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Facial recognition deficits as a potential endophenotype in bipolar disorder

Esther Vierck*, Richard J. Porter, Peter R. Joyce

Department of Psychological Medicine, University of Otago, Christchurch, PO Box 4345, Christchurch, New Zealand

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ABSTRACT

Bipolar disorder (BD) is considered a highly heritable and genetically complex disorder. Several cognitive functions, such as executive functions and verbal memory have been suggested as promising candidates for endophenotypes. Although there is evidence for deficits in facial emotion recognition in individuals with BD, studies investigating these functions as endophenotypes are rare. The current study investigates emotion recognition as a potential endophenotype in BD by comparing 36 BD participants, 24 of their 1st degree relatives and 40 healthy control participants in a computerised facial emotion recognition task. Group differences were evaluated using repeated measurement analysis of co-variance with age as a covariate. Results revealed slowed emotion recognition for both BD and their relatives. Furthermore, BD participants were less accurate than healthy controls in their recognition of emotion expressions. We found no evidence of emotion specific differences between groups. Our results provide evidence for facial recognition as a potential endophenotype in BD.

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1. Introduction

BD is considered a highly heritable (Bertelsen et al., 1977; Pauls et al., 1992; Cardno et al., 1999; McGuffin et al., 2003; Kieseppa et al., 2004) and genetically complex disorder (Wang et al., 2005; Craddock and Sklar, 2009). Researchers are attempting to segregate the observed behavioural symptoms into more stable endophenotypes, that is, markers with a clearer genetic link to facilitate genetic research (Gottesman and Gould, 2003). This technique has resulted in promising findings, with several clinical variables being found to show intrafamilial clustering of traits (O'Mahony et al., 2002; Goes et al., 2007) and links to specific genes have been suggested (Goes et al., 2007). Several cognitive functions, such as executive functions and verbal memory, are considered promising candidates for endophenotypes in BD. Such impairments have been found to be independent of mood state (Martínez-Arán et al., 2004; Robinson et al., 2006; Torres et al., 2007; Arts et al., 2008; Bora et al., 2009; Mann-Wrobel et al., 2011; Bourne et al., 2013) and appear to be heritable as BD relatives show similar although often weaker cognitive functioning deficits than BD participants (Zalla et al., 2004; Arts et al., 2008).

Emotional processing has been investigated to evaluate social cognition in BD. Some studies found that BD participants showed emotion recognition deficits when in a manic state (e.g., Lembke and Ketter, 2002; Getz et al., 2003). Similar findings were reported for BD participants in a depressed state (David and Cutting, 1990a, 1990b; Lfnclf and Kfuufs, 2002). In addition, there is evidence for impaired emotion processing in euthymic participants (Harmer et al., 2002; Bora et al., 2005; Pavuluri et al., 2007). Although findings are not consistent in this area, a recent meta-analysis (Samame et al., 2013), concluded that deficits in emotion recognition are evident in all the mood states of BD. Investigations into specific emotional expressions indicate impaired recognition of fear (Lembke and Ketter, 2002; Martino et al., 2011), disgust (Lembke and Ketter, 2002; Malhi et al., 2007), and happiness in BD patients (Almeida et al., 2010) although one study reported a recognition facilitation of disgust (Harmer et al., 2002). These studies evaluated emotion specificity in all three states of BD. A recent meta-analysis was able to confirm a general emotion processing deficit in BD participants, but failed to establish the role of specific emotions (Kohler et al., 2011). Some studies have focused on participants with a history of psychosis, with mixed findings. Daros et al. (2014) investigated emotion recognition in first-episode patients during a psychotic episode and after seven weeks of treatment. At both times happy and sad emotion recognition was impaired. Ruocco et al. (2014) also observed deficits in emotion processing in BD participants with psychosis, but Martino et al. (2011) found emotion recognition deficits to be independent of a history of psychosis. It is thus unclear whether psychosis per se has an impact on emotion recognition in BD.

In addition, emotional recognition deficits have been reported in at risk youth (Brotman et al., 2008a, 2008b) and in euthymic

* Corresponding author. Fax: +64 3 378 6540.
E-mail address: esther.vierck@otago.ac.nz (E. Vierck).

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paediatric participants with BD (Schenkel et al., 2007; McClure et al., 2005), but again findings are not consistent (Pavuluri et al., 2007). Psychotropic medication may influence emotion recognition. Samame et al. (2015) used meta-regression analysis to explore this issue and found a significant association between the recognition of disgust and the use of antipsychotics. Martino et al. (2011) found an association between antipsychotics and benzodiazepines with emotion recognition performance. In contrast, Ruocco et al. (2014) found no connection between antipsychotic use and emotion recognition.

To our knowledge only three studies of emotion recognition included first degree family members. Seidel et al. (2012) explored empathic abilities and found BD participants and their relatives slower than healthy controls in recognising the emotions displayed. Surguladze et al. (2010) reported greater activity in cortico-limbic areas, in response to emotional faces in BD patients and their first degree relatives, compared with healthy controls. These two findings suggest that aspects of emotion recognition may be familial. In contrast Rucco et al. (2014) found no evidence of familiality. They investigated BD participants with a history of psychosis and their first degree relatives. BD participants were less accurate than control participants in labelling angry and neutral emotion expressions but BD relatives did not differ in their performance from controls.

In the current study we examined facial emotion recognition in BD patients, their unaffected 1st degree relatives and a healthy control group. We hypothesised that BD probands and their family members would be less accurate and slower in the recognition of emotional expressions than control participants. We also hypothesised that BD participants with a history of psychosis would be more impaired than BD participants without such a history. We further predicted that certain facial emotional expressions, in particular fear and disgust, would be less well recognised by BD participants and their unaffected relatives than by healthy controls.

2. Methods

2.1. Participants

In total 100 participants took part in this study. Forty of these were healthy control participants (11 males, mean age 36.2 ± 11.3), 36 had BD (9 males, mean age 40.8 ± 11.6), and 24 participants were 1st degree unaffected relatives of the BD participants (7 males, mean age 33.2 ± 13.5). Relatives were mainly siblings (13) and children (7), but there were also four parents. We retained all 36 BD patients mainly to increase power in comparisons including this group, i.e. effects between control and BD participants, although 12 of the BD relatives did not participate as anticipated. The majority of the BD participants were classified as BD-I (32 including 9 males, mean age 42.3 ± 11.5), only eight individuals suffered from BD-II (no males, mean age 35.3 ± 10.5). Ethical approval was received from the Upper South Canterbury (New Zealand) Ethics Committee. BD participants and their relatives were recruited within mental health outpatient clinics, by advertising in the community, and through mental illness support organisations and residential mental health services. Control participants were recruited through advertisement on radio, in newspapers, and in the community. Control participants were screened for mood disorders with questions taken from the Mini International Neuropsychiatric Interview (MINI, Sheehan et al., 1998). They were also asked about any current or past mood disorders or any family history of mood disorder. Any signs of mood disorder either in their own or in their immediate family led to the exclusion of the participant. The demographic data is displayed in Table 1.

Table 1
Demographic data, mood and medication status for all participants.

	BD participants	BD relatives	Healthy controls
	$n=36$	$n=24$	$n=40$
Age (years), mean (SD)	40.8 (11.6)	33.2 (13.5)	36.2 (11.3)
Males *n* (%)	9 (25.0)	7 (29.2)	11 (27.5)
Mood status: *n* (%)			
Euthymic	19 (52.77)	20 (83.33)	40 (100)
Depression:			
Mild symptoms	11 (30.56)	4 (16.67)	
Moderate symptoms	5 (13.89)		
Mixed symptoms:	1 (2.78)		

For all BD participants and their relatives diagnosis was conducted with a modified version of the Structured Clinical Interview for DSM-IV (SCID, First et al., 1995). In addition, we used the Montgomery and Asberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979) to establish mood state in both of these participant groups. We further used the Young Rating Scale for Mania (Y-MRS; Young et al., 1978) to establish symptoms of mania in BD participants. We followed previously used categorisations (Snaith et al., 1986; McElroy et al., 2010) to evaluate scores on these measures. Y-MRS scores in the BD group ranged from 1 to 14, with most participants (13) considered euthymic with scores equal or below 7. One participant scored in the mild range but because this person also showed mild depressive symptom mixed symptomology best described this participant. In BD participants the MADRS ranged from one to 34. Nineteen participants were euthymic (MADRS score: <6), 11 participants showed mild depressive symptoms (MADRS score: 7–19) and five had moderate symptoms (MADRS score: 20–34). Of the 19 euthymic BD participants the information of the last episode was missing for one individual due to an assessment error. Time in months since the last acute phase differed considerably (range 1–300 months) with an average of 37.8 (SD 73.8) months. Twenty-two of the 36 BD participants had experienced psychosis as part of their mood episodes as established following DSM-IV criteria with the SCID. Half of the BD relatives had suffered from depression during their life, but at the time of testing depressive symptoms were rare. MADRS scores for this group ranged from 0-8. Twenty participants were classified as euthymic and four showed very mild symptoms of depression.

The types of medication taken are displayed in Table 1. Most BD participants used several types of medication. Overall, 16 participants used antidepressants, 11 lithium, 10 anticonvulsants, 12 atypical antipsychotics, 6 typical antipsychotics, 5 sleep medication, and 4 benzodiazepine. BD relatives took also a range of medication. Six relatives used antidepressants. One participant of this group suffered from epilepsy and used atypical antipsychotics, anticonvulsants and antidepressants. Another participant had a diagnosis of borderline personality and received atypical antipsychotics and hypnotics.

2.2. Materials

2.2.1. Facial expression recognition task

In this computer-based task faces displaying five of the basic emotions (anger, disgust, fear, happy, and sad) or neutral expressions were used. The faces were taken from the Ekman and Friesen Pictures of Affect Series (Ekman and Friesen, 1976) and were morphed so that each picture contained part of the emotional prototype and part of the neutral expressions. By varying the portions of each of these parts faces with varying intensity of emotional expression were created. Faces used in this study

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