www.elsevier.com/locate/euroneuro

Common and distinct neural correlates of emotional processing in Bipolar Disorder and Major Depressive Disorder: A voxel-based meta-analysis of functional magnetic resonance imaging studies

Giuseppe Delvecchio [a,b], Philippe Fossati [a,c], Patrice Boyer [a,c], Paolo Brambilla [a,d], Peter Falkai [a,e], Oliver Gruber [a,e], Jarmo Hietala [a,f], Stephen M. Lawrie [a,g], Jean-Luc Martinot [a,h], Andrew M. McIntosh [a,g], Eva Meisenzahl [a,i], Sophia Frangou [a,b,*]

[a] European College of Neuropsychopharmacology, Networks Initiative, Neuroimaging Network
[b] Section of Neurobiology of Psychosis, Institute of Psychiatry, King's College London, UK
[c] CNRS USR 3246, Emotion Center & Departement of Psychiatry, GH Pitié-Salpétrière, AP-HP, Université Pierre & Marie Curie, Paris, France
[d] IRCCS "E. Medea" Scientific Institute, Udine, Italy
[e] Department of Psychiatry and Psychotherapy, Georg August University Göttingen, Germany
[f] Department of Psychiatry, University of Turku, Finland
[g] Division of Psychiatry, School of Molecular Medicine, Edinburgh University, Scotland, UK
[h] INSERM CEA Research Unit 1000 "Imaging & Psychiatry", Paris Sud University, Orsay, and Maison de Solenn, Paris Descartes University, Paris, France
[i] Department of Psychiatry and Psychotherapy, Ludwig-Maximilians University, Germany

Abstract

Neuroimaging studies have consistently shown functional brain abnormalities in patients with Bipolar Disorder (BD) and Major Depressive Disorder (MDD). However, the extent to which these two disorders are associated with similar or distinct neural changes remains unclear. We conducted a systematic review of functional magnetic resonance imaging studies comparing BD and MDD patients to healthy participants using facial affect processing paradigms. Relevant spatial coordinates from twenty original studies were subjected to quantitative Activation Likelihood Estimation meta-analyses based on 168 BD and 189 MDD patients and 344 healthy

---

* Corresponding author at: Section of Neurobiology of Psychosis, Institute of Psychiatry, King's College London, De Crespigny Park, London SE5 8AF, UK. Tel.: +44 2078480903; fax: +44 2078480983.
E-mail address: sophia.frangou@kcl.ac.uk (S. Frangou).

controls. We identified common and distinct patterns of neural engagement for BD and MDD within the facial affect processing network. Both disorders were associated with increased engagement of limbic regions. Diagnosis-specific differences were observed in cortical, thalamic and striatal regions. Decreased ventrolateral prefrontal cortical engagement was associated with BD while relative hypoactivation of the sensorimotor cortices was seen in MDD. Increased responsiveness in the thalamus and basal ganglia were associated with BD. These findings were modulated by stimulus valence. These data suggest that whereas limbic overactivation is reported consistently in patients with mood disorders, future research should consider the relevance of a wider network of regions in formulating conceptual models of BD and MDD.

1. Introduction

Bipolar Disorder (BD) and Major Depressive Disorder (MDD) are amongst the leading causes of disability worldwide (Murray and Lopez, 1997). Although syndromal mania is unique to BD, both disorders present with recurrent depressive episodes as well as similar subsyndromal affective symptoms (Judd et al., 2002, 2003; Angst et al., 2010). Evidence from genetic studies also suggests both distinct and common contributions to their aetiology (McGuffin et al., 2003).

Current neurobiological models propose that mood disorders arise from disruption in prefrontal, limbic and subcortical regions (particularly the amygdala/hippocampus, and striatum) that support the adaptive regulation of affect (Savitz and Drevets, 2009). Within this general framework, much research effort in neuroimaging is directed towards identifying overlapping and diagnosis-specific brain abnormalities for BD and MDD. Several reviews and meta-analysis have attempted to summarise and synthesise the available evidence (Savitz and Drevets, 2009; Konarski et al., 2008). In the most recent quantitative meta-analysis (Kempton et al., 2011), we showed that volume reductions in the basal ganglia and hippocampus appear specific to MDD patients and differentiated MDD from BD. We now focus on the neural correlates of emotional processing in BD and MDD, which may relate more directly to the core abnormalities underpinning mood disorders. Our understanding of the neural circuitry involved in emotional processing in healthy individuals is mostly based on studies using facial affect as a probe (Phan et al., 2002; Murphy et al., 2003; Fusar-Poli et al., 2009; Vytal and Hamann, 2010). Facial affect processing is mediated by a distributed neural network that encompasses visual, limbic, and prefrontal regions (Phan et al., 2002; Murphy et al., 2003; Fusar-Poli et al., 2009; Vytal and Hamann, 2010). This network shows significant overlap with that implicated in mood disorders (Savitz and Drevets, 2009). We used Activation Likelihood Estimation (ALE) (Turkeltaub et al., 2002; Laird et al., 2005; Eickhoff et al., 2009), a quantitative meta-analytic approach which allows integration of neuroimaging results across studies, to investigate the neural correlates of facial affect processing in BD and MDD.

The main goals are threefold. First, to consolidate neuroimaging findings associated with emotional processing in patients with BD or MDD and to examine whether meta-analytic synthesis of this empirical evidence aligns with current theoretical models of mood disorders (Cerullo et al., 2009; Savitz and Drevets, 2009). Second, to determine whether stimulus valence modulates disease-related activity within the face processing network based on findings that neural activity and connectivity may differ between BD and MDD in response to positive and negative stimuli (Almeida et al., 2009; Almeida et al., 2010). Third, to identify common and distinct brain functional changes in BD and MDD.

2. Method

2.1. Data sources and inclusion criteria

Studies investigating facial affect processing in either BD or MDD patients were identified through a comprehensive MEDLINE, EMBASE and PsycINFO search of the English-language literature covering publications between January 2000 and December 2010. The search keywords were "mania", "depression", "bipolar disorder", "major depressive disorder" and "facial affect", "emotional processing", "fMRI" and their combinations as well as terms specifying individual facial affect (fear, happiness, sadness, anger and disgust). Additional articles were identified through the reference lists of these papers.

Studies were included if they (a) reported comparisons between patients with BD or MDD with healthy controls (b) employed functional magnetic resonance imaging (fMRI) (c) assessed brain activation by using human facial identities (d) used image subtraction methodology to identify foci of task-related neural changes contrasting an active (emotional faces) and control (neutral faces or shapes) condition, and (e) reported their results in standard stereotactic coordinates (either Talairach or Montreal Neurological Institute [MNI] space).

We excluded studies that (a) used facial affect stimuli to investigate processes not directly involved in emotional processing (e.g. memory, attention), (b) involved non-facial identities such as emotional pictures, (c) grouped together stimuli displaying positive and negative facial affect, and (d) used the same patient sample. The threshold of statistical inference varied but we accepted the results reported as significant based on the criteria of the primary studies.

2.2. Quantitative meta-analytical voxel-based procedure

We investigated facial affect processing in BD and MDD by focusing on the contrast between facial affect and control conditions using Activation Likelihood Estimation (ALE) implemented in GingerALE 2.0.4 (http://brainmap.org/Ale). This ALE version uses a random effect model and weighting for sample size of the original studies (Eickhoff et al., 2009). Coordinates of the foci of activation reported in the primary literature were transformed into Talairach space using the Lancaster transform (icbm2tal tool) in GingerALE. For each study, peaks were modelled as the centre of a 3D Gaussian distribution and a modelled activation (MA) map was then