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An association between affective lability and executive functioning in bipolar disorder

Sofie Ragnhild Aminoff [a,b,*], Jimmy Jensen [a,c], Trine Vik Lagerberg [b], Tone Hellvin [a,b], Kjetil Sundet [b,d], Ole A. Andreassen [a,b], Ingrid Melle [a,b]

[a] Institute of Clinical Medicine, University of Oslo. P. O. Box 1171 Blindern, N-0318 Oslo, Norway
[b] Psychosis Research Unit, Division of Mental Health and Addiction, Oslo University Hospital, Ullevål Hospital Building 49, P.O. Box 4950 Nydalen, N-0424 Oslo, Norway
[c] Department of Psychiatry and Psychotherapy, Charité Universitätsmedizin, Berlin, Germany
[d] Department of Psychology, Faculty of Social Sciences, University of Oslo, P. O. Box 1094 Blindern, N-0317 Oslo, Norway

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ABSTRACT

Studies suggest altered affect regulation manifested by affective lability in manic/mixed and euthymic states in patients with bipolar disorder (BD). Altered affect regulation may arise from disturbances in interactions between the cognitive and the emotional brain networks. However, the relationship between affective lability and executive function has not previously been studied. Our aim was to investigate affective lability, as measured with the Affective Lability Scale (ALS) in patients with BD ($N=32$) compared to healthy controls (HC) ($N=60$), and its relationship to executive functioning. We found significantly higher ALS scores in the BD than in the HC group, indicating a higher degree of affective lability in patients with BD. Subsample analysis revealed a significant positive relationship between affective lability and semantic set shifting abilities in BD only. These findings suggest that higher levels of affective lability compared with controls are a trait as well as state dependent in BD, and that disturbed affective lability may arise from an aberrant interaction between cognitive and emotional brain networks.

1. Introduction

Bipolar disorder (BD) is a severe mental disorder estimated to affect approximately 1% of the population (Merikangas et al., 2011). The disorder is characterized by manic, depressive and euthymic episodes. Although emotional disturbances are central, there has been little systematic research on emotion processing in individuals with BD (Johnson et al., 2007). Existing studies have mainly focused on emotion perception (Rocca et al., 2009), and less on emotion or affect regulation (Wessa and Linke, 2009). Affect dysregulation may appear as affective lability, or frequent and intense fluctuations in affect in response to both pleasant and unpleasant events (Thompson et al., 2011). Studies suggest heightened affective lability and intensity both in manic and mixed episodes (Henry et al., 2003) as well as trait affective lability in euthymic episodes in patients with BD (Henry et al., 2008). These findings have not yet been replicated.

It has been suggested that problems in emotion processing may be influenced by cognitive dysfunctions and ensuing disturbances in the interactions between the cognitive and emotional brain networks (Phillips et al., 2003). The prefrontal cortex and its related neural circuitry are critically involved both in executing many of the components underlying executive function (Walshaw et al., 2010) and in automatic affect regulation (Phillips et al., 2003). One hypothesis is that the clinical picture in BD in part can be understood as the result of an impairment in the cognitive control of emotion (Green et al., 2007). Cognitive control is considered one aspect of executive function, a cognitive system that resolves conflicts in cognitive processing, enabling adequate performance in the face of distraction (Melcher et al., 2008). Studies using interference control to measure executive function show that patients with BD display executive dysfunction on a group level (Arts et al., 2008; Bora et al., 2009). In the literature, there are few direct investigations of cognitive–emotional interactions in patients with BD (Malhi et al., 2005) and to our knowledge there are no studies investigating a possible relationship between executive function and affective lability.

The objective of the current study is to address the possible underlying mechanisms of affective lability by investigating the relationship between affective lability and executive functioning in a sample of stable, recently diagnosed patients with BD, compared with an age- and gender-matched group of healthy controls (HC). We aim to answer the following questions: Are there

* Corresponding author at: Psychosis Research Unit, Division of Mental Health and Addiction, Oslo University Hospital–Ullevål Hospital, Building 49, P.O. Box 4950 Nydalen, N-0424 Oslo, Norway. Tel.: +47 93 62 86 15; fax: +47 23 02 73 33.
E-mail address: s.r.aminoff@medisin.uio.no (S.R. Aminoff).

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differences in the levels of affective lability between HC and BD, and is there a relationship between affective lability and measures of executive functioning?

2. Methods

2.1. Subjects

The participants are part of the ongoing Thematically Organized Psychosis (TOP) study sample consecutively recruited (November 2006–September 2009) from outpatient and inpatient units of the major hospitals in Oslo, Norway. Inclusion criteria for the main study were age between 18 and 65 years, a diagnosis of DSM-IV BD, IQ >70, and no history of moderate/severe head injury or of neurological disorders. For the current study, we included consecutive patients that had completed the Affective Lability Scales (ALS) (Harvey et al., 1989) and were clinically stable without signs of severe depression (a score of <30 (Rush et al., 2000) on the Inventory of Depressive Symptomatology-Clinician rated (IDS-C)(Rush et al., 1996)) or mania (a score of <15 (Merikangas et al., 2007) on the Young Mania Rating Scale (YMRS) (Young et al., 1978)). This resulted in a patient group of 32 (BD type I, $n=26$, BD type II $n=4$, and BD not otherwise specified $n=2$) (Table 1), for the first research question. The majority of patients ($n=22$, 69%) were referred to the study at the time of their first treated manic episode.

The patients' neurocognitive function was assessed at inclusion to the study and after 1 year. Clinical status was assessed at shorter intervals with the ALS completed as soon as possible after the clinical episode. ALS was completed at inclusion ($n=8$), at 6 months ($n=11$) or at 1 year ($n=13$). We included only patients with simultaneous assessments of neurocognition and affective lability for the second research question, resulting in a sub-sample of $n=12$ stable patients. These subjects did not differ from the remaining 20 regarding demographical variables, IQ measures or current mood symptoms. In this sub-sample the majority ($n=10$) were euthymic (IDS-C≤13 and YMRS≤8) and ($n=10$) first episode patients.

Table 1
Sample characteristics.

	Bipolar disorder	Healthy controls	Group comparisons
	($N=32$)	($N=60$)	
Sex, *N* (%)			$\chi^2(1,92)=0.00, p=1.0$
Males	11 (34)	20 (33)	
Females	21 (66)	40 (67)	
Age (years), mean ± S.D.	30 ± 10	32 ± 10	$t(90)=1.01$, $p=0.315$
Md (range)	27 (18–59)	31.5 (19–56)	
Education (years), mean ± S.D.	14 ± 2	14.5 ± 2	$t(50)=1.62$, $p=0.111$
NART IQ, mean ± S.D.	112 ± 5	113 ± 5	$t(81)=0.59$, $p=0.560$
Diagnostic subgroup, *N* (%)			
Bipolar I disorder	26 (81)		
Bipolar II disorder	4 (12)		
Bipolar disorder, NOS	2 (6)		
Age at onset (years), mean ± S.D.	22 ± 8		
Time since first adequate treatment (years), *Md* (range)	1 (0–23)		
Duration of illness (years), *Md* (range)	4.5 (0–30)		
Polarity of presenting episode, *N* (%)			
Depressive	17 (53)		
Elevated/mixed	15 (47)		
History of psychosis, *N* (%)	27 (84)		
Symptom/function measures at the time of ALS			
GAF-F, mean ± S.D.	61 ± 12		
GAF-S, mean ± S.D.	64 ± 11		
IDS, mean ± S.D.	12 ± 9		
YMRS, mean ± S.D.	3 ± 4		
Medication at the time of ALS completion			
2nd generation antipsychotic, *N* (%)	10 (32)		
Antidepressant, *N* (%)	8 (26)		
Mood stabilizer, *N* (%)	19 (61)		

The HC group was drawn randomly from the statistical population registers of the Oslo region and contacted by mail. Participants were screened for history of physical and mental disorders, head injury, ongoing drug abuse and family history of severe mental disorders. There is no known gender effect on affective lability (Harvey et al., 1989) while the effect of age has not been investigated. We included two gender- and age-matched (±6 years) healthy controls per patient; four were later excluded due to history of severe head trauma or history of depression in close family leaving $n=60$ in the HC group. All assessments were administered at inclusion. There were no differences in age, education or IQ between the HC and BD groups (Table 1).

The Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate approved the study. Participants' written, informed consent was obtained.

2.2. Assessments

2.2.1. Clinical assessment

Patients were assessed by MDs, psychiatrists or clinical psychologists who had completed the TOP study's training and reliability program. Diagnostic assessments were based on the Structural Clinical Interview (SCID-I) for DSM IV (American Psychiatric Association, 1994). A good interrater reliability for diagnostic categories in the TOP study has previously been reported with a kappa of 0.77 (95% confidence interval = 0.60–0.94) (Ringen et al., 2008). History of psychosis, polarity of first presenting episode and age at onset were determined from the SCID interview. Depressive symptoms were measured by the IDS-C and manic symptoms by the YMRS. Global functioning and symptoms were assessed by the split version of the Global Assessment of Functioning scale (GAF) (American Psychiatric Association, 1994; Pedersen et al., 2007). Subjects in the control group were screened with the Primary Care Evaluation of Mental Disorders (Spitzer et al., 1994).

2.2.2. Assessment of affective lability

Affective lability was measured by the Norwegian version of the Affective Lability Scale (ALS) (Harvey et al., 1989). The ALS is a 54-item instrument where subjects rate their agreement to statements regarding the tendency to shift between what they consider to be their own baseline mood into anger, depression, hypomania and anxiety; as well as their tendency to oscillate between depression and hypomania and between depression and anxiety. Each item is rated on a 4-point scale (0–3) ranging from "very undescriptive" to "very descriptive". The items can be divided into subscales for six dimensions: labile depression, labile hypomania, biphasic oscillation, labile anger, labile anxiety and anxiety-depression oscillation with the total ALS score as the mean. Six patients with ≤2 ALS items missing had their missing items replaced with the mean score for that item across all patients. Internal consistency was good with Chronbach's alpha (α) for total ALS score: 0.97; depression subscale: 0.90; hypomania subscale: 0.86; biphasic subscale: 0.81; anger subscale: 0.67; anxiety subscale: 0.91; anxiety-depression subscale: 0.94; all corresponding closely to that of the original (Harvey et al., 1989). Based on this we used the total ALS score in the analyses.

2.2.3. Neurocognitive assessment

Neurocognitive assessment was carried out by psychologists trained in the standardized three-hour comprehensive neuropsychological test battery. Premorbid IQ was assessed with a Norwegian research version of the National Adult Reading Test (NART) (Sundet and Vaskinn, 2008). Short term and working memory was assessed with the Digit Span Test (total scaled scores) from the Wechsler Adult Intelligence Scale WAIS-III (Wechsler, 2003).

From the Delis-Kaplan Executive Function System (D-KEFS) (Delis et al., 2005) we included the Letter fluency condition phonetic verbal fluency); the Category fluency condition (semantic verbal fluency); and the Category switching condition (semantic set shift) — correct responses and shifts. We also included set loss- and repetition-errors across all three trials in the analyses, as well as individual trial error scores (raw scores). From the D-KEFS we also included the Inhibition and Inhibition/Switching conditions (verbal–interference control and –set shift) from the Color–Word interference test (CW). With the exception of errors in individual trials (without norms) we used age adjusted scale scores ($M=10\pm3$). Set-shifting was additionally measured by the Wisconsin Card Sorting Test (Kongs et al., 2000) where we used *T* scores.

2.2.4. Statistical analysis

All analyses were performed using PASW Statistics, version 18 (SPSS, Inc., 2009, Chicago,IL). For analyses of group differences we used chi square (χ^2) tables for categorical data, *t*-tests for normally distributed data and Mann–Whitney *U* Tests for data with skewed distribution. All tests were two-sided with a $p<0.05$. Bivariate associations were measured through Pearson or Spearman's rho correlations (depending on data distribution) with Bonferroni corrections ($p\leq$set at 0.007). Effect sizes based on correlation coefficients are small (0.10), medium, (0.30) and large (0.50). Due to the small sample size we present associations between affective lability and neurocognition as scatterplots.

3. Results

3.1. Affective lability in BD versus HC groups

Patients with BD ($N=32$) had significantly higher total ALS scores (1.09 ± 0.65) than the control group (0.46 ± 0.36), $U(92)=1.6$,