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Research report

Reduced insight in bipolar I disorder: Neurofunctional and neurostructural correlates
A preliminary study

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ABSTRACT

Background: To correlate measures of insight for own psychopathology to structural and functional brain imaging findings in 21 patients with DSM-IV bipolar I disorder.
Methods: Insight was assessed using the Scale to Assess Unawareness of Mental Disorder (SUMD). Resting single photon emission computed tomography (SPECT) and computed tomography (CT) was conducted in patients and 21 normal comparison subjects matched for age, gender and handedness.
Results: Reduced general insight and symptom awareness, but not symptom attribution, were significantly related to cortical and subcortical atrophy, respectively. No correlations between SPECT and insight measures were identified.
Limitations: Limited sample size and the use of resting state SPECT.
Conclusions: General and symptom awareness were related to measures of brain atrophy but not to neurofunctioning as measured by SPECT. Future research should consider the structure and function of specific cortical regions, including the frontal and parietal cortices.

1. Introduction

The neurological condition of anosognosia is characterised by a seeming lack of awareness of disabilities caused by brain injury or disease (Babinski, 1914). Lewis (1934) postulated that a disturbance of cerebral function may be implicated in loss of insight in both neurological disorders and functional psychoses. It has been demonstrated that 50–80% of patients with schizophrenia show poor insight into their illness (Amador and Gorman, 1998). Based on DSM-IV, one of the major differences between schizophrenia and other psychotic disorders is the lack of insight in schizophrenia. However, insight function is significantly affected in bipolar patients as well, especially during the manic phase but also to some extent in the remitted state (Dell'Osso et al., 2002; Ghaemi and Rosenquist, 2004; Varga et al., 2006).

Little is known about the neurobiological underpinnings of insight deficits in general, and the pathophysiology of bipolar disorder is incompletely understood. In schizophrenia, the potential relationship between prefrontal function and insight has been examined in a number of neuropsychological and structural imaging studies (i.e., Larøi et al., 2000; Flashman et al., 2001; Shad et al., 2004). As in schizophrenia, neuropsychological studies indicate that a selective prefrontal

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(and possibly parietal) dysfunction is present in bipolar disorder (i.e., Goldberg et al., 1995; Olley et al., 2005; Varga et al., 2006), but this does not necessarily imply that a selective structural–biochemical abnormality is present. In a review of CT and MRI studies in the major psychoses, Raz and Raz (1990) found that patients with schizophrenia and affective psychosis did not differ in terms of ventricular enlargement or abnormal widening of the cortical fissures. Bearden et al. (2001) reviewed neuroimaging studies of bipolar patients and found that one of the most prominent findings was the presence of white matter lesions (hyperintensities), located most frequently in the frontal lobes and basal ganglia. According to Strakowski et al. (2005), abnormalities in prefrontal cortical areas, striatum and amygdala seem to exist early in the course of the illness and could possibly predate illness onset. In contrast, abnormalities in the cerebellar vermis, lateral ventricles and other prefrontal regions (e.g., left inferior) appear to develop with repeated affective episodes, and may represent the effects of illness progression and associated factors (Strakowski et al., 2005).

Functional neuroimaging studies have demonstrated distinct alterations of cerebral blood flow during different states of bipolar illness (for reviews see Bearden et al., 2001; Strakowski et al., 2005). For example, Benabarre et al. (2004) found in a recent single photon emission computed tomography (SPECT) study regional decreased uptake of 99mTc-HMPAO in the frontal region and the basal ganglia in 17 bipolar I depressed patients. However, Tutus et al. (1998) found increased rCBF in the left frontal lobe in unmedicated unipolar depressed patients as compared to bipolar patients; a difference which disappeared during remission. There were no significant differences in rCBF between bipolar patients and healthy control subjects. PET studies have generally shown overall increased cortical metabolism when patients are in the manic state and decreased cortical metabolism in the same patients in the depressive state (O'Connell, 1995; Sarikaya et al., 1999; Friedman et al., 2006 for a review). Studies of euthymic patients suggest a combination of increased activity in anterior cingulate regions and decreased activity in other prefrontal areas, consistent with the presence of mild symptoms of both mania and depression (Friedman et al., 2006). However, the cause of the regional cerebral blood flow (rCBF) deficits is unknown.

The aim of the present study was to examine the possible relationship between reduced insight and neurofunctional and neurostructural measures in patients with bipolar I disorder, and to establish a relationship, as not yet formulated, between these markers and the psychopathology of the disorder itself. Neuropsychological tests were included to assess the neurocognitive correlates of insight failure, as already published in Varga et al., 2006. To the best of our knowledge, this is the first study where structural and functional neuroimaging measures have been combined with neuropsychological assessments to investigate structural and functional correlates of compromised insight in bipolar disorder.

2. Materials and methods

2.1. Subjects

Twenty-one bipolar I patients, recruited from in- and outpatient wards at Ulleval University Hospital, participated in the study. This group is a sub-set of our larger study group described in Varga et al. (2006). The Structured Clinical Interview for DSM-IV (SCID; 1994) was administered to verify the primary axis I diagnosis. A consensus group of two experienced psychiatrists was established (U.R.; S.O.), performing independent ratings based on the SCID protocols with excellent agreement. All patients were less than 60 years of age. The exclusion criteria were as follows: concomitant neurological disorder and/or brain organic conditions, chronic or long-term substance abuse, and electroconvulsive therapy within the last 3 months. Treatment given was part of a standard, clinical regime, and no attempts were made to control for specific medication or non-medication effects. At evaluation, all but two patients (90.5%) were taking mood-stabilisers (lithium $n=15$; valproic acid $n=3$; carbamazepine $n=1$). Three patients (14.3%) were using antipsychotics (olanzapine $n=2$; chlorprothixene $n=1$), 14.3% antidepressants (citalopram $n=3$), and 9.5% hypnotics (promethazin $n=1$; zopiclone $n=1$). In 19 of the 21 patients, the duration of stable treatment was 6 months or more. Most patients were in a phase of full ($n=12$) or partial ($n=1$) remission from their illness. Full remission requires a period of at least 2 months with no significant symptoms of mania or depression (APA, 1994). For partial remission, (a) the symptoms of a manic or depressive episode are either still present but full criteria are no longer met, or (b) there are no longer any significant symptoms of a manic or depressive episode, but the period of remission has been less than 2 months. One patient (4.8%) was manic at the time of examination, 19% were mildly depressed, 9.5% moderately depressed and 4.8% severely depressed (for the seven depressed patients, the mean MADRS score was 15.4; range 8–28). There were 10 men and 11 women, mean age 41 years (SD = 7.8) (see Table 1 for details). As control subjects, 21 healthy volunteers (10 men and 11 women) were recruited among acquaintances and personnel employed in various departments at Ulleval University Hospital; mean age 40 years (SD = 11.1). Inclusion criteria were no significant mental illness, no previous or present neurological disorders, no major head trauma, no alcohol and/or drug abuse, and no history of serious mental disorder among first-degree relatives.

2.2. Psychiatric scales and neurocognitive tests

A detailed description of the psychometric scales used in the present study has been presented elsewhere (Varga et al., 2006). These included: Global Assessment of Functioning — split version (GAF), Brief Psychiatric Rating Scale (BPRS), Montgomery–Asberg Depression Rating Scale (MADRS), Mania Rating Scale (MRS from SADS-C), Strauss–Carpenter Scale (SCLFS) and Clinical Global Impressions Scale (CGI). Degree of insight into own mental disorder and relevant symptoms was assessed with the Scale to Assess Unawareness of Mental Disorder (SUMD; Amador et al., 1993). The scale has been used in large samples in the DSM-IV field trials and is perhaps the most common scale in current use. The SUMD consists of 3 primary items (SUMD General, Awareness and Misattribution), scored on a Likert-type scale from 1 (good insight) to 5 (no insight). The patients were categorised as having generally "preserved" or "impaired" insight based on a threshold mean score of ≤ 3.0. The threshold score is identical to those used in other studies (e.g., Larøi et al., 2000; Varga et al., 2006). For the purpose of the present study, data analysis