

Cognitive functioning in a depressive period of bipolar disorder

Julita Świtalska, Alina Borkowska

Summary

Aim of the study. Study aims were to compare neuropsychological functioning of depressed bipolar patients and healthy controls and to estimate relationship between severity of depressive symptoms and cognitive functioning.

Method. Cognitive functions were examined in 30 depressed bipolar patients aged 18-68 (M=45,6, SD=12,6; 18 women and 12 men) who fulfilled ICD-10 criteria for depressive episode (Hamilton Depression Rating Scale score ≥ 11). The comparison group consisted of 30 healthy subjects aged 23-71 (M=46, 20 women and 10 men) matched in age, years of education and gender to bipolar group. A neuropsychological battery assessed executive functions and working memory.

Results. The bipolar patients in depression revealed neuropsychological deficits in working memory and some aspects of executive functions in comparison to healthy group. Only in WCST test both groups received similar results. Neuropsychological functioning seems to be independent of the severity of depressive symptoms.

Discussion. Different aspects of working memory and executive functions are impaired in depression period of bipolar disorder and they seem independent of the severity of depressive symptoms. These results are consistent with previous reports.

Conclusions. In patients with bipolar depression cognitive assessment should be taken into account in the diagnosis and the disturbances in executive functions and working memory should be treated with neuropsychological rehabilitation and / or pharmacotherapy.

bipolar disorder / neurocognitive impairment / depression

INTRODUCTION

The research results to date concerning bipolar affective disorder indicate the presence of cognitive deficits during both active episodes of the illness, as well as in periods of remission [1]. It has been found that disturbances in cognitive functioning are neither a side effect of pharmacotherapy, because they can be found in individuals not treated pharmacologically, nor a de-

rivative of other symptoms – changes in mental state, since they are present also during asymptomatic periods of the disorder [2]. Currently, it is assumed that they are part of the clinical picture of the illness. The observed cognitive dysfunctions concern mainly working memory and executive functions, which are associated with prefrontal brain areas, and verbal learning.

The discovery of the presence of cognitive disturbances during remission led the researchers to focus their activity mainly on the asymptomatic period of the illness, and they lost their interest on cognitive functioning of patients in active phases: depression and mania or hypomania. To date, little is known about the profile and level of cognitive deficits in patients with bipolar

Julita Świtalska¹, Alina Borkowska²: ¹Institute of Psychology, University of Łódź, ²Department of Clinical Neuropsychology, UMK in Toruń, Collegium Medicum in Bydgoszcz. **Correspondence address:** julitaswitalska@tlen.pl

disorder in active phases of the illness as well as about the relationship between severity of symptoms and cognitive functioning.

Recent studies indicate the presence of cognitive disturbances during depression. The observed abnormalities are mainly related to executive functions, working memory, verbal learning and verbal fluency [3-8]. Dolan et al [9] observed a significant correlation between the execution of tasks that measure memory and frontal brain functions and reduced brain flow in the frontal areas.

The aim of this study is to compare the cognitive functioning of patients with bipolar disorder who are in a phase of depression and cognitive functioning in healthy subjects. Different aspects of working memory and executive functions have been compared. The relationship between cognitive functioning and severity of depressive symptoms has also been estimated.

RESEARCH MATERIAL

30 individuals with diagnosis of bipolar disorder (determined by a psychiatrist using the diagnostic criteria for ICD-10) treated in the Second Department of Psychiatry CSK or in Babinski hospital in Lodz took part in this study. These individuals were aged 18-68 years (mean = 45.6, 18 women and 12 men) and during the study met criteria for a depressive episode. The study included people who received at least 11 points in the Hamilton scale. People with alcohol abuse or taking psychoactive substances, with a history of head trauma, during or less than six months after electroconvulsive therapy, with signs of the process of dementia or CNS injury, people suffering from neurological diseases, which are known to be associated with damage to the CNS and suffering from other mental disorders were excluded. Other psychiatric disorders were excluded by psychological and psychiatric interview and analyses of the history of the disease. In a few cases, the objective technical difficulties and disturbances in cooperation made the examination with all the tests impossible, so when presenting the results of a single test, I give the number of people who completed the given test.

The control group consisted of 30 people aged 23-71 years (mean = 46.2, 10 men and 20 women) selected so that the average age and number of years of education, and distribution of gender frequency was as similar to those in the study group as possible. The precondition for inclusion was lack of any mental disorders, including bipolar disorder. Other psychiatric disorders were excluded by psychological interview. People with alcohol abuse or taking psychoactive substances, with a history of head trauma, with signs of the process of dementia or CNS injury, or people suffering from serious neurological or somatic diseases, which can lead to damage to the CNS, were excluded. The subjects forming the control group came from the area of Lodz region.

METHOD

Research variables and the way of measuring

For measuring mood, the following instruments were used :

1. HDRS – Hamilton Depression Rating Scale – 17 item version, which measures the severity of depressive symptoms [10].

For assessment of cognitive functions, the following tools were used:

1. Reitan Trail Making Test A (TMT A) – a measure of psychomotor speed.

Reitan Trail Making Test B (TMT B) – allows the measurement of visuo-spatial working memory. This test is based on drawing a continuous line connecting alternating numbers and letters in the shortest time possible. This task requires from a subject to maintain in direct memory information about the two valid reaction criteria, to switch between them, as well as to control adequately the two separate processes. [11]

2. Wisconsin Card Sorting Test (WCST) – is used to assess the executive functions. I used a computerized version of the test developed by Heaton. In assessing a result one takes into account: the number of trials made in the study, the total number of correct answers and the number of errors made, the number of perseverative errors and perseverative responses, the number of non-perseverative errors, the number of correctly arranged categories, the number of responses in line with the logical concept and the number

of trials made before proper arrangement of the first category [12].

3. N-back test – used to test visual working memory and psychomotor skills; it also allows to measure response time. I used the 1-back version in the study – the task of the subject was to press on the computer keyboard a digit prior to this, which was visible at the moment.

4. Stroop Color-Word Interference Test – used to test verbal working memory. It is composed of two parts:

In Part A of the test (reading color names in black) the subject's task is to read a list of 50 words in the shortest possible time.

In Part B of the test (naming color of word – different), the subject's task is to name a color in which each word is printed, but the print color is different from the color described by the word. Assessing the test results, one takes into account the number of errors made (reading the name of the color instead of naming the print color) and the time in seconds, when the task was done. This test produces a situation of “conflict instruction” because the subject has to stop a function well learned – a routine – that is reading, and by following instructions, has to perform a non-standard action that is naming the print color. Here, as well, there is a situation of provocation of perseveration that is, a return to a previously trained way how to respond.

5. FAS Verbal Fluency Test – the FAS test is used to assess verbal fluency. The task of the subject in this test is to say words, as fast as possible, according to a given criterion, within 1 minute. In the study, I used a letter version, where the task of the subject is to say as many words beginning with F, A, S, as possible. The solution is the number of words in three letter categories, said within 3 minutes. Verbal Fluency Test is significantly reduced in patients with damage to the temporal areas of the brain, while the number of perseverated words, or words, which do not match the criterion, indicates dysfunction of “on-line” processes related to the functions of working memory [13].

Statistical Methods

To investigate the normal distribution, Shapiro-Wilk test was used. The variables that were

not distributed normally, were processed with non-parametric tests. For comparison of the parameters set in two test groups, the U Mann-Whitney test was used. For comparison of the frequency distributions of categories of discrete variables, chi – square test was used. As a measure of the assessment of the relationship strength between continuous variables, Pearson correlation coefficient was used. For comparison of the distribution of age and the number of years of education, Student's t-test was used. For the statistical evaluation, I used the statistical package SPSS 20.

RESULTS

Table 1 (*on the next page*) shows the characteristics of clinical variables and the comparison of demographic variables in the test groups.

There were no statistically significant differences between the means for age

and number of years of education and differences in the frequency distributions of gender in the compared groups.

All patients took mood stabilizers, most of them took also antidepressants and some participants took antipsychotics and anxiolytics.

Table 2 (*on the next page*) presents the correlation coefficients between the severity of depressive symptoms and the results of the neuropsychological tests in patients who are in a phase of depression.

In patients with depression, there were no statistically significant correlation between the severity of depressive symptoms and the results of the neuropsychological tests. We did not observe that greater severity of depressive symptoms significantly worsened performance of different aspects of working memory, executive functions, verbal fluency, slowed down psychomotor pace or prolonged reaction time.

Table 3 (*on page 31*) shows the neuropsychological test results obtained by patients with bipolar depression and healthy subjects.

In TMT test, A and B, patients with bipolar disorder who were in a period of depression obtained significantly worse results compared to healthy subjects. Both in the first part of the test, which measured psychomotor speed, as well as in the second part measuring visuo-spatial

Table 1. Demographic and clinical characteristics of depressed and healthy comparison subjects

Characteristics	Depressed group (N=30)		Healthy comparison group (N=30)		P
	M	SD	M	SD	t
Age (years)	45.6	12.6	46.20	12.206	0.86
Educational level (years)	13.5	3.2	13.83	2.743	0.70
Age at onset (years)	33.7	10.8	-	-	
Duration of illness (years)	12.4	8.4	-	-	
Total number of episodes	9.4	6.5	-	-	
Number of manic/hypomanic episodes	2.9	2.8	-	-	
Number of depressed episodes	6.5	4.6	-	-	
Number of hospitalizations	3.2	1.7	-	-	
Hamilton depression scale score	20.4	8.1	-	-	
	N	%	N	%	Chi ²
Female	18	60	20	67%	0.59
Male	12	40	10	33%	
Previous psychotic symptoms	10	33	-	-	
Mental disorders in family	6	20	-	-	
Bipolar Type I	13	43	-	-	
Medication					
Mood stabilizers	28	100	-	-	
Antidepressants	22	79	-	-	
Neuroleptics	10	36	-	-	
Anticholinergics	10	36	-	-	

N- number of people, M – mean, SD- standard deviation , p – level of significance

Table 2. The correlation coefficients between the severity of depressive symptoms and the results of the neuropsychological tests in depressed group

Variables	Severity of symptoms (Hamilton)	
	Depressed group	
	N	Person (r)
TMT A (sec.)	29	0.23
TMT A (errors)	29	-0.14
TMT B (sec.)	29	0.01
TMT B (errors)	29	-0.07
Stroop A	29	0.20
Stroop B	29	0.11
Stroop B (errors)	29	0.31

table continued on the next page

W C S T	Number of trials	30	-0.09
	Correct responses	30	-0.33
	Numer of errors	30	0.07
	Perseveratives responses	30	-0.01
	Perseveratives errors	30	0.02
	Nonperseveratives errors	30	0.12
	Conceptual level achieved (%)	30	-0.24
	Trials to complete first category	30	-0.01
	Categories completed	30	0.08

Table 3. Neuropsychological performance of depressed and healthy comparison subjects

Variables	Depressed group (N=30)					Healthy comparison group (N=30)					p test Manna-Whitney'a
	N	M	SD	Min.	Max.	N	M	SD	Min.	Max.	
TMT A (sec.)	29	54.83	35.02	22	169	30	34.73	20.05	13	100	0.001
ssTMT B (sec.)	29	152.07	122.82	46	634	30	84.67	51.79	34	284	0.002
TMT B (errors)	29	1.04	1.50	0	6	30	0.23	0.57	0	2	0.006
Stroop A (sec.)	29	28.14	8.585	20	57	30	21.83	2.77	16	29	0.001
Stroop B (czas)	29	84.34	30.07	49	164	30	60.10	18.45	40	127	<0.0005
Stroop B (errors)	29	2.66	4.29	0	18	30	0.87	1.57	0	6	0.042
WCST											
Number of trials	30	98.03	22.552	70	128	30	93.60	21.73	70	128	0.326
Correct responses	30	72.17	10.072	59	100	30	72.27	9.88	61	96	0.994
Numer of errors	30	25.87	19.285	6	69	30	21.33	14.62	5	55	0.416
Perseveratives re-sponses	30	15.93	14.357	4	55	30	11.63	9.00	4	39	0.414
Perseveratives errors	30	14.03	11.903	4	48	30	10.63	7.54	4	32	0.381
Nonperseveratives errors	30	11.87	9.202	2	43	30	10.70	8.17	1	33	0.573
Conceptual level achieved (%)	30	64.60	11.796	34	90	30	67.33	8.12	56	90	0.871
Trials to complete first category	30	24.47	20.104	10	65	30	17.17	12.97	10	65	0.041
Categories completed	30	4.73	2.132	0	6	30	5.73	0.64	4	6	0.113
N- back correct re-sponces	26	13.32	6.26	5	25	27	17.89	5.93	6	25	0.015
N- back reaction time	22	1289	406	362	1820	27	946.3	432.8	385	1788	0.005
FAS	30	11.44	3.49	3.67	19.67	30	16.64	4.23	8.67	25	<0.0005

working memory, patients received much longer execution time than healthy controls. Patients committed four times as many errors performing Part B of the test as healthy controls (statistically significant difference). This indicates disturbances in visuo-spatial working memory in patients with bipolar disorder who are in a period of depression.

Similarly, in parts A and B of Stroop test, patients received significantly worse results than healthy controls. It took a lot more time for them to complete both parts of the test, and they also committed significantly more errors in Part B of the test. This indicates the disturbances in verbal working memory.

In the Wisconsin Card Sorting Test, the depressed patients came out slightly worse than healthy subjects, the differences in most cases did not receive the level of statistical significance. Comparing the means, one could observe that the depressed patients generally committed more errors, made more perseverative errors and they gave more perseverative responses, and also completed less categories than healthy subjects. However, these differences did not receive the level of statistical significance. Some of the patients did not complete any category correctly, while the healthy subjects arranged correctly at least four categories. Only the number of trials needed for completion of the first category showed significant difference between the patients with depression – who came out significantly worse – and healthy controls. Based on the obtained results, it can be concluded that condition of executive functions measured by the WCST test in patients with depression and in healthy individuals is similar. The only significant difference in the execution of the WCST occurred in the number of trials needed for the first category and it indicates the difficulty in discovering the rules of resolving the test in patients with depression.

In the N-back test, depressed patients gave significantly fewer correct responses than healthy controls, indicating impaired visuo-spatial working memory. The reaction time in depressed patients was also significantly longer than in healthy subjects. In FAS test that measured verbal fluency, depressed patients gave significantly fewer words beginning with that letter than healthy controls.

DISCUSSION

In the group of depressed patients, there were no statistically significant correlation between the intensity of depressive symptoms measured by the Hamilton scale and performance in neuropsychological tests. I did not observe that higher severity of symptoms was associated with poorer functioning of working memory and executive functions, which suggests that in patients with depression, cognitive deficits are independent of the severity of symptoms.

Results are consistent with previous reports, where there was also no statistically significant association between cognitive functioning and severity of depressive symptoms. In Dixon's et al [4] study, in patients with bipolar disorder depressive symptoms were not in a statistically significant relationship with impaired executive functions. The Bearden's et al [14] study showed that the intensity of depressive symptoms did not correlate significantly with the intensity of memory dysfunctions, suggesting that memory impairment in depression is not secondary to depressive symptoms. Results different from mine occurred in Chaves' et al [15] study, indicating the deterioration of verbal fluency along with intensification of depressive symptoms.

The results of neuropsychological tests that measure various aspects of working memory in patients with bipolar disorder during depression were significantly worse than those of healthy subjects matched for age, sex and number of years of education.

In TMT test part A and B, patients with depression received almost twice as long execution time as healthy controls, suggesting a distinct disturbances in the visuo-spatial working memory. These patients also committed significantly more errors in Part B of the test, based on reacting in accordance with established patterns (making a trail in numerical or alphabetical order), instead of following the instructions, requiring a switch between the two criteria of action. On this basis, it can be concluded that in these patients, there are attention disorders involving difficulties in searching the perceptual field and in switching attention. Difficulties in execution of part A can also be related to impairment in sustained attention, and can also be the result of a general psychomotor slow down.

However, the significantly poorer execution of part B can also be caused by disturbances in the main control system, that is in executive functions. Research studies with neurosurgical patients show that the prolonged time in TMT test is associated with impaired functioning in the frontal brain. Also, the occurrence of errors in part B of TMT is associated with lesions in the frontal brain, while patients with damage to the dorsolateral part of the prefrontal cortex make significantly more errors than patients with damage to medial-basal areas [16]. Thus, significantly longer execution times of part B and committing more errors in patients with depression compared to healthy controls may be subject to disturbances in the functioning of dorsolateral area of prefrontal cortex of the brain.

Results similar to mine, Martinez-Aran et al. [8] obtained in their work. In their studies, patients with depression obtained significantly worse results in both parts of the test TMT than healthy controls. The execution times obtained in those studies, 51.2 seconds for Part A and 151.2 seconds for Part B are very similar to those that occurred in my work: 54.8 seconds for Part A and 152, 0 seconds for Part B. These results are consistent with previous reports of Martinez-Aran et al [7], in which patients with depression received prolonged execution times of part A (55.2 sec.) and Part B (154.3 sec.). Also in Basso's et al [3] studies, patients with depression obtained in the test TMT A and B significantly worse results than healthy individuals. The above contrasts with the results of research of Mahli et al [6], in which there were no statistically significant differences in execution of the TMT Parts A and B between patients with depression and healthy controls, but the weakness of this study is very small size of the groups ($n = 14$).

Execution of both parts of the Stroop test was significantly worse in patients with depression as compared to healthy subjects. These patients also committed significantly more errors in Part B of the test, involving reading words indicating the names of colors, rather than following instructions requiring the naming of the print colour. This shows the weakness of verbal working memory in those patients. These problems of the patients, with the successful completion of Part B of the Stroop test, reflect their difficulty with

the inhibition of the action well learned, that is reading and following the instruction requiring untypical action, that is naming of the print colour. This phenomenon is called the Stroop interference effect and it is the extending of the reaction time in case of processing incoherent stimuli [17]. However, in the case of patients with bipolar disorder who are depressed, this phenomenon goes beyond the norm (hence significantly worse performance than healthy subjects) and reflects the particular difficulties of patients in the processes of inhibition and cognitive control, that is in the operation of executive functions. Neuroimaging of brain during execution of Stroop test in patients with bipolar disorder which are in various phases of the illness, show reduced activity in the left prefrontal cortex in patients, regardless of the phase of the illness, compared to the control group consisted of healthy individuals. In patients in a period of depression, additionally increased activity was observed in the left ventral part of the prefrontal cortex [18]. Research made by Kronhaus et al [19], using functional magnetic resonance, imaging brain activity while performing Stroop test, confirmed the decrease in activity in the supraorbital and medial area of the prefrontal cortex in patients with bipolar disorder. Additionally, it was observed that depressive symptoms negatively correlated with decreased activity in the prefrontal areas of the brain (supraorbital cortex).

On this basis, it can be concluded that the difficulties in execution of the Stroop test by patients with depression reflect abnormal activity in the supraorbital area of the brain.

In the literature, there are reports of studies confirming the results obtained by me, showing significantly worse execution of the Stroop test in patients with bipolar disorder who are in a phase of depression, compared to healthy subjects. In the study by Martinez-Aran et al [8], patients with depression scored significantly worse in the Stroop test than healthy subjects. Similarly, in studies by Mahli et al [6], depressed patients came out significantly worse in the Stroop test than the control group consisting of healthy individuals. Other studies of Martinez-Aran et al. [7] also indicate the presence of dysfunction in verbal memory measured with the Stroop test.

In the WCST test, patients with depression only in one case obtained a score significantly worse than the control group consisting of healthy individuals. Depressed patients needed significantly more attempts to correct completion of the first category. In other measures of WCST, patients with depression came out slightly worse than healthy controls (differences did not achieve statistical significance). The WCST test measures the ability of an individual to discover the principle of laying out cards, then to maintain it in working memory and change to another when the previous rule expires. It measures the conceptual thinking (on the basis of analysis of available information, formulating the concept of laying out cards) and cognitive plasticity (change strategies of action in response to change in the rule of laying out cards). An important indicator of disturbances in cognitive plasticity are perseverative errors, involving a return to the previous, currently wrong, way of responding. Taking the test is related to the activity of the dorsolateral and ventrolateral prefrontal cortex of the brain. Dorsolateral part is responsible for discovery of the rule that governs laying out of the cards, and the ventrolateral part is responsible for changing the strategy [20]. Results obtained in my study indicate that patients with depression needed significantly more time to analyze the information context and to formulate a concept for the test solution than healthy controls, as evidenced by the significantly higher number of trials needed to correct completion of the first category. However, the results did not confirm the presence of disturbances in cognitive plasticity (no significant difference in the number of perseverative errors and the number of correctly arranged categories, comparing to the control group) and conceptual thinking (no difference in the percentage of responses consistent with the logical concept, comparing to the control group).

In the study by Martinez-Aran et al [8], patients with depression committed significantly more perseverative errors in the WCST than healthy controls, but there were no differences in the number of correctly arranged categories between patients and controls. On the other hand, in the studies by Mahli et al [6], there were no statistically significant differences in the WCST execution in patients with depression compared

to healthy subjects. Research made by Borkowska and Rybakowski [21] suggests that patients with bipolar disorder who are depressed have committed significantly more perseverative errors and have completed fewer categories in the WCST test than patients with unipolar depression.

Patients with depression obtained significantly worse results in the N-back test than healthy subjects. They gave less correct answers in the test and had also longer reaction times than those in the control group. This indicates disturbances in visuo-spatial working memory in these patients. Correct execution of the test requires from a subject to maintain a previous number in the working memory and pressing it on the keyboard when the next digit appears (version 1-back). A correct execution of the test is also dependent on effective hand-eye coordination and on stopping a forcing reaction to press the number currently seen on the monitor. Frangou studies [22] using functional magnetic resonance imaging while performing the N-back test in patients with bipolar disorder and healthy controls, indicated the differences in brain activity only at higher load of working memory (versions 1,2,3 – back). In healthy individuals, greater working memory load resulted in an increase of activity in the dorsal prefrontal cortex and anterior cingulate gyrus. In the group of patients, an increase of activity appeared in the upper part of the frontal area (B10), which is responsible for keeping the superior goal in mind, during processing of information of secondary importance.

There were few studies comparing working memory functions, measured by N-back test, in patients with bipolar disorder and healthy subjects. Report of the study by Harkavy-Friedman et al [23] indicates the presence of disturbances in the working memory measured by N-back test in patients with depression compared to healthy subjects. In the study by Drapier et al [24], patients in remission came out worse in the N-back test, version 2 and 3 back, than healthy subjects. Similar results were obtained in Adler's et al [25] studies, showing that patients scored worse in the 2 back version as compared to healthy subjects. On the other hand, in the studies by Monks et al [26], there were no statistically significant

differences in the 2-back test in patients with bipolar disorder and healthy subjects.

In the FAS test, measuring phonetic verbal fluency, patients with depression came out significantly worse than the control group consisting of healthy individuals. The differences turned out to be very significant ($p = 0.000$). Patients had clear difficulties in evoking in memory the words beginning with a given letter (often, after a few words given, the silence appeared and there were complaints that nothing else came to mind), which reflects the disturbances in the supervisory control of the executive functions. Results are consistent with previous findings that indicate a significantly worse functioning of phonetic verbal fluency measured by FAS test in the group of patients during depression compared to healthy subjects [3,8]. Many studies show worse functioning of verbal fluency in patients with severe episode of depression [27] and in patients with bipolar disorder in remission [28].

The study of the functioning of working memory and executive functions in depressive patients with bipolar disorder has predictive values and broad application. It allows to estimate the cognitive mechanisms of the difficulties faced by patients in daily functioning and it may have a contribution to the development of standards for diagnosis and treatment. My results indicate the presence of distinct disorders of working memory and of some aspects of executive function in depressive patients with bipolar disorder. The results suggest a great need of recognition of these deficits as an essential component of the clinical picture of the disease and necessity to include them in the process of diagnosis and treatment of bipolar disorder. The executive functions form an overriding system responsible for the integration and organization of the course of complex cognitive processes. Thanks to them human behavior becomes planned, deliberate, conscious and selective as well as flexible and controlled [29]. The executive functions and working memory play a very important role in everyday life, as they allow people to perform tasks and to satisfy needs and to adapt to changing environmental conditions and to cope with the requirements effectively. Disorders of executive function and working memory worsen psychosocial and occupational functioning and ex-

pose patients to experience failure and stress, which in turn can contribute to an onset of a next episode of illness. Treatment of patients with bipolar depression should take into account not only the stabilization of the mood, but also an improvement in cognitive function, which may occur as a result of neuropsychological rehabilitation and / or drug therapy.

It is impossible to exclude the impact of medications on cognitive functioning in patients with bipolar disorder. Undoubtedly, drugs are interfering condition, especially when comparing cognitive functioning of patients receiving medicines and healthy controls. An ideal solution would be to examine cognitive functioning of patients who do not take drugs, but in practice this is impossible because pharmacotherapy is a standard treatment of bipolar disorder, and it would be unethical to leave the suffering patient without treatment or delay it. On the other hand many studies report improvement of cognitive function after pharmacological treatment [8].

CONCLUSIONS

1. In the group of patients in the phase of depression, there were no statistically significant correlation between the intensity of depressive symptoms and cognitive functioning.
2. In patients with bipolar disorder who are in the phase of depression, compared to healthy subjects, the presence of distinct cognitive deficits in different types of working memory as well as in certain aspects of executive functions can be observed. On the other hand, there was no disturbance observed in the area of the executive functions measured by the WCST test (ability to formulate logical concepts and plasticity of thinking).
3. In patients with bipolar depression cognitive assessment should be taken into account in the diagnosis and the disturbances in executive functions and working memory should be treated with neuropsychological rehabilitation and / or pharmacotherapy.

REFERENCES

1. Robinson LJ., Ferrier N. Evolution of cognitive impairment in bipolar disorder: a systematic review of cross-sectional evidence. *Bipolar Disorders*. 2006; 8: 103-116.
2. Goswami U., Gulrajani C., Moore P.B., Varma A., Young A.H., Khastgir Sharma A.N., Ferrier I.N. (2002). Neurocognitive decline in bipolar mood disorder: role of mood stabilizers. *Journal of Psychopharmacology*, 16, A45.
3. Basso M., Neel J., Bornstein R.A., Lowery N., Purdie R. Neuropsychological impairment among manic, depressed, and mixed-episode inpatients with bipolar disorder. *Neuropsychology*. 2002; 16(1): 84-91.
4. Dixon T., Kravarity E., Frith C., Murray R.M., McGuire P.K. Effect of symptoms on executive function in bipolar illness. *Psychological Medicine*. 2004; 34(5): 811-821.
5. Gruber S., Rathgeber K., Braunig P., Gauggel S. Stability and course of neuropsychological deficits in manic and depressed bipolar patients compared to patients with major depression. *Journal of Affective Disorders*. 2007; 104: 61-71.
6. Mahli G.S., Ivanowski B., Hadzi-Pavlovic D., Mitchell P.B., Vieta E., Sachdev P. Neuropsychological deficits and functional impairment in bipolar depression, hypomania and euthymia. *Bipolar Disorders*. 2007; 9: 114-125.
7. Martinez-Aran A., Vieta E., Colom F., Reinares M., Benabarre A., Torrent C., Goikolea J.M., Corbella B., Sanchez-Moreno J., Salamero M. Neuropsychological performance in depressed and euthymic bipolar patients. *Neuropsychobiology*. 2002b; 46(supp 11): 16-21.
8. Martinez-Aran A., Vieta E., Reinares M., Colom F., Torrent C., Sanchez-Moreno J., Benabarre A., Goikolea J.M., Comes M., Salamero M. Cognitive function across manic or hypomanic, depressed and euthymic states in bipolar disorder. *American Journal of Psychiatry*. 2004b; 161: 262-270.
9. Dolan R.J., Bench C.J., Brown R.G., Scott L.C., Frackowiak R.S. Neuropsychological dysfunction in depression: the relationship to regional cerebral blood flow. *Psychological Medicine*. 1994; 24(4): 849-850.
10. Hamilton M. A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry*. 1960; 23: 56-62.
11. Bowie CR., Harvey PD. Administration and Interpretation of Trail Making Test. *Nature Protocols*. 2006; 1(5): 2277-2281.
12. Heaton RK., Chelune G.J., Talley J.L., Kay G.G., Curtiss G. Wisconsin Card Sorting Test. Manual. Revised and expanded. USA: Psychological Assessment Resources, Inc;1993.
13. Ruff R.M., Light R.H., Parker S.B., Levin H.S. Benton controlled oral word association test: Reliability and updated norms. *Archives of Clinical Neuropsychology*. 1996; 11(4): 329-338.
14. Bearden CE., Glahn DC., Monkul ES., Barrett J., Najt P., Villareal V., Soares J.C. Patterns of memory impairment in bipolar disorder and unipolar major depression. *Psychiatry Research*. 2006; 142(2-3): 139-150.
15. Chaves OC, Lombardo LE, Bearden CE, Woolsey MD, Martinez DM, Barrett JA, Miller AL, Velligan DI, Glahn DC. Association of clinical symptoms and neurocognitive performance in bipolar disorder: a longitudinal study. *Bipolar Disord*. 2011; 13(1): 118-123.
16. Mahurin R.K., Velligan D.I., Hazleton B., Davis J.M., Eckert S., Miller A.L. Trail Making Test errors and executive function in schizophrenia and depression. *The Clinical Neuropsychologist*. 2006; 20: 271-288.
17. Nęcka E., Orzechowski J., Szymura B. *Psychologia poznawcza*. Warszawa: ACADEMICA Wydawnictwo SWPS, PWN 2007.
18. Blumberg HP., Leung HC., Skudlarski P., Lacadie CM., Fredericks CA., Harris BC., Charney DS., Gore JC., Krystal JH., Peterson BS. A functional magnetic resonance imaging study of bipolar disorder: state – and trait-related dysfunction in ventral prefrontal cortices. *Archives of General Psychiatry*. 2003; 60(6): 601-609
19. Kronhaus DM., Lawrence NS., Williams AM., Frangou S., Brammer MJ., Williams SCR., Andrew ChM., Phillips ML. Stroop performance in bipolar disorder: further evidence for abnormalities in the ventral prefrontal cortex. *Bipolar Disorders*. 2006; 8(1): 28-39.
20. Frangou S., Dakhil N., Landau S., Kumari V. Fronto-temporal function may distinguish bipolar disorder from schizophrenia. *Bipolar Disorders*. 2006; 8, 47-55.
21. Borkowska A., Rybakowski JK. (2001). Neuropsychological frontal lobe tests indicate that bipolar depressed patients are more impaired than unipolar. *Bipolar Disorders*. 3: 88-94.
22. Frangou S., Donaldson S., Hadjulis M., Landau S, Goldstein SH. The Maudsley Bipolar Disorder Project: executive dysfunction in bipolar disorder I and its clinical correlates. *Biological Psychiatry*. 2005; 58(11): 859-64.
23. Harkavy-Friedman JM., Keilp JG., Grunebaum MF., Sher L., Printz D., Burke AK., Mann JJ., Oquendo M. Are BDI and BDII suicide attempters distinct neuropsychologically? *Journal of Affective Disorder*. 2006; 94: 255-259.
24. Drapier D., Surguladze S., Marshall N., Schulze K., Fern A., Hall M.H., Walshe M., Murray RM., McDonald C. (2008). Genetic liability for bipolar disorder is characterized by excess frontal activation in response to a working memory task. *Biological Psychiatry*. 2008; 64(6): 513-520.
25. Adler CM., Holland SK., Schmithorst V., Tuchfarber M.J., Strakowsski SM.. Changes in neuronal activation in patients with bipolar disorder during performance of a working memory task. *Bipolar Disorder*. 2004; 6 (6): 540-549.
26. Monks P.J., Thompson J.M., Bullmore E.T., Suckling J., Brammer M.J., Williams S.C., Simmons A., Giles N., Lloyd A.J., Harrison C.L., Seal M., Murray R.M., Ferrier I.N., Young A.H., Curtis V.A. A functional MRI study of working memory task in eu-

- thymic bipolar disorder: evidence for task-specific dysfunction. *Bipolar Disorder*. 2004; 6(6): 550-564.
27. Henry JD., Crawford JR. A meta-analytic review of verbal fluency deficits in depression. *Journal of Clinical and Experimental Neuropsychology*. 2005; 27: 78-101.
28. Rocca CC. de Almeida., Macedo-Soares MB., Gorenstein C., Tamada RS., Isler C.K., Dias RS., Almeida K.M., Schwartzmann AM., Amaral JA., Lafer B. Verbal fluency dysfunction in ethymic bipolar patients: A controlled study. *Journal of Affective Disorders*. 2008; 107(1-3): 187-192.
29. Jodzio K. *Neuropsychology of intentional action. Concepts of executive functions*. Warsaw: Wydawnictwo Naukowe SCHOLAR. 2008.