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Brief report

Cognitive inconsistency in bipolar patients is determined by increased intra-individual variability in initial phase of task performance

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ABSTRACT

Background: Bipolar patients show high intra-individual variability during cognitive processing. However, it is not known whether there are a specific fluctuations of variability contributing to the overall high cognitive inconsistency. The objective was to compare dynamic profiles of patients and healthy controls to identify hypothetical differences and their associations with overall variability and processing speed.
Methods: Changes of reaction times iSD during processing speed test performance over time was measured by dividing the iSD for whole task into four consecutive parts. Motor speed and cognitive effort were controlled.
Results: Patients with BD exhibited significantly lower results regarding processing speed and higher intra-individual variability comparing with HC. The profile of intra-individual variability changes over time of performance was significantly different in BD versus HC groups: $F(3, 207)=8.60$, $p < 0.0001$, $\eta_p^2=0.11$. iSD of BD patients in the initial phase of performance was three times higher than in the last. There was no significant differences between four intervals in HC group. Inter-group difference in the initial part of the profiles was significant also after controlling for several cognitive and clinical variables.
Limitations: Applied computer version of Cognitive Speed Test was relatively new and, thus, replication studies are needed. Effect seen in the present study is driven mainly by the BD type I.
Conclusions: Patients with BD exhibits problems with setting a stimulus-response association in starting phase of cognitive processing. This deficit may negatively interfere with the other cognitive functions, decreasing level of psychosocial functioning, therefore should be explored in future studies.

1. Introduction

Recent research has demonstrated that patients with bipolar disorder (BD), and to a lesser extent with other mood disorders, are characterized by significant disturbances within the dynamic dimensions of information processing, such as cognitive speed (Antila et al., 2011; Bearden et al., 2001; Bora et al., 2009). Additionally, cognitive processing speed, as typically measured with the Digit Symbol Tests (see Wechsler, 1997), is not only substantially impaired in BD patients, but it also significantly contributes to a broad range of cognitive dysfunctions in this group which differentiated patients and healthy controls (Antila et al., 2011). It was also demonstrated that the processing speed might be an important candidate for endophenotype of the disease (Daban et al., 2012). Further, likely as a result of disturbances within the dynamics of information processing, these patients' both cognitive and psychomotor performance is often intra-individually variable, as expressed by a standard deviation or variance of individual reaction times sequence (Brotman et al., 2009; Bolbecker et al., 2014; Gallagher et al., 2015). For example, significantly high intra-individual variability in patients with BD was observed in various cognitive and timed measures examining attention (Gallagher et al., 2015), sub-second timing perception (Bolbecker et al., 2011) and in conflict monitoring task (Patino et al., 2013), in which increased IIV was detected in adolescents at risk for bipolar disorder.

Cognitive speed, and processing consistency are associated with structural, functional and metabolic properties of the cerebral white matter (Turken et al., 2008; Fjell et al., 2011; Johnson et al., 2015). This is of vital importance considering well-documented link between

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the abnormalities of the white matter and the response to various forms of treatment (Bollettini et al., 2015) as well as the functional outcome in BD patients (Moore et al., 2001).

Despite a growing interest in processing speed impairment in bipolar disorder, to the best of our knowledge, there has been no research that directly addressed the question of the response time variability changes over time of cognitive speed test performance in this specific population. Further, the general single score of intra-individual variability indicates only the general level of processing stability, and does not allow for the evaluation of probable fluctuations in cognitive consistency over time. Importantly, such fluctuations in cognitive consistency may then contribute to a generally higher intra-individual variability in BD patients. Therefore, the purpose of the present study was to investigate temporal profiles of intra-individual variability during the performance of a cognitive speed test in a group of patients with BD and demographically comparable healthy controls. Specifically, we aimed at identifying potential intra-profile group differences, which may contribute to differences in overall results of processing speed test and intra-individual variability. Due to the psychopathological specificity of studied group, several clinical variables were controlled.

2. Methods

2.1. Participants and procedure

All patients with BD were enrolled in the statutory research of the Department of Clinical Neuropsychiatry at the Medical University of Lublin, Poland. Patients were diagnosed with BD according to DSM-IV-TR criteria. In the time of the assessment carried by certified clinical psychiatrist, all were in a clinical remission state (Hypomania Check List, 32 R1 version [HCL-32] (Angst et al., 2005) score ≤14, and Beck Depression Inventory ≤16 (Beck and Steer, 1993). Participants with a history of alcohol or substance abuse, neurological illnesses or neurodegenerative disorders, mental retardation as well as those actually treated with benzodiazepines were not included the study. The same criteria were applied to healthy controls who were selected by pairs with patients. Additionally, none of the controls suffered form psychiatric problems or had a first-degree relative with a psychiatric disorder. From the initial group of 50 patients, 3 individuals did not obtain the minimum score in the Reliable Digit Span Test (Meyers and Volbrecht, 1998), 2 did not complete the main cognitive speed task, and 3 had records indicating changes in clinical diagnosis. Thus, these 8 patients were excluded from the analyses.

The study was conducted during two meetings. During the first meeting, the clinical evaluation was performed, whereas mood and cognitive assessment was carried out during the second meeting. Both patients with BD (n=42) and controls (n=42) did not differ demographically, except for occupational status (see Table 1). Patients and controls gave written informed consent before entering the study. Ethical approval for the study was granted by the local Bioethics Committees of Medical University of Lublin.

2.2. Cognitive testing

All participants completed the computer version of Cognitive Speed Test (eCST) designed on the basis of Symbol Coding/Digit Symbol and other analogues tests being a part of various neuropsychological batteries, including WAIS (Wechsler, 1997), and BACS (Keefe et al., 2004), as a tablet software developed in cooperation between the Medical University of Lublin, and Lublin University of Technology. Development of the original assessment tool was necessary to get all the raw data containing temporal parameters of task performance, which was the main material for the analysis. To all study participants, the test was displayed on the same hardware (Lenovo Yoga 2 tablet with 13,3″ screen, resolution Quad HD 2560×1440 IPS, Android™ 4.4 system). The detailed description of the test was concluded in the Supplementary materials.

Table 1
Demographic, clinical, pharmacological and cognitive variables.

Variables	HC (n=42)	BD (n=42)	*p*-Value
Demographic and Clinical:			
Age (mean years)	29.04	32.50	n.s.[a]
Gender (% female)	54.3%	60%	n.s.[b]
Employment (% employed)	73%	43%	0.001[b]
Education (mean, yrs)	14.43	13.55	n.s.
Parental education (mean, yrs)	12.26	11.35	n.s.
Duration of illness (mean, months)	0	59.37	
Number of hospitalizations (mean)	0	3.65	
Beck Depression Inventory (mean, total)	2.5	14.27	< 0.0001
HCL-32[c] (mean, total)	3.1	12.37	< 0.0001
BD type I (%)	0%	65%	
BD type II (%)	0%	35%	
Pharmacological:			
Number of medications (mean)	0	1.65	
Anticonvulsants (% using)	0%	57%	
Atypical antipsychotics (% using)	0%	42%	
Antidepressants (% using)	0%	25%	
Lithium (% using)	0%	15%	
Cognitive:			
RDS[d] (mean, total)	11.65	10.60	n.s.
FTT[e] (mean, 5 trials)	55.30	48.02	< 0.001
Processing speed (mean, number of processed stimuli)	83.17	43.70	< 0.0001
Reaction time (mean, milliseconds)	1133.98	2171.37	0.0006
Intra-individual variability (mean, iSD)	384.79	1784.07	< 0.0001

[a] Student's *t*-test used to compare group means for dimensional variables, 2-tailed p-values.
[b] Fisher's Exact Test used to compare categorical variables.
[c] Hypomania Check List, 32R1 version (Angst et al., 2005).
[d] Reliable Digit Span (Meyers and Volbrecht, 1998).
[e] Finger Tapping Test (PARINC® apparatus).

The cognitive effort was assessed with the Reliable Digit Span method, with ≤7 point. cutoff. Of note, according to the neuropsychological literature (Meyers, Volbrecht, 1998), this symptom validity test may not only be used to control for hypothetical insufficient effort put in completion of cognitive tasks but also for the inclusion criteria, as in the present study.

Manual motor speed was assessed with the Finger Tappig Test, mechanical PARINC® apparatus was used and procedure of assessment was conducted according to Reitan and Wolfson (1985) instruction.

2.3. Data analysis

The main eCST outcome was a set of data representing such parameters as: reaction times, number of stimuli processed during given time period, and indicator of intra-individual variability, expressed as an individual Standard Deviation (iSD) from sequence of valid responses. With the data depicting all reaction times, it was possible to conduct an analysis of the iSD variability over time of the performance. Due to the fact that most patients processed approximately around 40 stimuli, the rows of their reaction times (RT), enabling the calculation of the iSD for whole task, have been divided into four parts. In this way, the iSD was calculated for the first ten RT's, and a second set of ten RT's and further divided into two consecutive intervals. Mixed model repeated measure ANOVA (group x within-profile variability) with η_p^2 as an effect size indicator, the Bonferrori correction for multiple comparisons and, in case of comparison significance, the Bonferroni's post hoc test for identifying results generating differences in ANOVA model was used. Lastly, in order to control possible impact of side variables (age, education, RDS, FTT, scales of mood disorders) on differences between intra-individual