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Mental rotation task in bipolar disorder

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Summary

Aim. Bipolar disorder (BD) significantly affects level of cognitive and motor functioning. Studies on cognitive function in BD shows i.a. deficits in visuospatial processing and visuospatial memory. However, studies have not used Mental Rotation Task to evaluate these functions so far. Our aim is to introduce this method to assess abovementioned deficits in euthymic BD patients.

Method. 31 euthymic BD patients and 27 healthy volunteers matched for age and years of education were recruited. All participants performed digital version of Mental Rotation Task. In this task, participants were asked to compare two figures rotated against each other and declare its similarity or difference indicating whether the figures are identical or whether they constitute their own mirror image.

Results. The test revealed significantly longer reaction times in the group of BD patients when images were rotated by – 90, – 45, 45, 90 degrees, or not rotated at all. There was no significant difference in condition of – 135, 135 or 180 degrees. The accuracy rate was significantly lower in the patient group than in the control group for the entire test and in each condition. The correlation between the average response time and the accuracy rate turned out to be insignificant.

Conclusions. Our results are consistent with studies presenting visuospatial deficits in bipolar disorder. In this study we show for the first time that mental rotation deficits are present in euthymic state of BD patients.

Key words: visuospatial processing, affective disorders, PEBL

Introduction

Mental rotation is the ability of the human mind to create mental representations of two – and three-dimensional objects, and rotate the imagined object in space. The test using mental rotation was first presented by Shepard and Metzler [1]. The task is to present the subjects with a pair of objects, rotated against one another by a specific degree. The subject is assessed on accuracy and speed of distinguishing whether presented images are the same, or they are mirror images (enantiomorphs). The computer version of this test, available in the Psychology Experiment Building Language (PEBL) test battery [2], provides the ability to measure response time with even greater accuracy. Mental rotation task presumes sequential cognitive processing, divided into certain stages: creating a mental image of an object, rotating the image mentally until it is possible to draw a comparison, making the comparison, deciding whether the objects are the same or not, and reporting the decision [3].

Evidence shows that both manic and depressive episodes in bipolar disorder (BD) have a significant long-term effect on brain function and its structures. The most significant changes observed in the course of these episodes in neuroimaging studies include changes in the volume and function of areas such as the prefrontal cortex [4], basal ganglia (e.g., caudate nucleus) [5] and the cerebellum [6]. They increase with the duration of the illness [7] and lead to impairment of cognitive and motor function [8–16].

The body of research into cognitive functions of BD patients, including various aspects of visuospatial processing and visuospatial memory, is growing. Data show such decline both in euthymia [17–19], and during manic or depressive episodes [17, 20]. Visuospatial working memory were assessed using the Delayed Matching to Sample Test [21], VS-N-Back task [19], and visuospatial measures from the Cambridge Neuropsychological Test Automated Battery (CANTAB), among others, Spatial Working Memory Test [21], Spatial Recognition Test, Spatial Span Test [20, 21], while visual searching speed, visual scanning and other visuospatial deficits were evaluated using the Judgement of Line Orientation and the Trail Making B [17].

Despite many neuropsychological paradigms having been tested on BD patients, no published study described deficits using the mental rotation paradigm. We believe that examining BD patients' performance in this task might improve the understanding of clinical picture of the illness associated with cognitive functioning in BD.

Methodology

Participants

In this study we enrolled 31 patients meeting DSM-5 Criteria for BD [22–24] and 27 healthy volunteers. Among patients with BD, 16 people met criteria for type I and 17 for type II. The participants were all right-handed, as measured by the Neurological Evaluation Scale (NES) [14, 25]. All patients were recruited from the Department of Adult Psychiatry of the University Hospital in Krakow.

Both outpatients and those admitted to the hospital, were in the state of symptomatic remission. Patients from the hospital were examined one day before their discharge. Inclusion criteria were as follows: euthymia (defined as <11 points in the Montgomery-Åsberg Depression Rating Scale – MADRS [26] and <5 points in the Young Rating Scale for Mania – YMRS [27]) and therapy with dibenzoxazepine antipsychotic drugs (olanzapine, clozapine, quetiapine). Patients treated with mood stabilizers – lamotrigine or valproic acid – were also included in the study. Those medications provide a comparable profile of potential neurological side effects and thus the group was relatively homogenous in terms of pharmacotherapy. Exclusion criteria were as follows: a history of alcohol or drug abuse, severe, acute or chronic neurological and somatic diseases, severe personality disorders, and pharmacological treatment other than described above.

The control group comprised of mentally healthy volunteers, recruited via authors' social network. Interviewed by an experienced psychiatrist, they all reported a negative history of mental and neurological disorders thus meeting the inclusion criteria of the study. The patient and control groups were matched for age and years of education (Table 1).

Table 1. **Sample characteristics**

Group	BD	Healthy controls
Age (mean age ± SD)[a]	41.97 ±14.36	38.93 ± 21.69
Sex (men/women)[b]	6/25	13/14
Years of education (mean ± SD)[c]	15.71 ± 2.16	15.72 ± 1.72
Duration of treatment (mean ± SD)	11.07 ± 7.67	-
Antipsychotic medication (number of patients, mg, mean daily doses ± SD)		
Clozapine	n = 2 250.00 mg ± 70.71	-
Olanzapine	n = 6 14.17 mg ± 4.91	-
Quetiapine	n = 17 382.35 mg ± 133.39	-
Normothymic medication (number of patients, mg, mean daily doses ± SD)		
Valproic acid	n = 5 640.00 mg ± 288.10	-
Lamotrigine	n = 2 130.00 mg ± 42.43	-

[a] *T*-test = 0.64; $p = 0.53$; [b] Chi-square test = 5.43; $p = 0.02$; [c] *T*-test = – 0.02; $p = 0.98$

All participants signed a written informed consent to participate in the study. All procedures performed in this study were in accordance with the ethical standards of the Jagiellonian University Bioethics Committee.

Mental Rotation Task

The computer version of mental rotation task used in this study is available in a standard battery of tests in PEBL (Psychology Experiment Building Language) software [2]. The instruction was translated into Polish by the authors of the study, and subsequently an independent reverse translation was performed to assess its relevance. The test instruction was explained to the participants before the test began, according to the original version. During the test, subjects were presented with 64 stimuli, each consisting of a pair of two-dimensional shapes, rotated against one another by – 135, – 90, – 45, 0, 45, 90, 135, or 180 degrees. They were either the same shape, or mirror images. The task was to press the "S" button with their left index finger if the two shapes shown on the screen were same, but rotated against one another, and "D" with their right index button, when they were mirror images of each other (Figure 1).

Figure 1. **Mental rotation task**

Data analysis

The study analyzed intergroup differences in accuracy and reaction time. The reaction time (RT) was calculated as the time from the appearance of the pair of shapes on the screen to the response by pressing either "S" or "D" button. Both RT and accuracy were compared separately for each angle. Because distribution of the obtained results was not normal, Mann-Whitney *U* test, was used.

The relationship between accuracy rate and average response time was assessed using Pearson correlation coefficient. Correlation coefficient was estimated both for the entire test score and scores for each condition, i.e., angles the presented shapes were rotated against one another.

Results

Groups did not differ with respect to age and years of education and variances proved to be homogeneous for both groups. The accuracy rate of the entire test was significantly lower in the patient group than in control group ($p < 0.001$) (Table 2).

Table 2. **Results**

Angle of rotation	Accuracy (average number of correct answers ± SD)		Mann-Whitney *U* test	Mean reaction time (ms ± SD)		Mann-Whitney *U* test
	BD	Healthy controls		BD	Healthy controls	
-135°	5.29 ± 2.02	6.67 ± 1.27	-2.44*	6571 ± 5974	4484 ± 3224	1.13
-90°	5.32 ± 1.56	6.93 ± 1.30	-4.13***	7535 ± 10079	3969 ± 3749	3.02**
-45°	5.13 ±1.94	7.07 ± 1.07	-3.87***	6359 ± 8523	3664 ± 4735	2.20*
0°	5.64 ± 1.87	7.07 ± 1.10	-3.14**	9039 ± 24107	3036 ± 1589	1.98*
45°	5.81 ± 1.60	7.26 ± 1.20	-3.67***	5913 ± 5785	3048 ± 1582	2.49*
90°	5.42 ± 1.84	7.07 ± 1.00	-3.32***	6376 ± 5666	4102 ± 3262	2.17*
135°	5.42 ±1.59	6.52 ± 1.78	-2.78**	6886 ± 7022	5168 ± 8188	1.90
180°	4.90 ±1.74	6.11 ± 1.19	-2.67**	7296 ± 8207	4239 ± 2608	1.23

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

The recorded reaction times were significantly higher in the patient group when images were rotated by – 90 ($p < 0.01$), – 45, 45, 90 degrees, or not rotated at all ($p < 0.05$). When the shapes were rotated against one another by – 135, 135 or 180 degrees, there were no significant differences between groups. The correlation between the average response time and the accuracy rate proved to be insignificant, taking into account both the entire test score and scores for each condition (angle of rotation).

Discussion

Our study is the first one to use Mental Rotation task in evaluating BD patients. Our results are consistent with other studies presenting visuospatial deficits in this disorder. Pan et al. [19] found that in patients in remission the efficiency of processes using visual-spatial working memory deteriorated significantly faster with increased load than in healthy controls. Lower results in euthymic patients have also been demonstrated in the Corsi Block Test (CBT), the Visual Patterns Test (VPT), and other task based on performance of visual working memory [28]. These studies also confirmed the deficits in executive functions in BD [28].

In mental rotation task used in this study, the characteristic distribution of reaction time was observed – its significant increase occurred in the conditions of 0 to 90 degrees. For larger angles of rotation, the response time of patients and healthy

individuals appeared to be equal. There are at least two possible causes of these differences. It can be hypothesized that smaller angle of rotation requires shorter spatial processing than larger angles, but requires full efficiency since the initiation of the processing. If initiation of cognitive processing is impaired, it gives rise to significant time differences between persons with BD and healthy individuals right at the very beginning of the task. However, this assumption does not explain the fact that reaction times even out between group in rotation angles greater than 90 degrees. It can be suggested that when there is less pronounced difference between stimuli – in this case smaller angles of rotation – their differentiation requires longer analysis in the case of people with BD.

It is suspected that mental rotation impairment present in BD may be due to disturbances on neuronal level. In healthy subjects performing mental rotation task, functional Magnetic Resonance Imaging studies (fMRI) show diffuse activity in parietal lobe [29], especially superior parietal cortex, centered in the intraparietal sulcus and extending to the transverse occipital sulcus [30] – areas responsible for creating mental spatial maps, which code intended actions targets' location. There is also activation of precentral gyrus bilaterally [29], especially in supplementary motor area – activation is due to mental simulation of the object manipulation [31], and therefore inherent to performing the task, and not due to necessity of performing a motor action of pressing a button in response to the stimulus. Similar role is ascribed to the inferior frontal cortex [32], that is motor simulation occurring during the task. Parietal cortex, but also basal ganglia (especially caudate nucleus) were activated during mental rotation task in a PET imaging study [33]. Deficits in mental rotation have been also described after damage to right basal ganglia [34]. A recent study using continuous Theta Burst Stimulation to downregulate the cerebellar hemisphere activity found increased reaction times in versions of Mental Rotation task, when the procedure was performed on left cerebellar hemisphere [35]. This suggests cerebellar involvement in the task.

Neuroimaging studies show various structural and functional changes in the above-mentioned regions in BD patients – especially in the prefrontal region [36, 37], as well as parietal region [38] and limbic subcortical structures [39]. In the basal ganglia – particularly in the caudate nucleus – studies show decreased metabolism [40] or increased blood flow [41]. Caudate nucleus has also been found to be enlarged in volume-based morphometry study of BD patients [5]. Differences in activity in supplementary motor area (SMA) in BD patients have been described in the literature, and they consist of increased activation during manic periods, and hypoactivation in depressive episode during the performed task [42]. Also cerebellar structural and functional abnormalities has been shown in BD patients [43]. It should be borne in mind that the limitation of many of those studies was the recruitment of patients during manic or depressive episodes.

Of the cognitive and executive dysfunctions, an aspect to consider are decreased attention and psychomotor speed in BD patients [44]. This decrease of psychomotor speed might affect reaction times in mental rotation task. It should not, however, be

a factor in the accuracy rate, the decrease of which was observed in our study. It also does not explain the presence of differences in reaction time for rotation conditions of 0 to 90 degrees and absence of these differences for rotation conditions of 135 degrees and more.

Another factor that could potentially affect the results of cognitive assessment in BD is impulsiveness. Powers et al. [45] studied the influence of impulsivity in BD patients on cognitive functions. Inverse correlation between the performance in various cognitive tests (cognitive flexibility, verbal fluency, visual scanning, graphomotor speed) and impulsivity was found in DB patients with no history of substance abuse. However, this study did not evaluate visuospatial processing. To our best knowledge, no data, even in healthy subjects, is available to see how impulsivity relates to visuospatial processing, or to Mental Rotation Task in particular. In our study, lack of correlation between average response time and the accuracy rate suggests that patients' worse result was not due to the so-called trade-off between speed and correctness, that is patients' reaction time pattern did not influence the accuracy rate.

It is extremely difficult to assess the effect of pharmacotherapy on task performance. Patients were undergoing pharmacotherapy using only atypical antipsychotics, such as quetiapine, clozapine or olanzapine and mood stabilizers – lamotrigine, or valproic acid. The effects of atypical antipsychotics were studied predominantly in schizophrenia patients, and not BD, and this is mostly the literature on which we base the assumptions about their potential interference with the testing protocol. It is known that atypical antipsychotics cause fewer extrapyramidal side-effects [46], and as such are less likely to influence the results of the tested paradigm. It has been shown in certain neurocognitive studies, that atypical neuroleptics do not affect the participants' performance of the Serial Reaction Time Task [47] and Saccadic Adaptation [48], while the decremental effect was present in the case of classical neuroleptics. However, in a study conducted by Mazhari and Moghadas Tabrizi [49], using Mental Rotation Task in patients with schizophrenia, there was no difference found between groups receiving atypical and typical antipsychotics.

The issue of the effect of pharmacological treatment on cognitive function in BD was addressed by Sweeney et al. [21], who did not find correlation between different classes of antipsychotics and performance in CATNAB test battery. Pavuluri et al. [17] compared medicated euthymic and unmedicated manic patients' cognitive functions, finding no effect of medication on participants' performance. Atagun et al. [50] investigated the effect of lithium and valproate on motor and sensory performance in BD. He found decreased tapping speed associated with valproic acid – an effect which might affect the reaction times in the case of mental rotation task, but not the accuracy rate.

The most significant limitations of this research are: low number of subjects in groups, lack of equinumerous groups in terms of gender, and applied therapy (atypical antypsychotic medication and mood stabilizers). Moreover, to assess the actual deficit of the visuospatial processing, we should examine the drug naive patients, what is im-

possible and ethically questionable in present circumstances. However, as mentioned before, most research prove no impact of atypical antipsychotics or mood stabilizers on visuospatial processing.

Conclusions

Our study is the first one describing mental rotation deficits in patients with BD in euthymia. Our study adds to the growing body of evidence of cognitive impairments persisting in BD patients even in euthymia.

Conflict of interests – none to declare. Authors' contributions – all authors contributed equally to the paper.

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