

ORIGINAL ARTICLE

# Therapeutic response to complex cognitive-behavioral and pharmacological treatment in patients with social phobia

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## Abstract

**INTRODUCTION:** Many different approaches were created and used in the treatment of patients with social phobia, still, the pharmacoresistancy is an important problem. Exact predictors of the therapeutic response are not known yet. The aim of our study was to prove the efficacy of our treatment program and identify predictors of therapeutic response to complex pharmacotherapeutical and cognitive behavioral treatment in pharmacoresistant patients.

**METHODS:** We analyzed data for 50 probands diagnosed with social phobia hospitalized in the psychotherapeutical department of Department of Psychiatry, University Hospital Olomouc. We investigated basic demographic data (age, disease duration, age of onset), index of used antidepressant and scores of main rating scales (LSAS, CGI, BAI, BDI, DES a DES-T). We also evaluated an influence of personality disorders.

**RESULTS:** There was an statistically significant decrease in symptomatology in all rating scales during the treatment. Change in LSAS (ratio of initial to last measured score) positively correlated only with age of onset of the disorder. Level of dissociation measured by DES correlated with initial BAI score, in the case of DES-T with initial BAI and BDI. We proved statistically significant differences in the initial BAI score when splitting the group into responders and non-responders by final CGI. There was no statistically significant result if we concentrate on influence of personality disorders.

**CONCLUSIONS:** In our study we proved efficacy complex therapeutical program in the treatment of pharmacoresistant patients with social phobia.

## INTRODUCTION

Social phobia belongs to a group of anxiety disorders. It is characterized by fear and avoidance of situations in which a person can be observed and judged by others (Prasko & Lankova 2006). It is often a disorder with a chronic course (Kessler *et al* 2005). It is usually associated with decreased quality of life (Stein & Kean 2000; Safren *et al* 1996). The data concern the annual prevalence varies among different authors,

usually it is given between 6.8 to 13.3% (Kessler *et al* 1994; 2005). Although the representation of this disorder in the population is relatively high, a therapeutic approach that would cure all patients has not yet been developed. As well as in other psychiatric disorders, the problem of resistance to a treatment occurs.

In the case of treatment with psychiatric medication (standard is the use of SSRIs (Prasko *et al* 2008) approximately 50% of patients do not respond sufficiently to this treatment (Ameringen *et al* 2004).

Alternatively, the effective treatment option is use of cognitive behavioral therapy (Clark *et al* 2003, Kawaguchi *et al* 2013). However even that doesn't bring relief to all patients, the effect size of this treatment is 0.70 (Acarturk *et al* 2009). When treating patients with social phobia, we face the question whether will be the therapeutic approach effective in certain patient and thus which one to select. This choice could be facilitated by identification of predictors of successful response or of resistance to a treatment. There may be some demographic and clinical characteristics linked with the resistance to pharmacological treatment – the increased presence of anxiety and depressive symptoms prior to the treatment, the age, the age of onset of the disease and the presence of comorbid personality disorders (Ameringen *et al* 2004). Predictors of the response to therapy using both cognitive behavioral therapy and psychiatric medication were summarized in work of Mululo *et al* (2012). This article summarizes results of 24 studies. As predictors of response were identified the age of disease onset and severity of illness, presence of comorbid anxiety disorders and low expectations from therapy.

## OBJECTIVES

The aims of our study were to assess the effectiveness of a comprehensive treatment program – the combination of cognitive behavioral therapy (CBT) and antidepressant in patients resistant to psychopharmacs suffering from social phobia, and determine whether any demographic clinical patient's characteristics can predict the success or failure of treatment in a complex six-week therapeutic program, including both pharmacotherapy and daily group cognitive behavioral therapy.

## HYPOTHESES

1. Some demographic characteristics have influence on a response to the treatment in patients with social phobia:
  - The response to the complex treatment is related to patient's age, age of onset, duration of the disorder.
2. The treatment is affected by the following clinical features:
  - The severity of social phobia, the severity of anxiety symptoms, severity of depressive symptoms, comorbidity with personality disorder, the degree of dissociation.
3. The treatment is influenced by the dosage of psychopharmacs

## METHOD

The evaluation included patients suffering from generalized form of social phobia resistant to antidepressant treatment recommended to an intensive program

during hospitalization. The study enrolled outpatients who had been treated by recommended antidepressants in adequate doses within the previous year, who received the last antidepressant in adequate dosage at least for three months and because of the therapeutic resistance were accepted into a therapeutic program.

### Inclusion criteria:

- Age between 18 and 55
- Established diagnosis of social phobia using the ICD-10 classification
- Signed informed consent
- Resistance to treatment

### Exclusion criteria:

- The presence of depressive episode
- Drug addiction
- History of schizophrenia
- Mental retardation
- Endocrine disorders

The diagnosis of social phobia was determined by two independent psychiatrists according to ICD-10 (1996) before treatment. Several scales were used to assess clinical state. Overall psychopathology was assessed by using a CGI scale (Clinical Global Impression, Guy, 1976) at the beginning and end of the treatment. Also the scale for subjective evaluation of symptoms of depression BDI (Beck Depression Inventory, Beck *et al* 1996) and anxiety BAI (Beck Anxiety Inventory; Beck *et al* 1988; Beck & Steer 1993) were used at the beginning and at the end of the treatment. In addition, there were used questionnaires to assess the presence of dissociation: DES (Dissociative Experience Scale; Bernstein & Putman 1986) and LSAS (Liebowitz Social Anxiety Scale; Liebowitz *et al* 1987). The primary observed parameter of the response to the treatment was a 25% drop in the rating by LSAS. Remission was defined as the total score CGI-S score 1 or 2 at the end of the treatment.

### A brief description of used assessment scales:

LSAS (Liebowitz *et al* 1987) – Liebowitz Social Anxiety Scale consists of 24 items related to different social situations in which it is evaluated the measure of anxiety as well as degree of avoidance behavior.

BAI (Beck *et al* 1988; Beck & Steer 1993) – Beck Anxiety Inventory consists of 21 items with a four-point Likert scale, in which the proband marks out symptoms of anxiety experienced last week, and the degree of inconvenience the anxiety brings.

BDI (Beck *et al* 1996) – Beck Depression Inventory contains 21 items in which the individual indicates one of the four options that applies to him the best. The items are related to the characteristic features of depression such as sad mood, pessimism, or change of weight.

CGI (Guy 1976) – clinical global impression of severity of psychopathology. The source of evaluation is a comprehensive assessment of the patient by psychiatrist. In its subjective version (CGI-S) the patient

**Tab. 1.** Basic demographic and clinical data of the file.

	Age	Onset of disorder	Duration of disorder	Antidepressant index (n=46)	Anxiolytic index (n=9)
Average ± SD	29.96±11.68	20.64±12.05	9.56±10.00	30.00±17.76	0.42±0.49

SD – standard deviation

himself assesses the overall condition of the severity of symptoms on scale from 1 to 7. Each of the level of severity has it's own described characteristics.

DES (Bernstein & Putman 1986) – Dissociative Experience Scale is a questionnaire describing 28 kinds of experience, the patient marks how often this experience happens to him or her on the 10 cm line segment. The questionnaire was translated into czech in a comparable format (Ptacek *et al* 2007). We also evaluated the degree of pathological dissociation using the Dissociative Experience Scale Taxon (DES-T), which studies only 8 out of the 28 questionnaire items DES (questions 3, 5, 7, 8, 12, 13, 22 and 27), evaluating depersonalization, derealization, altering personal identity and quality of pathological dissociation (Waller & Ross 1996).

#### Treatment method

All the patients have undergone group CBT treatment while taking antidepressants, alternatively in combination with antipsychotics or anxiolytics. Drugs were used according to the recommended procedures for the treatment of social phobia (Praško *et al* 2008). Patients were treated with conventional doses of antidepressant medication, mainly with which they were recommended to the treatment and there were no major changes in the pharmacotherapy. The doses of drugs were modified minimally (exceptionally mild increase to the upper limit of dosage, reduction or discontinuation of benzodiazepines).

The average dose of antidepressant was 29.52±23.31 mg equivalent of paroxetine at the beginning and 28.25±17.68 mg equivalent of paroxetine at the end of treatment. In 12 cases the antidepressant therapy was combined with anxiolytics in an average dose of 0.65±0.42 mg of alprazolam equivalent. In 9 cases the antidepressant therapy was combined with antipsychotic of second generation, three patients were also treated with anticonvulsant. Ten patients who were taking antidepressants in the past without effect, rejected antidepressant treatment and were treated only with CBT without pharmacological support. All the patients participated in a structured group CBT program lasting six weeks. This program contains the standard steps composed of psychoeducation, creating a hierarchy of phobic situations, cognitive restructuring of anxious thoughts, social skills training and hierarchical exposure therapy. Part of the second half of the treatment program is a work with conditional assumptions and core beliefs (schemas). The program was completed by occupational therapy and sport activities.

#### Statistical evaluation

The statistical program Prism3 was used to evaluate the results. Demographic data and average total scores in each rating scale were evaluated by using descriptive statistics. There were detected averages of medians, standard deviations and character of data distribution. To compare the initial and final scores (the last reporting assessment – LOCF = last observation carried forward) the paired t-tests were used. The relations between categories were assessed by using correlation coefficients and linear regression. The relation of alternative variables (sex, yes/no, duration of the disease less than 15 years more than 15 years) to improvement or remission was evaluated by Fisher's test. The 5% level of statistical significance was considered acceptable at all the statistical tests. The study was approved by the local ethics committee. The research was conducted in accordance with the latest version of the Declaration of Helsinki and recommendations for the good clinical practice (Guideline for Good clinical practice, EMEA 2002). Patients signed informed consent.

## RESULTS

In this study, we present the results of patients admitted to intensive CBT program for the treatment of anxiety disorders from January 2010 to December 2013.

#### Group description:

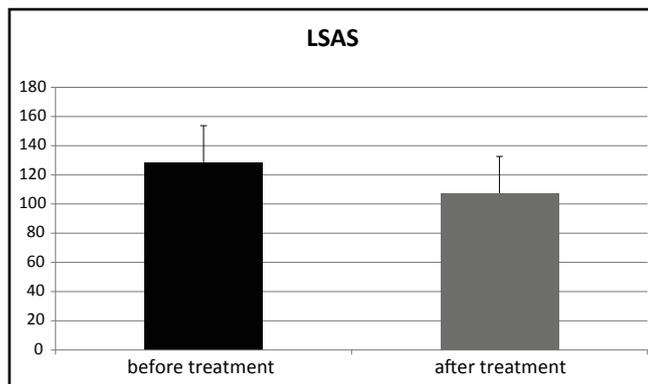
The data of 58 patients of average age 29.96±11.68 was evaluated. The group included 21 women (42.0%). The first symptoms of social phobia appeared in an average of 20.64±12.05 years of age (range of beginning of the disorder 5 to 48 years), the disease lasted an average of 9.56±10.00 years (Table 1). 40 patients (80.05%) were single, 9 were married (18.0%), 1 patient was divorced (42.0%). A positive psychiatric family history was found in 21 patients (48.7%). 11 patients had only primary education (22.0%), 14 were apprenticed (28.0%), 18 had secondary education (36.0%) and 5 of the patients (10.0%) had a college education.

Patients with diagnosis of personality disorder (20 patients, i.e. 40% of the sample) suffered mainly from borderline disorder (10 patients, i.e. 50% of the personality disorders), then avoidant personality disorder (5 patients, i.e. 25% of the personality disorders), 2 suffered from narcissistic personality disorder, 1 patient from obsessive compulsive and 1 patient from histrionic personality disorder. Mixed personality disorder was found in 1 patient. In 13 patients (i.e. 26%

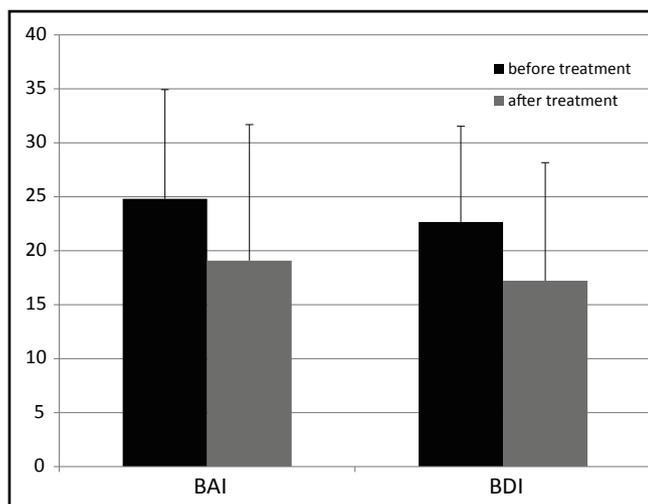
**Tab. 2.** Medians and standard deviations of ratings scales.

Scale	Number of probands	Median ± SD	Statistics
LSAS-1	n=37	128.6±25.15	t-test: t=3.569 df=70; p≤0.001
LSAS-L	n=35	107.4±25.28	
BAI-1	n=50	24.80±10.12	t-test: t=2.492 df=97; p≤0.05
BAI-L	n=49	19.08±12.60	
BDI-1	n=50	22.66±8.87	t-test: t=2.717 df=97; p≤0.01
BDI-L	n=49	17.22±10.95	
CGI-1	n=49	4.25±1.11	t-test: t=5.876 df=94; p≤0.0001
CGI-2	n=47	2.94±1.07	

SD – standard deviation, LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week, LSAS-L – the last assessment of Liebowitz Social Anxiety Scale, BAI-1 – Beck Anxiety Inventory assessed in first week, BAI-L – the last assessment of Beck Anxiety Inventory, BDI-1 – Beck Depression Inventory assessed in first week, BDI-L – the latest assessment of Beck Depression Inventory, CGI-1 – Clinical Global Impression scored in first week, CGI-2 – the last rating of Clinical Global Impression



**Fig. 1.** The decrease in median of total score in LSAS scale. unpaired t-test: t=3.569; df=70; p≤0.001. LSAS - Liebowitz Social Anxiety Scale.



**Fig. 2.** The decrease in median of total score in BAI and BDI scales during the treatment. unpaired t-test: t=2.717; df=97; p≤0.01; unpaired t-test: t=2.2492; p≤0.05. BAI - Beck Anxiety Inventory; BDI - Beck Depression Inventory.

of the sample) accented characteristics of personality were found, mostly features of borderline personality disorder.

There was a statistically significant decrease in symptoms in all rating scales (Table 2, Figure 1 and Figure 2) during the treatment.

The change in LSAS during treatment

We defined the change in LSAS as the ratio between the initial and final total score of the scale. The change in LSAS significantly negatively correlated with BAI at the beginning (Pearson r=-0.379, p≤0.05), but there was no relation either to any of the demographic parameters (age, duration of disease) except of the age of onset of the disorder (Spearman r=0.3261; p≤0.05), or to other clinical parameters (scores in other ratings scales) or to the degree of dissociation evaluated by DES or DES taxon (Table 3). Therefore we cannot predict the change in LSAS on the basis of any of these characteristics. The change in LSAS correlates positively with the age of onset of the disorder – the later the social phobia appears, the more significant the change is.

The rate of dissociation and relations to other variables

It seems that the rate of dissociation evaluated in DES scale does not correlate with any demographic characteristics, such as age, the onset of disorder or duration of illness. DES correlates with the anxiety at the beginning and at the end of the treatment. In our study, however, it did not correlate with level of depression, as it is common for example at OCD (Prasko *et al* 2009) or at panic disorder (Pastucha *et al* 2009). The score of DES scale also does not correlate with any of the parameters of change (change in CGI, LSAS) (Table 4).

DES taxon (nonparametric distribution of values) that detects more pathological dissociative phenomena than DES, correlated with both – the initial degree of anxiety and depression. However, it did not correlate with any of the examined demographic factors or parameters of change (change in CGI, LSAS) (Table 5).

Comparison of responders and non-responders

At the end of the therapy a total of 22 patients (44%) achieved score 1 or 2 in CGI.

When we compared, in the basic demographic and clinical data, the group of patients who achieved remission criteria to the group of patients who did not reach this criteria, the only difference between these groups was an statistically significant higher level of anxiety, rated by BAI (t-test, t=2.020, df=48, p≤0.05) in the group of non-responders than in the responders group. (Table 6).

When comparing responders and non-responders in qualitative data, it turned out that there were 8 patients with personality disorder and 15 without personality disorders in the group of responders and 14 patients with personality disorder and 13 without personality disorders in the group of non-responders.

**Tab. 3.** Correlation between the change in LSAS / ratio of the first and the last evaluation and other demographic and clinical characteristics.

	Age	Onset of disorder	Duration of disorder	Antidepressant index	BAI-1	BDI-1	CGI-1	LSAS-1	DES-1	DES-1 taxon
Pearson r	0.00153		-0.05858		-0.09519	-0.2026	-0.1284	0.3214	0.2687	
Spearman r		0.3261		-0.09925						0.1888
p-value	ns	p<0.05	ns	ns	ns	ns	ns	ns	ns	ns

BAI-1 – Beck Anxiety Inventory assessed in first week, BDI-1 – Beck Depression Inventory assessed in first week, CGI-1 – Clinical Global Impression scored in first week, LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week, DES-1 – Dissociative Experience Scale assessed at first week, DES-T-1 – DES subscale measuring pathological dissociation, ns – non-significant result

**Tab. 4.** Correlation of DES at the beginning and demographic and clinical characteristics.

	Age	Onset of disorder	Duration of disorder	Antidepressant index	BAI-1	BDI-1	CGI-1	LSAS-1	LSAS change	CGI change
Pearson r	0.1131		-0.03973		0.6417	0.1922	0.01871	0.09208	0.2687	-0.0275
Spearman r		0.03874		0.1932						
p-value	ns	ns	ns	ns	<b>p≤0.0001</b>	ns	ns	ns	ns	ns

BAI-1 – Beck Anxiety Scale Inventory assessed in first week, BDI-1 – Beck Depression Inventory assessed in the first week, CGI-1 – Clinical Global Impression scored in first week, LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week, LSAS change – the ratio between the initial and the final score in the Liebowitz Social Anxiety Scale, CGI change – the ratio between the initial and the final score in Clinical Global Impression, ns – non-significant result

**Tab. 5.** Correlation of DES taxon at the beginning and the demographic and clinical characteristics.

	Age	Onset of disorder	Duration of disorder	Antidepressant Index	BAI-1	BDI-1	CGI-1	LSAS-1	LSAS change	CGI change
Spearman r	0.07686	0.1091	-0.05044	0.1607	0.4983	0.2842	0.1167	0.214	0.1315	-0.1105
p-value	ns	ns	ns	ns	<b>p≤0.0005</b>	<b>p≤0.05</b>	ns	ns	ns	ns

BAI-1 – Beck Anxiety Inventory assessed in first week, BDI-1 – Beck Depression Inventory assessed in first week, CGI-1 – Clinical Global Impression scored in first week, LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week, LSAS change – the ratio between the initial and the final score in the Liebowitz social Anxiety scale, CGI change – the proportion between the initial and the final score in Clinical Global Impression, ns – non-significant result

**Tab. 6.** Demographic and clinical characteristic of responders and non-responders.

	Age	Onset of disorder	Duration of disorder	Antidepressant index	BAI-1	BDI-1	CGI-1	LSAS-1	DES-1	DES-T-1
responders	30.32±11.91	20.82±11.67	9.01±11.35	28.89±18.11	21.64±9.72	20.73±11.05	3.96±1.09	124.7±29.32	11.19±9.44	5.03±6.78
non-responders	29.68±11.71	20.50±12.54	10.00±8.99	32.14±18.53	27.29±9.89	24.18±6.51	4.50±1.07	132.0±21.19	13.35±13.05	9.52±13.33
statistics	t=0.1903 df=48	MW U= 276.0	t=0.3462 df=48	MW U= 231.5	<b>t=2.020</b> <b>df=48</b>	t=1.379 df=48	t=1.773 df=48	t=0.8764 df=35	t=0.6499 df=47	MW U= 219.0
p-value	ns	ns	ns	ns	<b>p≤0.05</b>	ns	ns (p≤0.08)	ns	ns	ns

BAI-1 – Beck Anxiety Inventory assessed in first week, BDI-1 – Beck Depression Inventory assessed in first week, CGI-1 – Clinical Global Impression scored in first week, LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week, DES -1 – Dissociative Experience Scale assessed in first week, DES-T-1 – DES subscales measuring pathological dissociation, ns – non-significant result

10 patients in the group of responders and 16 patients in the group of non-responders to the treatment suffered from comorbid anxiety disorder or depression (chi<sup>2</sup>: ns). The difference in the frequency of personality disorders between both groups was not statistically significant (chi<sup>2</sup>: ns). There were 15 men and 7 women in the group of responders, 14 men and 14 women in

the group of non-responders (chi<sup>2</sup>: ns). In the group of responders there were 18 single patients, 4 married and no divorced patients, in the group of non-responders there were 22 single patients, 5 married and 1 divorced patient, the groups do not significantly differ (chi<sup>2</sup>: ns). Regarding employment, in the group of responders there were 5 patients employed, 9 students, 6 unem-

ployed and 1 in disability pension. In the group of non-responders to the treatment there were 7 patients employed, 8 students, 11 unemployed and 2 in disability pension. There was not a statistically significant difference in the frequency of individual subgroups ( $\chi^2$ : ns).

Patients with personality disorder versus patients without personality disorders

The demographic data in patients without personality disorders and patients with personality disorders did not differ in any of the monitored variables (age, onset and duration of the disorder). The difference was not found even in the dose of antidepressant (converted to paroxetine index) (Table 7).

The group of patients without personality disorder was not statistically significantly different from the group of patients with personality disorder in LSAS, BAI, BDI, CGI scales at the beginning of the treatment. Also, there was no significant difference in the extent of dissociation rated by DES or DES-T (Table 7).

When we compared the scores in rating scales between patients without personality disorder (n=28) and patients with personality disorder (n=22) using two-way ANOVA, it appeared that there was not sta-

tistically significant difference between both groups in LSAS scale in the first and the last assessment (two way-ANOVA:  $F=0.3569$   $df=28$ : n.s.) (Figure 3). Similarly in BAI (two-way ANOVA:  $F=0.4562$   $df=44$ : n.s) (Figure 4), BDI (two-way ANOVA:  $F=0.5761$   $df=44$ : n.s) (Figure 4) and CGI (two-way ANOVA:  $F=1.239$   $df=40$ : n.s.) (Figure 5) (Table 8).

**DISCUSSION**

We had two main objectives in our study. The first one was to prove the efficacy of a complex therapeutic program and the second was to find connections between some demographic data, doses of antidepressants and severity of symptoms, assessed by the number of basic scales. Our study group consisted of 50 patients, which approximately corresponds to the number of patients evaluated in other studies (Chen *et al* 2007; De Menezes *et al* 2008; Feske *et al* 1996). The average age of onset of the disorder was several years higher than in the work of Kessler *et al* (2005), and then it is in the works of other authors (Ameringen *et al* 2004; Dalrymple *et al* 2007).

An interesting finding is that in our sample there were 80% of probands single. If we look more closely at

**Tab. 7.** Demographic and clinical characteristic of patients without personality disorder and patients with personality disorder

	Age	Onset of disorder	Duration of disorder	Antidepressant index	CGI-1	DES-1	DES-T-1	LSAS-1	BAI-1	BDI-1
Without personality disorder	30.21±12.31	22.25±12.4	8.86±10.24	33.46±18.53	4.18±1.22	13.86±12.08	9.5±12.98	126±26.63	25.89±10.64	23.11±9.11
With personality disorder	29.64±11.1	18.59±11.53	10.45±9.85	27.5±17.73	4.36±0.95	10.4±10.67	4.84±7.16	132.5±23.16	23.41±9.48	22.09±8.73
Statistics	t=0.1719 df=48	MW U= 253.5	t=0.5554 df=48	MW U= 209.5	t=0.5849 df=48	t=1.040 df=47	t=1.482 df=47	t=0.7580 df=35	t=0.8592 df=48	t=0.3988 df=48
p-value	ns.	ns.	ns.	ns.	n.s.	ns.	ns.	ns.	ns.	ns.

BAI-1 – Beck Anxiety Inventory assessed in first week, BDI-1 – Beck Depression Inventory assessed in first week, CGI-1 – Clinical Global Impression scored in first week, LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week, DES-1 – Dissociative Experience Scale assessed in first week, DES-T-1 – DES subscale measuring pathological dissociation, MW U – Mann Whitney U-test, ns – non-significant result

**Tab. 8.** Scores in CGI, LSAS, BAI and BDI at patients without personality disorder and with personality disorder.

	CGI-1	CGI-2	LSAS-1	LSAS-2	BAI-1	BAI-2	BDI-1	BDI-2
Without personality disorder	4.179±1.219	2.778±0.974	126±26.63	102.4±25.62	25.89±10.64	17.26±11.61	23.11±9.11	15.22±11.46
With personality disorder	4.364±0.9535	3.15±1.182	132.5±23.16	115±23.65	23.41±9.48	21.32±13.65	22.09±8.728	19.68±10
Statistics	two-way ANOVA: $F=1.239$ ; $df=40$		two way-ANOVA: $F=0.3569$ ; $df=28$		two-way ANOVA: $F=0.4562$ ; $df=44$		two-way ANOVA: $F=0.5761$ ; $df=44$	
p-value	n.s		n.s.		n.s		n.s	

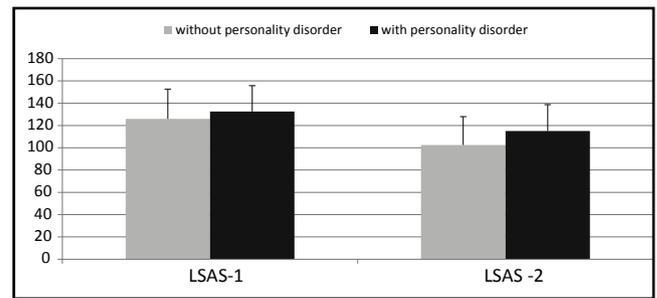
CGI-1 – Clinical Global Impression scored in first week, CGI-2 – Clinical Global Impression scored in second week, LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week, LSAS-2 – Liebowitz Social Anxiety Scale assessed in the second week, BAI-1 – Beck Anxiety Inventory assessed in first week, BAI-2 – Beck Anxiety Inventory assessed in second week, BDI-1 – Beck Depression Inventory assessed in first week, BDI-2 – Beck Depression Inventory assessed in second week, ns – not significant result

the data, it turns out that there were only women in the group of married and divorced patients. None of the 29 men with social phobia could enter into marriage, while every second woman was not able to enter into marriage. Therefore we can speculate that social phobia is a worse handicap for men to enter into marriage than for women. This difference in marital status between men and women was not found in patients with panic disorder (Kamarádová *et al* 2013).

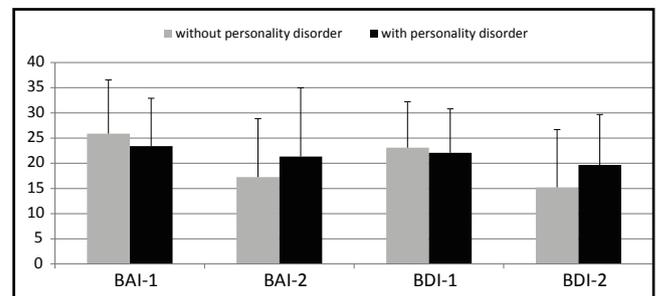
According to the statistical decrease of scores in basic scales in the group of all the patients, the therapeutic program can be described as relatively successful, even if only 44% of patients reached the remission. However they were patients with chronic form of social phobia and also resistant to the previous antidepressant treatment. The aim of the study was to determine whether predictors of therapeutic response to complex CBT program for pharmacologically resistant patients suffering from generalized form of social phobia can be found.

Our preliminary hypotheses came up to expectations only partially. In the first hypothesis we assumed that lower age at the time of the treatment, shorter duration of disorder and higher age of onset of disorder are associated with lower resistance to the treatment and vice versa. Significant proved to be only the age of onset of disorder from those three factors. In our group the higher age of onset of disorder was associated with a better response to the treatment evaluated by change in LSAS. This finding of ours is consistent with the work of Dalrymple *et al* (2007) and Borge *et al* (2010) where lower age of onset was associated with worse response to the treatment. There exists a study which does not validate this connection (Chen *et al* 2007), a different study claims the opposite (Ameringen *et al* 2004). One possible explanation for these different findings could be the fact that all of these studies, like ours, used a small sample of patients and it did not have a sufficiently representative sample considering the population. Another explanation may be that the patients who are treated in our workplace are usually those who repeatedly fail to respond to the outpatient antidepressant treatment, thus it is selection, unlike in the studies above.

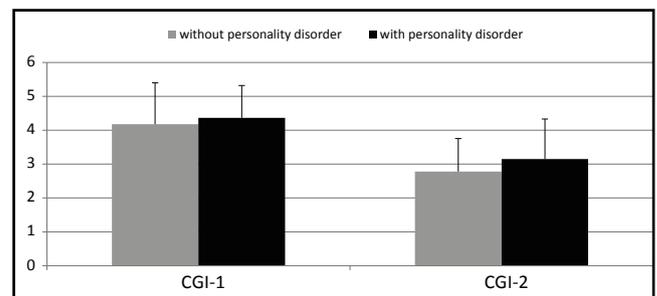
We divided the group of patients into responders and non-responders based on the value of the final CGI. In this division the difference between the groups was in the initial level of anxiety assessed by questionnaire BAI. This questionnaire is not specific to social phobia and it is used to monitor the severity of anxiety symptoms in other disorders. It is possible to claim that the level of anxiety at the beginning of the therapy is associated with a lower probability of achieving response. When using scale more specific to social phobia to evaluate anxiety-LSAS, the relation was not proved. The negative result brought the study of Stein *et al* (2002), which strived to demonstrate the link between the LSAS score and the rate of response to the treatment with paroxetine.



**Fig. 3.** Average scores in LSAS during the treatment in patients without personality disorder and with personality disorder. LSAS-1 – Liebowitz Social Anxiety Scale assessed in first week; LSAS-2 – Liebowitz Social Anxiety Scale assessed in last week; Without personality disorder LSAS-1 versus LSAS-2: paired t-test:  $t=3.991$ ;  $df=20$ ;  $p\leq 0.001$ ; With personality disorder LSAS-1 versus LSAS-2: paired t-test:  $t=3.029$ ;  $df=13$ ;  $p\leq 0.01$ ; two way-ANOVA (personality x duration):  $F=0.3569$ ;  $df=28$ ; n.s.



**Fig. 4.** Average scores in BAI and BDI during the treatment in patients without personality disorder and with personality disorder. BAI-1 – Beck Anxiety Inventory assessed in first week; BAI-2 – the latest assessment of Beck Anxiety Inventory; BDI-1 – Beck Depression Inventory assessed in first week; BAI-2 – the latest assessment of Beck Depression Inventory; Without personality disorder BAI-1 versus BAI-2: paired t-test:  $t=3.760$ ;  $df=26$ ;  $p\leq 0.001$ ; With personality disorder BAI-1 versus BAI-2: paired t-test:  $t=1.047$ ;  $df=21$ ; n.s.; BAI: (two-way ANOVA:  $F=0.4562$ ;  $df=44$ ; n.s.); Without personality disorder BAI-1 versus BAI-2: paired t-test:  $t=4.420$ ;  $df=26$ ;  $p\leq 0.0005$ ; With personality disorder BAI-1 versus BAI-2: paired t-test:  $t=1.047$ ;  $df=21$ ; n.s.; BDI (two-way ANOVA:  $F=0.5761$ ;  $df=44$ ; n.s.).



**Fig. 5.** Average scores in CGI during the treatment in patients without personality disorder and with personality disorder. CGI-1 – Clinical Global Impression scored in first week; CGI-2 – the last rating of Clinical Global Impression; Without personality disorder CGI-1 versus CGI-2: paired t-test:  $t=5.225$ ;  $df=26$ ;  $p\leq 0.0001$ ; With personality disorder CGI-1 versus CGI-2: paired t-test:  $t=3.526$ ;  $df=19$ ;  $p\leq 0.005$ ; two way-ANOVA (personality x duration):  $F=0.3569$ ;  $df=28$ ; n.s.

Other monitored parameters were the degree of dissociation and pathological dissociation measured by DES or DES-T. It turned out that the degree of dissociation correlates only with the level of anxiety. In case of pathological dissociation with the degree of depression assessed by BDI. Dissociation is a phenomenon which occurs also in healthy individuals. Compared to a healthy population it is higher in patients with anxiety disorders (Pastucha *et al* 2009; Raszka *et al* 2009; Kamarádová *et al* 2013). The explanation of higher BAI score in patients with increased DES may be that the rate of dissociation correlates with anxiety itself. Similarly, expected impact of comorbid disorders, including personality disorders, was not found. This finding may be surprising, but it corresponds to the findings of other authors (van Velzen *et al* 1995, 1997; Mersch *et al* 1995). However, there are also studies which claimed the opposite (Turner 1987). As we noted above there were represented primarily resistant patients in our sample and the frequency of personality disorders was unusually high. Another explanation may be that we evaluated the therapeutic effect of CBT, when the treatment includes work with cognitive schemas, while the authors noted above regarded to the effect of pharmacotherapy. The dosage of psychiatric medication did not affect the result. At the same time a higher degree of dissociation and the presence of comorbid personality disorder were not associated with a statistically significant difference in the dose of drugs. The cause probably is, that there were patients resistant to pharmacotherapy, who have been receiving adequate doses of psychiatric drugs, and therefore there was no scope for the differences between individual groups.

#### Limitations of the study:

Our study has several limitations. The main one is the low number of probands and the unavailability of data in some patients. Other limitations are using of subjective assessment scales and the difference in pharmacotherapy in individual patients.

#### CONCLUSION

Further studies with a larger number of patients and long-term self-rating monitoring are necessary to determine predictors of therapeutic effect in patients with pharmacoresistant generalized form of social phobia. In the future it may help to select the optimal therapeutic strategy for a particular patient according to patient's input characteristics. Considering that the current treatment options cannot help all the patients and many affected remain. Social phobia belongs to a group of anxiety disorders. It is characterized by fear and avoidance of situations in which a person can be observed and judged by others (Prasko & Lanková 2006). It is often a disorder with a chronic course (Kessler *et al* 2005). It is usually associated with decreased quality of life (Stein & Kean 2000; Safren *et al* 1996)

resistant to the treatment, it is necessary to search for alternative therapeutic approaches, especially for patients with comorbid depression, personality disorder or a higher degree of dissociation.

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