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A voxel-based morphometry study of gray matter correlates of facial emotion recognition in bipolar disorder

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ABSTRACT

Facial emotion recognition (FER) is one of the many cognitive deficits reported in bipolar disorder (BD) patients. The aim of this study was to investigate neuroanatomical correlates of FER impairments in BD type I (BD-I). Participants comprised 21 euthymic BD-I patients without Axis I DSM IV-TR comorbidities and 21 healthy controls who were assessed using magnetic resonance imaging and the Penn Emotion Recognition Test (ER40). Preprocessing of images used DARTEL (diffeomorphic anatomical registration through exponentiated Lie algebra) for optimized voxel-based morphometry in SPM8. Compared with healthy subjects, BD-I patients performed poorly in on the ER40 and had reduced gray matter volume (GMV) in the left orbitofrontal cortex, superior portion of the temporal pole and insula. In the BD-I group, the statistical maps indicated a direct correlation between FER on the ER40 and right middle cingulate gyrus GMV. Our findings are consistent with the previous studies regarding the overlap of multiple brain networks of social cognition and BD neurobiology, particularly components of the anterior-limbic neural network.

1. Introduction

Social cognition is concerned with the cognitive processes underlying the extremely diverse and flexible social behaviors observed in primates (Adolphs, 2009). Among social cognition components, facial emotion recognition (FER) is an essential element in everyday social and interpersonal function (Green et al., 2007; Cusi et al., 2012; Mercer and Becerra, 2013). Social cognitive impairments have been described in euthymic patients with bipolar disorder (BD) (Rocca et al., 2009). Although, some studies did not find FER deficits in euthymic BD patients (Bora et al., 2005; Malhi et al., 2007; Vaskinn et al., 2007; Jogia et al., 2008; Hassel et al., 2009; Almeida et al., 2010), most of the studies and a recent metanalysis reported moderate and stable FER impairments in BD patients (McClure et al., 2003; Bozikas et al., 2006; Summers et al., 2006; Guyer et al., 2007; Brotman et al., 2008; Konarski et al., 2008; Rocca et al., 2009; Derntl et al., 2009; Kohler et al., 2011; Martino et al., 2011; Lahera et al., 2012). These impairments seem to be influenced by a limited number of demographic and clinical factors, such as self-reported depression, age at time of testing and years of education (Kohler et al., 2011). The diversity of results could be related to the heterogeneity of study designs, including sample and task selection (Mercer and Becerra, 2013).

Two neural circuits have been involved in the synergic processing of emotional facial stimuli (Palermo and Rhodes, 2007). The first, face-responsive visual processing circuit has three different functions: recognition of color, shapes and motion (primary areas of the occipital lobe, lateral temporal lobe and posterior parietal cortex) (Matsumoto et al., 2005); categorization of facial features (fusiform gyrus); and extraction of information regarding emotional expression (superior temporal sulcus) (Ishai, 2008). The second, affective circuit is engaged in the evaluation and modulation of emotions and is composed by the pre-frontal cortex (PFC), insula, amygdala (Hariri and Weinberger, 2003), striatum and thalamus (Adolphs, 2009).

Studies have reported brain structural alterations in BD patients, compared with healthy subjects, in components of the

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limbic–thalamic–cortical and the limbic–striatal–pallidal–thalamic–cortical networks (Konarski et al., 2008; Matsuo et al., 2009). These areas are the same ones implicated in FER; therefore, the elucidation of the neuroanatomical correlates of social cognition impairments may contribute to the identification of the neural vulnerability to BD (Cusi et al., 2012). Moreover, in BD patients, functional magnetic resonance imaging (MRI) studies evaluating neural activation during FER, report different activation of ventromedial PFC, cingulate, hippocampus and amygdala, when compared to healthy subjects (Dickstein et al., 2007; Malhi et al., 2007; Hassel et al., 2008, 2009; Pavuluri et al., 2009; Chen et al., 2011). To the best of our knowledge, no studies evaluated the correlation among FER and gray matter volume (GMV) in BD patients using voxel-based morphometry (VBM).

In this study, we aimed to investigate the possible neuroanatomical correlates of FER impairments in euthymic type I BD patients (BD-I). We hypothesized that, compared to healthy subjects, BD patients present FER impairments, GMV changes in FER-related neural networks and that FER performance is correlated to GMV impairments in BD subjects. The aim of this study was to investigate the possible neuroanatomical correlates of FER impairments in euthymic type I BD patients (BD-I).

2. Methods

2.1. Study sample and assessment schedules

We screened 43 BD-I patients aged between 18 and 65 years, and 21 of those fulfilled the inclusion criteria for the study. These patients were compared to 21 healthy subjects. We recruited the patients in the *Núcleo de Transtornos Afetivos* (a tertiary service specialized in Affective Disorders) from the Federal University of Minas Gerais (UFMG) in the city of Belo Horizonte, Brazil. All patients were evaluated by a psychiatrist using the Mini International Neuropsychiatry Interview Plus protocol (MINI-PLUS), and they all met DSM-IV-TR criteria for BD-I. The Research and Ethics Committee of UFMG approved the study, in accordance with the Helsinki Declaration of 1975. Written informed consent was obtained from all the participants after a complete description of the study was provided. All participants were right-handed (scores above 40 on the Edinburgh Inventory) (Oldfield, 1971). We included only BD-I patients in euthymia, defined as a score less than eight on the Young Mania Rating Scale (YMRS) and in the 21-item version of the Hamilton Depression Rating Scale (HDRS21) (Williams,1988; Bozikas et al., 2006). Out of 43 patients initially evaluated, 18 were excluded due to psychiatric comorbidities (10 with anxiety disorders, 8 with alcohol abuse or dependence), 1 due to use of a pacemaker and 3 patients for not being right-handed. We chose to select right-handed, euthymic BD-I patients, without Axis I DSM IV-TR comorbidities, based on the evidence that psychiatric comorbidities and handedness may influence brain morphology (Cusi et al., 2012). One healthy control was excluded due to artifacts during image acquisition.

The healthy subjects were selected from the same community as the BD-I patients. They were evaluated by a psychiatrist using the MINI-PLUS, and those who had current or past Axis I DSM-IV-TR psychiatric disorders or had first-degree relatives with any Axis I DSM-IV-TR psychiatric disorder were excluded.

2.2. Facial emotion recognition assessment

The ER40 is a computerized test that assesses categorical identification of facial expressions of emotion (Fig. 1). We used a Portuguese version of the ER40. Subjects were asked to use a computer mouse to choose the most appropriate emotion label from a list of five (happiness, sadness, anger, fear, or no emotion). Forty square photographs with eight actors with hair were used: eight neutral expressions, four emotional expressions of low intensity and four emotional expressions of high intensity for each one of the four emotions. Across emotional categories, stimuli were balanced for models' gender and ethnicity, with 21 white and 19 non-white faces (Gur et al., 2001).

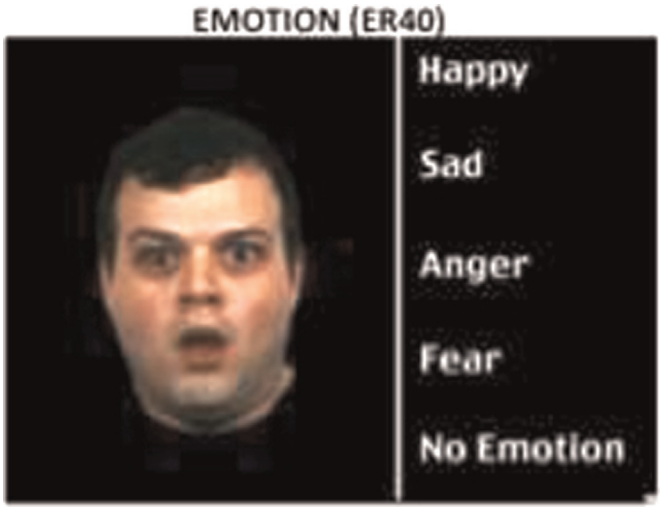

Fig. 1. Example of Penn Emotion Recognition Test (ER40) stimuli (Gur et al., 2010).

2.3. Image acquisition

Imaging data were acquired using a 1.5 T Phillips scanner (Philips Medical Systems, Eindhoven, The Netherlands) using a T1-3D SPGR sequence. Contiguous axial images across the entire brain were acquired with the following parameters: echo time = 6 ms, repetition time = 35 ms, flip angle = 45, acquisition matrix = 288 × 288, and a voxel size of 0.85 mm × 0.85 mm × 1 mm (190 slices).

2.4. Image processing and analysis

The VBM analysis was carried out using Statistical Parametric Mapping, version 8 (SPM8; http://www.fil.ion.ucl.ac.uk/spm) running under Matlab 2009b (http://www.mathworks.com/index.html). Briefly, we first oriented all MRI datasets manually in order to place the anterior commissure at the origin of the three-dimensional Montreal Neurological Institute (MNI) coordinate system. The images were then segmented into gray matter (GM) and white matter partitions using the unified segmentation procedure described by Ashburner and Friston (2005). The Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) algorithm (Ashburner, 2007) was then used to spatially normalize the segmented images; this procedure maximizes the sensitivity and accuracy of localization by registering individual structural images to an asymmetric custom T1-weighted template derived from the participants' structural images rather than a standard T1-weighted template based on a different sample (Ashburner, 2007). These fully normalized images were resliced with trilinear interpolation to a final voxel size of 1.5 × 1.5 × 1.5 mm^3. An additional "modulation" step consisted of multiplying each spatially normalized GM image by its relative volume before and after normalization; this ensured that the total amount of GM in each voxel was preserved. Finally, the resulting GM images were smoothed using an 8-mm isotropic kernel at full width half-maximum (FWHM) to ensure normal distribution of the data as required by subsequent statistical parametric tests.

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