A 5% level of statistical significance was adopted for all statistical tests. The study was approved by the local ethics committee. The research was conducted in accordance with the latest version of the Helsinki Declaration and Recommendations for Good Clinical Practice (EMEA 2002). Patients signed informed consent.

Treatment

Patients were treated with usual doses of antidepressants. Medication of patients at the start of treatment mostly remained the same as those recommended by their outpatient psychiatrists. Doses of benzodiazepines were reduced, and doses of antidepressants were increased in patients who received subnormal doses. The average doses of medication are in Table 1.

Patients participated in daily group therapy in the CBT program lasting six weeks (30 two-hour meetings). CBT program consisted of psychoeducation, planning, cognitive restructuring activities, exposure therapy (in comorbid OCD with response prevention), working with cognitive schemas and problem-solving strategy. The work was supervised once per week by experienced therapists. The program was completed by practicing communication, ergotherapy, and sports.

RESULTS

Sample description

The study included 151 depressed patients (99 women, 52 men) who were hospitalized for moderately severe depressive episode in period from 1st January 2010 to 31st December 2014. Depressive disorder was diagnosed in 16.69% of patients from the total of 905 of patients hospitalized during this period. These patients were hospitalized at the psychotherapeutic department because of depressive episodes that were pharmaco- resistant to outpatient psychiatric treatment. The patients were referred for systematic psychotherapeutic intervention by their outpatient psychiatrists. During the study period, 140 patients with a depressive episode completed at least three weeks of therapy. Eleven patients ended their participation in the study after the first two weeks, so their scale results were not included in statistical analyses (6 patients refused to fill out questionnaires, 3 felt improved so asked for early release from hospital and 2 were transferred to a department without psychotherapy because they did not want to continue in psychotherapy). The complete sample and the subset of patients who finished at least

three weeks of therapy are described in Table 2. Patients, who were excluded from the study, did not significantly differ in basic demographic and clinical characteristics of those retained for the evaluation the of treatment effectiveness.

Results of treatment

In further analyzes, data from patients who completed at least three weeks of treatment were used. During the treatment, there was a significant decrease in overall severity of the disorder (subjectively and objectively) as well as in self-assessment scales of anxiety and depression (Table 3, Figure 1).

The improvement of CGI-I, our primary criterion for evaluation, was not significantly associated with demographic factors, such as higher age, onset of illness, duration of the disease, nor with subjectively evaluated severity of the disorder at baseline (assessed

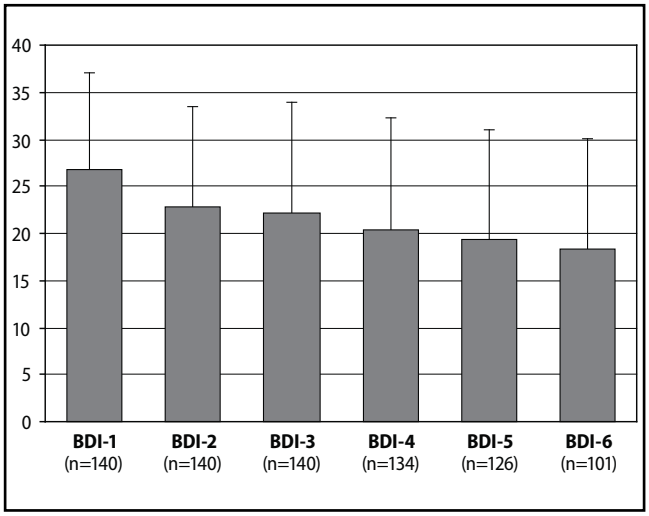

Fig. 1. BDI during treatment. One-way analysis of variance: F= 9.212 df=773; $p<0.0001$.

Tab. 2. Demographic and clinical data of the whole sample of patients and patients who finished at least three weeks of treatment.

Variables	Whole sample (n=151)	Patients who finished at least three weeks of treatment (n=140)
Age	44.52±11.76	44.17±11.76
Gender (M: F)	62:99	50:90
Family psychiatric burden (yes: no)	72:79	68:72
Length of disease	8.33±8.47	8.46±8.56
Age of illness onset	36.17±14.38	35.68±14.35
Education: vocational training / secondary school / university	15:43:59:34	13:41:56:30
Employed / unemployed	86:65	79:61
No pension / pension	112:39	105:35
Marital status: single / married / divorced / widowed	39:69:34:9	36:63:32:9
Objective CGI – severity	4.52±1.18	4.39±1.10
Subjective CGI – severity	4.40±1.38	4.32±1.38
Antidepressants: average dose adjusted to a daily dose of paroxetine	49.56±26.84 (n=133)	48.84±24.85 (n=123)
Anxiolytics: average dose adjusted to a daily dose of diazepam	10.08±7.50 (n=40)	16.27±12.33 (n=35)
Antipsychotics: average dose adjusted to a daily dose of risperidone	1.47±1.18 (n=67)	1.69±1.31 (n=53)
No psychiatric comorbidity: psychiatric comorbidity	97:54	89:51
Without personality disorder: with personality disorder	122:29	112:28
No somatic comorbidity: somatic comorbidity	135:16	124:16

Tab. 3. The average scores in assessment scales at the start (BAI-1, BDI-1, oCG1-1, sCGI-1) and end of treatment (BAI-L, BDI-L, oCG1-L, sCGI-L).

	BAI-1	BAI-L	BDI-1	BDI-L	oCGI-1	oCGI-L	sCGI-1	sCGI-L
Patients who completed at least three weeks of treatment	22.63±12.41	18.13±13.23	26.98±10.25	18.77±12.09	4.39±1.10	2.76±1.36	4.32±1.38	2.98±1.22
Paired t-test	t=4.924 df=138; ***p*<0.0001**		t=10.58 df=138; ***p*<0.0001**				t=9.970 df=138; ***p*<0.0001**	
Mann-Whitney test					Mann-Whitney U=3743; ***p*<0.0001**			

by sCGI, BAI and BDI), with doses of medication, severity of insomnia, any of the evaluated quality of life parameters (evaluated with Q-LES-Q) and the degree of dissociation (assessed with DES). It was significantly positively correlated only with oCGI severity at baseline (Table 4).

However, the improvement in subjective assessment (by sCGI-I) correlated with many parameters (increased age, later onset of the disease, greater disease severity at baseline in both overall and subjective evaluation of the severity, anxiety and depressive symptomatology).Furthermore, it was negatively correlated with most quality of life parameters, such as H (Home), F (Feelings), L (Leisure), Sr (Social relations) and G (General).Subjectively perceived overall improvement was not related to disease duration, doses of medication, severity of sleep disorders at baseline, sub scores of Q-LES-Q W (Work), Ph (Physical Health), nor with the degree of dissociation at baseline (Table 4).

A secondary criterion of improvement was a decrease in depression in the subjective scale BDI. The findings were mostly similar to those associated with the primary criterion, except the correlation with subjCGI at baseline and with BAI at baseline. Unlike the primary criterion of the improvement in severity of depression, the BDI was significantly related to a subscore of Q-LES-Q work (W) (Table 4).

There were no statistically significant differences in average declines of oCGI and BDI during treatment depending on gender, education, employment, pension, psychiatric comorbidity, particularly personality disorder or severe somatic comorbidity (Table 5).However, there was a significantly greater decrease in BDI in single patients compared to those who were married. This difference was not found for changes in oCGI.

When dividing the patients into three groups (achieved remission, slightly improved, unimproved) it was found out that the unimproved group had a significantly higher severity of illness (objective and subjective), anxiety, and depression at baseline and an overall higher age in comparison with the other two groups. However, the groups did not differ in the rate of dissociation, comorbid psychiatric/somatic disorders, comorbid personality disorder or doses of medica-

Tab. 4. The correlation ofCGI-I and BDI changes with demographic and clinical data.

Variables	oCGI-I		sCGI-I		BDI 1 – BDI last	
	Correlation coefficient (Spearman)	Statistical significance	Correlation coefficient (Spearman)	Statistical significance	Correlation coefficient (Spearman)	Statistical significance
Age	–0.0159	n.s.	0.2100	***p*<0.05**	–0.2078	***p*<0.05**
Age of disease onset	–0.0856	n.s.	0.1811	***p*<0.05**	–0.2452	***p*<0.005**
Length of disease	0.0700	n.s.	0.0865	n.s.	0.1045	n.s.
Obj CGI 1 severity	0.2467	***p*<0.005**	0.4942	***p*<0.0001**	0.6999	***p*<0.0001**
Subj CGI 1 severity	0.0806	n.s.	0.3062	***p*<0.0005**	0.0358	n.s.
BAI 1	0.07377	n.s.	0.1969	***p*<0.05**	–0.0972	n.s.
BDI 1	0.1599	n.s. (*p*=0.063)	0.2714	***p*<0.005**	0.2271	***p*<0.01**
Index of antidepressants	–0.0029	n.s.	0.1533	n.s.	0.0450	n.s.
Index of anxiolytics	0.242	n.s.	–0.14	n.s.	0.2035	n.s.
Index of antipsychotics	0.2433	n.s.	–0.0688	n.s.	0.2125	n.s.
Scale of severity of insomnia	0.07866	n.s.	0.0879	n.s.	–0.0496	n.s.
Q-les.Q - Ph	–0.0588	n.s.	–0.151	n.s.(*p*=0.078)	–0.0995	n.s.
Q-les-Q - H	0.01991	n.s.	–0.2133	***p*<0.05**	0.0510	n.s.
Q-les-Q - W	–0.2551	n.s. (*p*=0.0512)	0.0433	n.s.	–0.3242	***p*<0.05**
Q-les-Q-F	–0.05156	n.s.	–0.2258	***p*<0.01**	–0.0374	n.s.
Q-les-Q-L	–0.1680	n.s. (*p*=0.0514)	–0.0906	***p*<0.05**	–0.1186	n.s.
Q-les-Q-Sr	0.0541	n.s.	–0.2219	***p*<0.05**	0.0332	n.s.
Q-les-Q-G	–0.1288	n.s.	–0.1853	***p*<0.05**	–0.1030	n.s.
DES	0.0922	n.s.	0.1139	n.s.	–0.0070	n.s.
DEST	0.1128	n.s.	0.1442	n.s.	–0.0327	n.s.

Tab. 5. The average values of changes in oCGI a BDI between start and end of treatment by qualitative demographic parameters and comorbidities.

Variables	oCGI-1 – oCGI-L		BDI-1 – BDI-L	
	AVERAGE VALUES	STATISTICAL SIGNIFICANCE	AVERAGE VALUES	STATISTICAL SIGNIFICANCE
Male (n=50)	1.66±1.15	Mann-Whitney test;	9.72±9.67	Unpaired t-test;
Female (n=90)	1.61±1.15	MW U=2191; n.s.	7.06±8.53	t=1.688 df=138; n.s.
Primary education (n=13)	1.62±1.93	Kruskal-Wallis test;	9.69±10.44	One way ANOVA;
Vocational (n=41)	1.46±1.14	KW statistics=0.6687; n.s.	5.83±7.72	F=1.299 df=139; n.s.
Secondary (n= 56)	1.71±1.20		8.36±9.88	
University (n= 30)	1.79±1.06		9.60±7.84	
Employed (n=79)	1.54±1.04	Mann-Whitney test;	7.28±7.57	Unpaired t-test;
Unemployed (n=37)	1.74±1.28	MW U=2210; n.s.	8.95±10.58	t=1.090 df=138; n.s.
No pension (n=105)	1.52±1.06	Mann-Whitney test;	7.46±8.58	Unpaired t-test;
Pension (n=35)	1.94±1.35	MW U=1520; n.s.	9.66±10.14	t=1.254 df=138; n.s.
Single (n=36)	2.00±1.15	Kruskal-Wallis test;	12.19±11.47	One way ANOVA;
Married (n=63)	1.44±1.03	KW statistics=6.107; n.s.	6.68±6.71	F=3.790 df=139; ***p<0.05***
Divorced (n=32)	1.66±1.29		6.72±8.97	
Widowed (n=9)	1.33±1.23		5.11±8.05	
No psychiatric comorbidity (n=89)	1.52±1.04	Mann-Whitney test;	7.53±8.08	Unpaired t-test;
Psychiatric comorbidity (n=51)	1.82±1.31	MW U=2024; n.s.	8.84±10.47	t=0.8302 df=138; n.s.
No personality disorder (n=112)	1.59±1.10	Mann-Whitney test;	7.69±8.34	Unpaired t-test;
With personality disorder (n=28)	1.79±1.32	MW U=1432; n.s.	9.29±11.39	t=0.8387 df=138; n.s.
No somatic comorbidity (n=124)	1.61±1.13	Mann-Whitney test;	7.63±8.86	Unpaired t-test;
Somatic comorbidity (n=16)	1.81±1.33	MW U=929; n.s.	10.94±9.87	t=1.387 df=138; n.s.

tion (Table 6). There were also no differences between groups in gender, employment, education, pension, onset of disease or length of illness. Groups differ only in a rate of single individuals, which were significantly more in the group that achieved remission.

DISCUSSION

At the start of treatment, the mean BDI scores for depression were 26.98±10.25, which indicates moderate depression. Severity of anxiety with BAI at the start of treatment was yielding the average score of 22.63±12.41. This score indicates moderate anxiety disorder. It is not surprising because the diagnosis of another psychiatric disorder (mostly anxiety disorder, somatoform disorder, OCD, PTSD) was found out in many (Table 2). A rate of dissociation of patients with major depressive disorder in our study was similar to dissociation in patients with anxiety disorders (Ball *et al.* 1997). We measured dissociation by DES. The average score was 13.67±13.65. In the Czech population, a similar level of dissociation (12.8±13.5) was found in patients with obsessive-compulsive disorder (Raszka *et al.* 2009) and panic disorder (11.79±13.34) (Kamarádová *et al.* 2013). These average scores are very similar.

The response to therapy was defined in two different ways. The first includes achievement of clinical remission and evaluation of therapeutic improvement at the end of treatment assessed objectively by psychiatrist (obj CGI) and subjectively by the patient (sub CGI). The degree of improvement was also evaluated by a decrease in subjective rating scale BDI. According to the results clinical improvement achieved 69.3% of patients, but clinical remission at the end of treatment was reached only by 33.6% of patients. However, our patients were resistant to outpatient treatment, so this result is not surprising. The aim of our study was to determine whether clinical improvement and remission were associated with particular demographic, clinical and social factors.

Our assumptions were only partially proved. Regarding demographic factors we expected that younger patient age, shorter duration of illness and later onset of depression would be associated with better results in therapy. There is a probable relationship between age and treatment effect, which was evident in two (sub CGI, BDI) of three parameters (obj CGI, subj CGI, BDI) of improvement in treatment, which negatively correlated with age also when comparing patients according to remission (mean age of patients who got to remission was significantly lower than in patients who partly remitted or did not improve). The duration of disease did not correlate with improvement in any of the evaluated parameters, and the length of illness was practically the same in remitted and non-remitted patients. Our results concerning the duration of the

disorder are inconsistent with the findings of Pigott and Sean (1997) and Saxena *et al.* (2002), who found a correlation between poor therapeutic response and longer duration of disease. However, these studies were focused on patients with OCD while our research was about depressive patients. Another possible reason may be that most of our patients were recruited from individuals who were already resistant to pharmacological treatment in outpatient care.

Our *the prior* expectations regarding the effects of age of disease onset were not supported. Patients with later onset of illness had worse treatment outcomes than patients with earlier disease onset in two of the three parameters for evaluation of improvement (sub CGI-I and BDI 1-BDI last, but not obj CGI-I). Mean age of illness onset in remitted patients was numerically lower when compared to two other groups (slightly improved, not improved); the difference was not statistically significant.

When examining the relationship between severity of psychopathology at baseline and therapeutic effect we confirmed the relationship between lower rates of depression, anxiety and overall severity of disease at the beginning of therapy and positive therapeutic effect measured after 6 weeks of treatment. These findings were also further confirmed by correlation of the subjective improvement with initial scores of anxiety and depression. It was similar when sample was divided into groups based on the achievement of remission. Patients, who remitted, had the lowest scores at baseline in all assessment scales; the difference between the three outcome groups (remitters, slight improvers, non-improvers) was statistically significant. There were no significant differences in doses of medication between the three outcome groups.

Furthermore, we assumed that the rate of dissociation at baseline would negatively affect the therapeutic response. However, the dissociation rate did not correlate with changes in any of the evaluated parameters. Differences in the average scores of DES also did not differ in groups sorted by remission. On the other hand, there was a trend for higher dissociation in the group that did not improve at all. These results do not correspond with the findings of Rufer *et al.* (2005), and

Tab. 6. Comparison of demographic and clinical data of patients whom(1) get to remission, (2) have still mild symptoms of disorder and (3) do not improve or their condition worsening course/end of treatment.

	Remission (n=47)	Mild symptoms of the disorder (n=50)	Unimprovement or worsening of the condition(n=43)	Statistics
Age	39.89±13.78	45.42±9.97	47.07±9.91	One way ANOVA; F=5.013 df=139; ***p*<0.01**
Age of disease onset	31.63±15.93	37.50±12.58	38.00±13.83	One way ANOVA; F=2.915 df=139; n.s.
Length of disease	8.23±9.51	7.91±8.22	9.33±7.96	Kruskal-Wallis test; KW statistics =2.38; n.s.
ObjCGI 1 – severity	3.94±0.89	4.40±1.09	4.88±1.12	Kruskal-Wallis test; KW statistics = 15.36; ***p*<0.001**
SubjCGI 1 – severity	3.92±1.30	4.12±1.42	5.02±1.10	Kruskal-Wallis test; KW statistics=17.82; ***p*<0.0001**
BAI-1	19.76±11.32	21.42±11.74	26.55±13.25	one way ANOVA; F=3.702 df=134; ***p*<0.01**
BDI-1	23.23±8.43	26.38±10.96	31.14±10.19	one way ANOVA; F=7.176 df=134; ***p*<0.005**
DES	10.71±11.28	16.09±15.74	14.82±13.32	Kruskal-Wallis test; KW statistics=3.596; n.s.
DES-T	4.35+9.09	11.75±16.44	8.10±14.23	Kruskal-Wallis test; KW statistics=5.790; n.s.
Male: female	18:29	16:34	16:27	chi-square: n.s.
Education: B: V: S: U	6:8:17:16	5:18:21:6	2:15:18:8	chi-square: n.s.
Employed: unemployed	26:21	29:21	24:19	chi-square: n.s.
No pension: pension	36:11	37:13	32:11	chi-square: n.s.
Marital status S: M: D:W	21:15:9:2	8:24:15:3	7:24:8:4	chi-square: ***p*<0.05**
Antidepressants converted dose	45.09±25.96	48.15±22.54	53.25±26.08	one way ANOVA; F=1.095 df=122; n.s.
Anxiolytics converted dose	18.04±13.94	13.41±9.89	16.95±13.01	one way ANOVA; F=0.4401 df=34; n.s.
Antipsychotics converted dose	2.115±1.845	1.513±1.109	1.467±0.7923	one way ANOVA; F=1346 df=52; n.s.
No psychiatric comorbidity: with psychiatric comorbidity	28:19	34:16	27:16	chi-square: n.s.
No personality disorder: with personality disorder	36:11	41:9	35:8	chi-square: n.s.
No somatic comorbidity: with somatic comorbidity	43:4	42:8	39:4	chi-square: n.s.

Spitzer *et al.* (2007), who found worse effect of psychotherapy in patients with higher levels of dissociation.

Although more than two-thirds of patients suffered from comorbid psychiatric disorder, we discovered that psychiatric disorder or personality disorder comorbidity had no relationship with treatment response or state of remission. The same results were in the case of somatic comorbidity. Rate of patients with comorbid personality disorder (20.7%) was relatively high.

Despite our assumptions, the comorbidity with personality disorder was not associated with therapeutic response to treatment or remission. The average doses of antidepressants and antipsychotics were similar in both groups. In our previous study (Sedlackova *et al.* 2013) we found similar results: there were no significant differences in the course and results of treatment associated with the number and length of hospitalizations, doses of medication, the number of depressive episodes or comorbid personality disorder. Other studies found analogous results that comorbid personality disorder has no adverse effect on depression treatment (Blom *et al.* 2007; Kool *et al.* 2005; Maddux *et al.* 2009; Mulder *et al.* 2003; Russell *et al.* 2003).

However, there are also studies proving that comorbid personality disorder in depressive individual can lead to reduced efficacy of treatment of depression (Newton-Howes *et al.* 2006; Sato *et al.* 1994). This effect is more evident in case of comorbidity of depression with two or more personality disorders (Sato *et al.* 1994), which was proved in some studies by longer time for getting to remission in these individuals (Bagby *et al.* 2008; Levenson *et al.* 2012).These findings are not consistent with the studies of psychotherapeutic approaches. Levenson *et al.* (2012) studied depressive patients who were treated with interpersonal therapy. He found no differences in the results of treatment regarding presence of one comorbid personality disorder (except bipolar personality disorder). O'Leary and Costello (2001) found that comorbid personality disorder predicts a longer time for getting to remission during the acute treatment of depression, but in the 18 months follow up the presence of personality disorder was not a predictor of more frequent relapses.

Different findings regarding comorbid personality disorder may be due to varying evaluation methods (using different questionnaires, interviews), several types of treatment (only pharmacotherapy, or psychotherapy, various psychotherapeutic approaches or different hospital environment) and specifics of the patient (personality characteristics, coping strategies, voluntariness of hospitalization, rate of cooperation, pharmaco-resistance etc.).

We found also interesting results in the field of social factors. We assumed that patients with a higher quality of life, especially in the family or in a broader social relations and work, married individuals, with higher level of education, employed, would have better treatment results. However, most of our premises were not proved. Only higher quality of life measured at the beginning of treatment was associated with a higher rate of subjectively evaluated improvement in the course of treatment. It was correlated with all the factors except quality of life at work, which was, on the other hand, associated with lower severity of depression. It means that the more the patients felt satisfied at work, the lower his/her depressive scores were.

Conversely, one social factor was associated with exactly the opposite pattern than we expected. We observed that single patients had better treatment results than married ones. That was proved by a greater decrease of depression and a higher percentage of single people in the remission group compared with partly remitted/not improved groups. This finding is unexpected, but it is in accordance with the results of our other study about panic disorder (Kamaradova *et al.* 2013).

CONCLUSION

The results suggest that clinical variables, such as the lower severity of psychopathology, depression, and anxiety, lower age, or singleness may be associated with a worse response to complex treatment of patients with major depressive disorder. However, the results do not indicate that treatment of patients suffering from depression and comorbid psychiatric disorder, personality disorder or somatic disorder was less effective than in patients without any comorbidity.

REFERENCES

1 Bagby RM, Quilty LC, Segal ZV, *et al.* (2008). Personality and differential treatment response in major depression: a randomized controlled trial is comparing cognitive-behavioural therapy and pharmacotherapy. Can J Psychiatry. **53**(6): 361–370.
2 Ball S, Robinson A, Shekhar A, Walsh K (1997). Dissociative symptoms in panic disorder. J Nerv Ment Dis. **185**: 755–760.
3 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.
4 Beck AT, Steer RA, Ball R, Ranieri W (1996). Comparison of Beck Depression Inventories -I and -II in psychiatric outpatients. J Pers Assess. **67**(3): 588–597.
5 Bennabi D, Aouizerate B, El-Hage W, Doumy O, Moliere F, Courtet P, Nieto I, Bellivier F, Bubrovsky M, Vaiva G, Holztmann J, Bougerol T, *et al.* (2015). Risk factors for treatment resistance in unipolar depression: A systematic review. J Affect Disord. **171**:137–141.
6 Bernstein EM, Putnam FW (1986). Development, reliability, and validity of a dissociation scale. J Nerv Ment Dis. **174**(12): 727–735.
7 Blom MB, Spinhoven P, Hoffman T, *et al.* (2007). Severity and duration of depression, not personality factors, predict short-term outcome in the treatment of major depression. Journal of Affective Disord. **104**: 119–126.
8 Bousoño M, Galan J, Prieto E, Sanjuan J (2011). Depressive symptoms in patients with schizophrenia or schizoaffective disorder, prevalence, and the importance of subjective evaluation. 4D study. Eur Psychiat. **26**.
9 Celikel FC, Kose S, Cumurcu BE, Erkorkmaz U (2009). Cloninger's temperament and character dimensions of personality in patients with major depressive disorder. Compr Psychiatry. **50**: 556–561.

10 Corruble E, Ginestet D, Guelfi JD (1996). Comorbidity of personality disorders and unipolar major depression: a review. J Affect Disord. **37**: 157–170.
11 Dulin PL, Passmore T (2010). Avoidance of potentially traumatic stimuli mediates the relationship between accumulated lifetime trauma and late-life depression and anxiety. J Traumatic Stress. **23**(2): 296–299.
12 EMEA (2002). http://www.ema.europa.eu/pdfs/human/ich/013595en.pdf 20.3.2009
13 Endicott J, Nee J, Harrison W, Blumenthal R (1993). Quality of Life Enjoyment and Satisfaction Questionnaire: A New Measure. Psychopharmacology Bulletin. **29**: 321–326.
14 Engel GL (1977). The need for a new medical model: a challenge for biomedicine. Science. **196**: 129–136.
15 Faul F, Erdfelder E, Lang AG, Buchner A (2007). G*Power 3: A flexible statistical power analysis programs for the social, behavioral, and biomedical sciences.Behavior Research Methods. **39**:175–191.
16 Goenjian AK, Roussos A, Steinberg AM, SotiropoulouCh, Walling D, KakakiM, Karagianni S (2011). Longitudinal study of PTSD, depression, and quality of life among adolescents after the Parnitha earthquake. J Affect Disord. **133**(3): 509–515.
17 Gorwood P, Rouillon F, Even C, Falissard B, Corruble E, Moran P (2010). Treatment response in major depression: effects of personality. BJP. **196**: 139–142.
18 Grace J, O´Brien, JT (2003). Association of life events and psychosocial factors with early but not late-onset depression in the elderly: implications for possible differences in etiology. Int J Geriatr Psychiatry. **18**: 473–478.
19 Guy W (ed.) (1976). ECDEU Assessment manual for psychopharmacology. Rockville, U.S. DHEW.
20 Hansen PEB, Wang AG, Stage KB, Kragh-Sorensen P (2003). Comorbid personality disorder predicts suicide after major depression: a 10-year follow-up. Acta Psychiatr Scand. **107**: 436–440.
21 Honzak R (1999). Deprese. Praha; Galén.
22 Kamaradova D, Prasko J, Grambal A, Diveky T, Cerna M, Silhan P, *et al.* (2013). Prediktory terapeutické odpovědi pacientů s panickou poruchou identifikované pomocí demografických a klinických dat.Čes a slov Psychiat. **109**: 577–583.
23 Kool S, Schoevers R, de Maat S, *et al.* (2005). Efficacy of pharmacotherapy in depressed patients with and without personality disorders: a systematic review and meta-analysis. J Affect Disord. **88**(3): 269–278.
24 Levenson JC, Wallace ML, Fournier JC, *et al.* (2012). The role of personality pathology in depression treatment outcome with psychotherapy and pharmacotherapy. J Consult Clin Psychol. **80**(5): 719–729.
25 Low GD, Hubley AM (2007). Screening for depression after cardiac events using the Beck Depression Inventory-II and the Geriatric Depression Scale. Social Indicators Research. **82**(3): 527–543.
26 Machalkova L, Miksova Z (2013). Percepce únavy a hodnocení spánku v kontextu pracovního režimu všeobecných sester. Medicina pro praxi. **10**(8–9): 308–310.
27 Maddux RE, Riso LP, Klein DN, *et al.* (2009). Select comorbid personality disorders and the treatment of chronic depression with nefazodone, targeted psychotherapy, or their combination. J Affect Disord. **117**(3): 174–179.
28 Mezinárodní klasifikace nemocí – 10. revize (1996). MKN-10 (1. vydání); Maxdorf Praha.
29 Morin CM (2003). Measuring outcomes in randomized clinical trials of insomnia treatments. Sleep Med Rev. **7**: 263–279.
30 Mulder RT, Joyce PR, Luty SE (2003). The relationship of personality disorders to treatment outcome in depressed outpatients. J Clin Psychiatry. **64**(3): 259–264.
31 Müllerova H, Libigerova E, Prouzova M, Blazkova M, Krepela J, Matejkova P, Mrozek J (2001). Mezikultúrní přenos a validace dotazníku kvality života Q-LES-Q. Psychiatrie. **5**(2): 80–87.
32 Newton-Howes G, Tyrer P, Johnson T (2006). Personality disorder and the outcome of depression: meta-analysis of published studies. Br J Psychiatry. **188**: 13–20.
33 O'Leary D, Costello F (2001). Personality and outcome in depression: an 18-month prospective follow-up study. J Affect Disord. **63**(1–3): 67–78.
34 Pigott TA, Sean S (1997). Pharmacotherapy of obsessive-compulsive disorder. Int Rev Psychiatry. **9**: 133–147.
35 Prasko J, Espa-Cervena K, Zavesicka L. Nespavost, zvládání nespavosti. Praha: Portál 2004.
36 Preiss M, Vacíř K (1999). Beckova sebeposuzovací škála pro dospělé – BDI-II. Brno: Psychodiagnostika.
37 Ptacek R, Bob P, Paclt I, Pavlat J, Jasova D, Zvolsky P, Raboch J (2007). Psychobiology of dissociation and its clinical assessment. Neuroendocrinol Lett. **28**(2): 191–198.
38 Razska M, Prasko J, Koprivova J, Novak T, Adamcova K (2009). Psychological dissociation in obsessive-compulsive disorder is associated with anxiety level but not with severity of obsessive-compulsive symptoms. Neuroendocrinol Lett. **30**(5): 624–628.
39 Rodkjaer L, Laursen T, Balle N, Sodemann M (2009). Depression in patients with HIV is under-diagnosed: a cross-sectional study in Denmark. HIV Medicine. **11**: 46–53.
40 Rufer M, Held D, Cremer J, Fricke S, Moritz S, Peter H, Hand I (2006). Dissociation as a predictor of cognitive behavior therapy outcome in patients with obsessive-compulsive disorder. Psychother Psychosom. **75**: 40–46.
41 Russell JM, Kornstein SG, Shea MT, *et al.* (2003). Chronic depression and comorbid personality disorders: response to sertraline versus imipramine. J Clin Psychiatry. **64**(5): 554–561.
42 Sato T, Sakado K, Sato S, Morikawa T (1994). Cluster a personality disorder: a marker of worse treatment outcome of major depression? Psychiatry Res. **53**(2): 153–159.
43 Saxena S, Maidment KM, Vapnik T, Golden G, Rishwain T, Rosen RM, Tarlow G, Bystritsky A (2002). Obsessive-compulsive hoarding: symptom severity and response to multimodal treatment. J Clin Psychiatry. **63**: 21–27.
44 Sedlackova Z, Prasko J, Sedlacek M, Ociskova M, Latalova K, Kamaradova D (2013). Komorbidita depresivní poruchy a poruchy osobnosti – účinnost léčby.Čes a slov Psychiat. **109**(6): 577–583.
45 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): 682–627.
46 SPSS Inc. Released (2008). SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.
47 Takahashi M, Shirayama Y, Muneoka K, Suzuki M, Sato K, Hashimoto K (2013). Personality Traits as Risk Factors for Treatment-Resistant Depression. PLoS One. **8**(5): e63756.
48 Waller NG a 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.