*Psychiatria Danubina, 2010; Vol. 22, No. 4, pp 528–534* *Original paper*


# COGNITIVE DYSFUNCTION, DISSOCIATION AND QUALITY OF LIFE IN BIPOLAR AFFECTIVE DISORDERS IN REMISSION

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received: 02.08.2010; revised: 24.10.2010; accepted: 15.11.2010

## *SUMMARY*

***Background:*** *Bipolar disorders are often associated with cognitive deficits, which have an influence on social functioning and the course of the illness. These deficits have an impact on occupational ability and social integration.*

***Subjects and methods:*** *To ascertain cognitive function, level of dissociation and quality of life and their interrelations in patients with bipolar affective disorder in remission.*

*Data from D2 Attention Test, Verbal Fluency Test and Trial Making Test, Dissociative Experiences Scale (DES). Quality of Life Satisfaction and Enjoyment (Q-LES-Q) and M.I.N.I. (MINI-international neuropsychiatric interview were statistically analyzed.*

***Results:*** *There are no significant correlations between applied cognitive tests and dissociation scale DES. There are no significant correlations between applied cognitive tests and dissociation scale DES. There were no differences between employed and unemployed patients in DES, pathological DES and in any of Q-.LES-Q domains.*

***Conclusions:*** *We need further research to explore the role of cognitive functions and dissociation in bipolar affective disorder and its relationship to cognitive functions, emotional regulation, biological factors and therapy outcome.*

***Key words:*** *bipolar disorder - cognitive functions – dissociation – occupation - quality of life*

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## INTRODUCTION

The clinical presentation of bipolar affective disorders often has an episodic course, with individuals switching from distinct affective episodes of depression, mania or hypomania, and euthymia. Although mood disturbances are the sine qua non of bipolar disorder, contemporary research has pointed increasingly to non-affective elements of psychopathology associated with this diagnosis. Problems with work and social functioning persist for lengthy periods in many patients with bipolar disorder after the resolution of manic or depressive episodes, even in the absence of subsyndromal affective symptoms (Basso et al. 2002, Thompson et al. 2005). These problems point to other factors that likely mediate functional recovery, including the ability to plan and think clearly, understand connection between everyday life situations and emotions, solve problems with understanding of the context of the situation, use emotions as a tool for understanding interpersonal situations, remember important information and others which can be problematic if the person dissociates.

### Cognitive impairment in bipolar disorder

A cross-sectional study compared 4 groups: manic or hypomanic bipolars, depressed bipolars, euthymic bipolars, and healthy controls using a neuropsychological test battery (Martinez-Aran et al. 2004). Each of the three bipolar groups showed significant impairments in verbal memory and executive functions in comparison with controls. The most recent meta-analysis available used 45 studies comparing 1423 euthymic bipolar patients with 1524 healthy controls (Bora et al. 2009). The results showed group differences with medium to large effect sizes for measures of executive function, verbal memory, psychomotor speed, and sustained attention. Cognitive deficits have an influence on social functioning and the course of the illness. The principal conclusion of these studies comparing various disease states within bipolar disorder is that the cognitive impairment in euthymia is not substantially different from that in the manic or depressive state (Latalova et al. 2010a). These deficits have an impact on occupational ability and social integration. A recent review has identified 13 studies addressing the relationship between cognitive impairments and functional outcomes in euthymic bipolar patients in comparison with healthy controls (Wingo et al. 2009). Significant relationships between cognitive impairments and functional outcomes were reported in 12 of the 13 studies reviewed.

### Dissociation in bipolar disorder

Dissociation as a clinical psychiatric condition has been defined primarily in terms of the fragmentation and splitting of the mind and perception of the self and the body. Its clinical manifestations include altered

perceptions and behavior, including derealization, depersonalization, and distortions of perception of time, space, and body. Several studies confirmed the close association between depressive symptoms and dissociation (Lipsanen et al. 2004, Maaranen et al. 2005). A high level of dissociation is typical also for patients with borderline personality disorders (Pastucha et al. 2009; Zanarini et al. 2000). Our results suggest that the level of psychological dissociation in bipolar patients is higher than in healthy controls (Latalova et al. 2010b). If the disorder developed earlier, the level of pathological dissociation was higher.

### Quality of life in bipolar disorder

The effects of treatment using QoL as an indicator have been studied in the field of clinical psychiatry, including treatments and rehabilitation for bipolar disorder and schizophrenia (Michalak et al. 2005; Sidlova et al. 2010). The Quality of Life Enjoyment and Satisfaction scale (Q-LES-Q) (Endicott et al. 1993) for subjective assessment of QoL, has been used in bipolar patients in various clinical and research contexts (Ozer et al. 2002, Perlis et al. 2004, Revicki et al. 2003, Ritsner et al. 2005). The quality of life in bipolar patients has been compared with patients with schizophrenia, showing that there are higher mean scores in most Q-LES-Q summary scales in patients with bipolar disorder and this has also been shown in some summary scales in comparison with healthy controls in another study. The relationship between level of dissociation, cognitive functions and quality of life is unknown.

### Goals and hypotheses

The aim of our study was to examine the cognitive function, level of dissociation and quality of life and their interrelations in patients with bipolar affective disorder in remission.

We hypothesized that higher levels of cognitive dysfunction is related to a higher level of dissociation and lower quality of life in bipolar patients in remission. The second hypothesis is that patient with a job have better cognitive functions, lower level of dissociation and higher of quality of life.

## SUBJECTS AND METHODS

The subjects were outpatients diagnosed with bipolar disorder according to ICD-10 research diagnostic criteria (1996). Their written consent to participate in the research was given. Patients fulfilling all of the following criteria were enrolled in the study: (a) presence of life time bipolar disorder, (b) now in clinical remission (CGI-S one or two). Demographic data, including age, sex, age of the onset of the disorder, duration of disorder, number of psychiatric hospital admissions, numbers of manic and depressive episodes, were obtained from the interview. The diagnosis of lifetime bipolar disorder was confirmed according to the patients´ documentation and clinical interview. At the time of evaluation all the patients were in clinical remission as confirmed by an experienced psychiatrist (Clinical Global Impression – Severity; CGI-S one or two). Diagnosis was confirm with M.I.N.I. (MINI-international neuropsychiatric interview; Sheehan et al, 1998) evaluated by an experienced psychiatrist. Doses of drugs were converted to defined daily doses using data provided by the Czech State Institute for Drug Control (2010).

### Assessment

Cognitive functions were examined using D2 Attention Test, Verbal Fluency Test and Trial Making Test.

The D2 test is a self-administered and time – limited examination of selective attention. It measures quickness of elaboration, quality of effort and keeping the rules. The aim of the test is to find out d-letters with two lines in a time interval of 8 minutes. A standard test has 14 rows, every row with 47 marks. The marks used in the test are “d” and “p” letters with one to four vertical lines, placed alone or in pairs above or below the letter. The tested person has 20 seconds for every row. The score of overall achievement represents the sum of all processed items minus the overall sum of all the errors (Balcar 2000).

The Verbal Fluency Test is very useful in diagnosis of organic diseases. The patient is instructed to say as many words as he knows, if the first letter will be N, then K and then P. The words should not be names of places, states, towns, countries and first names (also surnames). The time for every letter is 1 minute. The administrator should count how many words the patient has said for every letter. The raw score represents the whole summation of all the words said by the patient (Preiss et al. 2002).

The Trial Making Test is a self – administered test used in diagnosis of organic diseases and to examine the patients psychomotor tempo, selective attention, concentration and flexibility. It consists of two parts, part A and part B. The instruction in part A is to connect numbers from 1 to 4 in the example form and from 1 to 25 in the administration form. In part B the patient is instructed to connect numbers and letter from the alphabet, e.g. 1 – A – 2 – B etc.

The administrator should note the time the patient needs for part A and part B. The raw score represents the whole time the patient needs to administer the test (Preiss et al. 1995).

Psychological dissociative symptoms were examined using the Dissociative Experiences Scale (DES) (Carlson et al. 1991, Carlson & Putman 1993). The DES is a self-administered 28-item inventory of psychological dissociation, where participants are asked

to indicate on a visual analog scale how often they experience the dissociative symptoms (in percentage of time). The Czech version of the scale is comparable to the original version in terms of its test-retest reliability, validity and factor structure (Ptacek et al. 2007). Pathological DES was measured by a Dissociative Experiences Scale Taxon (DES-T) (Waller et al. 1996). Based on the items of DES number 3, 5, 7, 8, 12, 13, 22 and 27. These items measure identity alteration, depersonalization, derealization, discontinuation of awareness, dissociative amnesia, and auditory hallucinations.

Quality of Life Satisfaction and Enjoyment (Q-LES-Q) is 93 questions divided into 8 domains answered mainly as a five-point Likert - type scale. It is mostly self-completed, possibly with the help of investigator (Ritsner et al. 2005). Q-LES-Q is useful for assessment of life satisfaction and enjoyment in patients with schizophrenia, schizoaffective and mood disorder patients (Endicott et al. 1993). It takes from 20 to 40 minutes, according to the health status of the patient. The domains physical health, feelings, leisure, social relations and overview of the quality of life are completed by patients and the domains, work, home and school only where relevant (Müllerova et al. 2001).

***Ethical issues:*** The investigation was carried out in accordance with the latest version of the Declaration of Helsinki and ICH-GCP guidelines (The International Conference on Harmonization, Good Clinical Practice, 1999). All participants signed an informed consent before entering the study.

***Data analysis:*** The patient's demographic and baseline clinical characteristics were analyzed using column statistics. Normal distribution of the demographic and clinical variables was determined by the Shapiro-Wilk W test. Differences between employed and unemployed patients were analyzed using unpair t-tests for independent groups and the Mann-Whitney test. For the analysis of categorical data we used the $chi^2$ test or Fisher´s exact test. The relationships between variables with normal distribution were calculated using Pearson correlation analysis, while Spearman correlation was used for variables with non-normal distribution of DES. The level of significance was set at $p<0.05$. All analyses were conducted using STATISTICA 9.0 software.

## RESULTS

Twenty three patients (11 males and 12 females) with bipolar affective disorder in clinical remission between 23 and 70 years of age (mean age 46.17±14.11) from the Outpatient department of Psychiatry Clinic of University Hospital Olomouc were recruited for this study. All patients had been hospitalized for bipolar disorder at some time in their past history. All used psychotropic medication, mood stabilizers (n=21; mean defined daily dosage of mood stabilizers were 0.91±0.45); antipsychotics (n=17; mean defined daily dosage of antipsychotics were 1.01±0.56); anti-depressants (n=10; mean defined daily dosage of antidepressant was 1.3±0.54); and some of them also benzodiazepines (n=8; mean defined daily dosage of benzodiazepines was 0.91±0.53). Doses of drugs were converted to defined daily doses using data provided by the Czech State Institute for Drug Control (SÚKL, 2010).

Demographic and clinical variables, mean scores of rating scales, DES and cognitive test scores see in table 1.

**Table 1.** Mean demographic and clinical variables, DES and cognitive test scores

| | |
|---|---|
| Age | 46.17±14.11 |
| Sex | |
| Male | 11 |
| Female | 12 |
| Education | |
| Basic | 7 |
| Secondary school without graduation | 3 |
| Secondary school with graduation | 8 |
| University | 5 |
| Marital status | |
| Single | 8 |
| Married | 12 |
| Unmarried living with partner | 0 |
| Divorced | 3 |
| Widower | 0 |
| Employment status | |
| Yes | 10 |
| No | 13 |
| Modd stabilizers DDD (n=21) | 0.91±0.45 |
| Antipsychotics DDD (n=17) | 1.01±0.56 |
| Antidepressants DDD (n=10) | 1.3±0.54 |
| Benzodiazepines DDD (n=8) | 0.91±0.53 |
| Age of the disorder onset | 32.78±8.09 |
| Length of the disorder | 13.52±9.15 |
| Number of manias | 2.61±2.15 |
| Number of depressions | 2.65±1.82 |
| Number of hospitalizations | 2.65±2.85 |
| Length of the clinical remission (years) | 1.48±2.57 |
| Number of suicidal attempts (n=10) | 1.30±0.48 |
| DES | 13.27±9.23 |
| Pathological DES | 1.71±2.82 |
| TMT-A | 47.00±17.88 |
| TMT-B | 116.30±69.32 |
| D2 | 359.70±92.53 |
| Verbal fluency | 34.09±10.86 |

DDD = Daily Defined Dose; DES=Dissociative Experience Scale; TMT-A=Trial Making Test A; TMT-B=Trial Making Test B; D2=D2 Test

## Cognitive tests and DES correlations with clinical variables

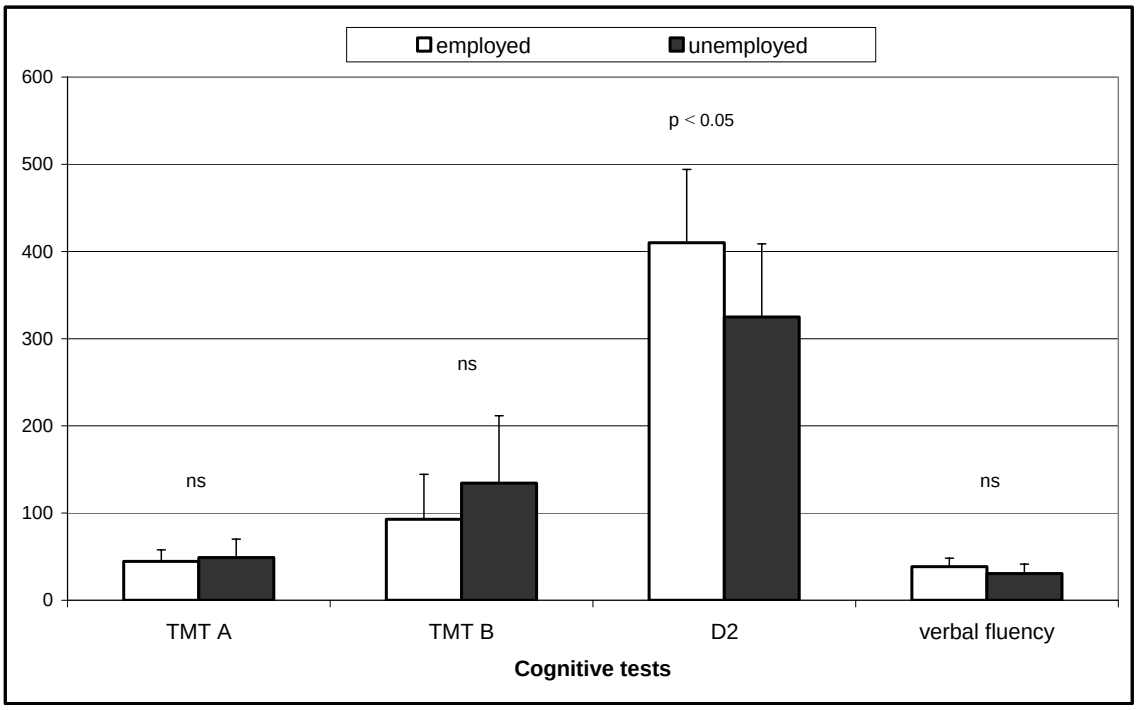
Main results of Pearson's and Spearman's correlations are presented in Table 2. There were no statistically significant correlations between cognitive and clinical variables. Positive association were found between number of manic episodes and DES (Spearman's r=0.42; p<0.05) and between mean dosage of mood stabilizers and DES (Pearson's r=0.4462, p<0.05).

The comparisons of cognitive tests in employed and unemployed bipolar patients show statistically significant difference between these subgroups only in the D2 test (410.00±84.19 versus 324.90±83.96; t=2.334; df=20; p<0.05) (Figure 1).

**Table 2.** Pearson's and Spearman's correlation coefficients between cognitive tests, DES, pathological DES and main clinical variables

| Variables | Age of the disorder onset | Duration of the disorder | Age of the patient | Number of manias | Number of depression | Number of hospitalizations | Number of suicidal attempts | Mean dosage of thymostabilisers | Mean dosage of antipsychotics |
|---|---|---|---|---|---|---|---|---|---|
| TMT-A | $^{P}$ 0.41 | $^{P}$ 0.19 | $^{P}$ 0.36 | $^{S}$ 0.01 | $^{P}$ 0.15 | $^{S}$ -0.07 | $^{S}$ 0.12 | $^{P}$ 0.08 | $^{P}$ 0.08 |
| TMT-B | $^{P}$ 0.36 | $^{P}$ 0.18 | $^{P}$ 0.32 | $^{S}$-0.08 | $^{P}$ 0.37 | $^{S}$ -0.03 | $^{S}$ 0.04 | $^{P}$ 0.09 | $^{P}$ 0.09 |
| D2 | $^{P}$ -0.18 | $^{P}$ 0.17 | $^{P}$ 0.01 | $^{S}$ -0.20 | $^{P}$ -0.28 | $^{S}$ -0.06 | $^{S}$ 0.17 | $^{P}$ -0.29 | $^{P}$ -0.29 |
| Verbal fluency | $^{P}$ -0.18 | $^{P}$ -0.02 | $^{P}$ -0.12 | $^{S}$ -0.01 | $^{P}$ -0.36 | $^{S}$ -0.30 | $^{S}$ 0.09 | $^{P}$ -0.08 | $^{P}$ -0.22 |
| DES | $^{P}$ 0.25 | $^{P}$ 0.06 | $^{P}$ 0.19 | $^{S}$ 0.42* | $^{P}$ 0.03 | $^{S}$ -0.10 | $^{S}$ 0.10 | $^{P}$ 0.45* | $^{P}$ -0.13 |

$^{P}$ = Pearson's r; $^{S}$ = Spearman's; r; *p<0.05




TMT-A= Trial Making Test A; TMT-B= Trial Making Test B; D2= D2 Test

**Figure 1.** Comparison of cognitive tests in employed and unemployed bipolar patients in remission

## Quality of life domains correlations with clinical variables

The correlation matrix of the scores for each of Q-LES-Q domains and clinical variables showed that the number of manic episodes has positive correlation with domain feelings (Spearman's r=0.55; p<0.01), number of hospitalizations with domain work (Spearman's r=0.65; p<0.05) and number of hospitalizations with domain leisure time (Spearman's r=0.42; p<0.05). The correlation matrix of the scores of Q-LES-Q did not show correlation of any of the domains with the age, illness onset, illness duration and number of depression episodes, and any of the clinical data with domains physical health, household, social activities and general. (see Table 3).

The results of QoL comparisons according the employment status are presented in table 5. The comparisons of Q-LES-Q domains in employed and unemployed bipolar patients show a statistically significant difference between these subgroups only in the Q-LES-Q sum (323.30±30.72 versus 252.20±35.23; t=5.063, df=21; p<0.0001) (see Table 4).

**Table 3.** Mean scores of Q-LES-Q domains and correlations with sociodemographic and clinical data

| | Mean | SD | Correlations | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Age | Illness onset | Illness duration | Number of manias | Number of depressions | Number of hospitalizations |
| Physical health | 46.35 | ±10.19 | P 0.09 | P 0.04 | P 0.10 | S -0.10 | P 0.03 | S 0.029 |
| Feelings | 51.30 | ±9.73 | P 0.05 | P 0.08 | P 0.02 | S -0.55 ** | P -0.08 | S -0.02 |
| Work (n=10) | 56.30 | ±6.29 | P -0.03 | P -0.04 | P -0.01 | S 0.58 | P -0.14 | S 0.65 * |
| Household | 43.10 | ±5.66 | P 0.34 | P 0.28 | P 0.29 | S 0.29 | P 0.02 | S 0.24 |
| School/study(n=0) | | | | | | | | |
| Leisure | 26.74 | ±3.02 | P -0.01 | P -0.08 | P 0.07 | S 0.19 | P 0.23 | S 0.42 * |
| Social activities | 39.57 | ±9.73 | P -0.10 | P 0.05 | P -0.19 | S -0.33 | P -0.14 | S -0.13 |
| General | 57.22 | ±6.78 | P 0.20 | P 0.22 | P 0.11 | S 0.14 | P -0.07 | S -0.01 |
| Q-LES-Q sum | 283.10 | ±48.59 | P 0.09 | P -0.02 | P 0.15 | S -0.14 | P -0.09 | S -0.33 |

P = Pearson's r; S = Spearman's; r; *p<0.05; **p<0.01

**Table 4.** Comparison of the quality of life according employment status

| Status | | Somatic | Feelings | Work | Household | School | Leisure | Social | General | Q-LES-Q sum |
|---|---|---|---|---|---|---|---|---|---|---|
| Employed n=10 | Mean | 49.30 | 53.10 | 56.30 | 41.50 | - | 25.80 | 37.80 | 59.50 | 323.30 |
| | SD | 10.20 | 9.61 | 6.29 | 6.47 | - | 2.97 | 12.15 | 5.44 | ±30.72 |
| Unemployed n=13 | Mean | 44.08 | 49.92 | - | 44.70 | - | 27.46 | 40.92 | 55.46 | 252.20 |
| | SD | 9.97 | 9.98 | - | 4.47 | - | 2.96 | 7.63 | 7.37 | ±35.23 |
| Statistics: unpair t-test | | ns | ns | - | ns | - | ns | ns | ns | p<0.0001 |

Q-LES-Q = Quality of Life Satisfaction and Enjoyment

## Cognitive function, dissociation and quality of life

Most of Q-LES-Q domains (Physical health, Feelings, Work, Household, Leisure, Social activities) did not show any correlation with any of the cognitive tests, but domain "General" highly correlated with 3 of the cognitive tests (negatively with TMT-B: Pearson's r=-0.54, p<0.01, positively with D2 test: Pearson's r=0.54, p<0.01 and negatively with Verbal fluency test: Pearson's r=-0.42, p<0.05). There were not any correlations between DES or pathological DES scores and scores of cognitive tests. Pathological DES is only negatively correlated with the Social activity domain of Q-LES-Q (Pearson's r=-0.58, p<0.01) (see Table 5).

**Table 5.** Q-LES-Q domains correlations with cognitive tests DES

| | TMT-A | TMT-B | D2 | Verbal fluency | DES | pathDES |
|---|---|---|---|---|---|---|
| Physical health | P -0.35 | P -0.16 | P 0.06 | P 0.25 | P -0.19 | P -0.18 |
| Feelings | P -0.36 | P -0.21 | P 0.32 | P 0.34 | P -0.40 | P -0.13 |
| Work (n=10) | P -0.28 | P -0.34 | P -0.15 | P 0.13 | P 0.19 | P 0.34 |
| Household | P -0.02 | P 0.07 | P -0.10 | P -0.11 | P 0.05 | P 0.01 |
| School/study(n=0) | | | | | | |
| Leisure | P -0.34 | P -0.26 | P 0.07 | P 0.10 | P -0.36 | P -0.06 |
| Social activities | P -0.37 | P -0.19 | P -0.08 | P 0.04 | P -0.14 | P -0.58 ** |
| General | P -0.39 | P -0.54 ** | P 0.54 ** | P -0.42 * | P 0.02 | P 0.33 |
| Q-LES-Q sum | P -0.34 | P -0.34 | P 0.40 | P 0.49 * | P -0.13 | P -0.02 |
| DES | P 0.17 | P -0.13 | P -0.08 | P 0.12 | | |
| pathDES | P 0.08 | P -0.20 | P 0.34 | P 0.30 | | |

P = Pearson's r; * = p<0.05; ** = p<0.01; pathDES= pathological dissociation

## DISCUSSION

The study confirmed our hypotheses only partially. We hypothesized that higher level of cognitive dysfunction is related to a higher level of dissociation and lower quality of life in bipolar patients in remission, but this is not true in our patients. There are not any significant correlations between applied cognitive tests and dissociation scale DES. It seems that dissociation is not part of cognitive impairment, but it is an independent (probably active) process. Also there are not any significant correlations between DES and Q-LES-Q domains. There was only one significant correlation between pathological DES and Q-LES-Q domain Social activities. This finding can indirectly strengthen previous considerations. Dissociation is the process which frequently grows up from interpersonal traumatic experience and could increase the problems in social adaptation, which could be seen in patients with high social problems and high levels of dissociation, like borderline personality disorder (Pastucha et al. 2009). Our findings could indirectly confirm this speculation: patients with higher levels of dissociation reported lower level of quality of life in the domain Social activities.

We found highly significant correlations between Q-LES-Q domain General and three of four applied cognitive tests (TMT-B, D2 test and Verbal fluency test), and between sum Q-LES-Q and Verbal fluency test. How to interpret these findings is difficult. Domain General of Q-LES-Q contains general items of feelings well and these feelings could be ensured by cognitive functions like attention, memory and verbal ability.

The second hypothesis was that employed patients will have better cognitive functions, lower level of dissociation and higher of quality of life. This could be true in the D2 test. Employed bipolar patients significantly differ from unemployed in this cognitive task, but not in other cognitive tests. There were no differences between employed and unemployed patients in DES, pathological DES and in any of Q-.LES-Q domains.

Our study has substantial limitations that should be considered.

To assess the level of dissociation, we used self-report questionnaires. Future research should corroborate these questionnaires with clinician-rated instruments. Also the subjective self-rating measurements of QoL were used with unknown reliability in this population. QoL in our study was measured with the Quality of Life Enjoyment and Satisfaction (Q-LES-Q) which is not a QoL questionnaire specific to bipolar disorder.

A further limitation of our study is in relatively small sample size of the patients, which made impossible the evaluation of different subgroups. Patients were medicated and possible side-effects could influence the cognitive functioning and dissociation. The cognitive effects of the medications used in bipolar disorder may well go in either direction, even with the same drug. Meta-regressions indicated that medication was associated with impaired psychomotor speed and sustained attention (Bora et al. 2009): Studies that reported a higher proportion of patients an antipsychotics reported lower psychomotor speed and more omission errors, antidepressants were associated with lower psychomotor speed and more impaired performance on Trail Making Test A. These associations between medications and test performance of course do not necessarily imply that medications had any direct causative effect on the performance. In our study the dosage of mood stabilizers positively correlated with DES but not with cognitive tests.

## CONCLUSION

We need further research to explore the role of cognitive functions and dissociation in bipolar affective disorder and its relation to the cognitive functions, emotional regulation, biological factors and therapy outcome. Research into cognitive impairments in bipolar disorder has yielded results that lead to revisions of the clinical approach to the illness.

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## Acknowledgement

This paper was supported by the research grant NT11047 IGA MZ ČR

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