Decreased gray matter density in orbitofrontal and anterior cingulate cortex in subjects with bipolar I disorder

LC Foland-Ross[1], LL Altshuler[2], SY Bookheimer[2], SK Madsen[1],
J Townsend[2], JK Shen[2], C Penfold[2], K Ahlf[2], J Fischer[2], PM Thompson[1]

[1]University of California, Los Angeles, Dept. of Neurology
[2]University of California, Los Angeles, Dept. Psychiatry and Biobehavioral Sciences

Introduction: Structural neuroimaging studies have reported various abnormalities in prefrontal cortex in bipolar disorder (BD). Previous findings have varied, perhaps because of the inclusion of patients treated with lithium, a medication shown to increase gray matter volume (Moore et al., 2000; Lancet, 7:356). Past studies also relied on traditional volumetric mapping methods, which may be insensitive to subtle neuroanatomic changes.

Method: 20 lithium-free bipolar I euthymic subjects (8f, 36.6±12.8yrs) and 20 pairwise age- and gender-matched healthy subjects (8f, 36.6±13.0yrs) were scanned on a 1.5T scanner. Data were analyzed to provide a measurement of cortical gray matter density (GMD, Thompson et al., 2004; NeuroImage, 23:S2). Cortical pattern matching (CPM) methods were used to associate homologous brain regions across subjects (Thompson et al., 2000; Hum. Br. Mapp. 9:81-92). Spatially normalized GMD maps were analyzed to assess group differences using an analysis of variance model at each point along the cortex. P values describing the significance of between-group differences were color-coded to visualize these differences; permutation methods were used to correct for multiple comparisons. The relationships between GMD and different medications were explored using correlation analyses at each surface point. Medications found to have significant associations with GMD were retained and modeled as covariates in a post-hoc point-wise analysis of variance to determine the effects of diagnosis after controlling for medication.

Results: Relative to healthy subjects, patients showed non-significant decreases in cortical GMD in diffuse areas of cortex. After controlling for quetiapine, an antipsychotic medication used in the treatment of BD, significant decreases in GMD in patients were detected right orbitofrontal (BA11, $p=0.028$) and bilateral anterior cingulate cortices (BA32/33, $p<0.05$). Decreases in GMD were also present in somatosensory (BA1/5/7), motor (BA4), and posterior cingulate (BA23) cortices.

Discussion: The CPM methods employed in this study were able to detect gray matter reductions in orbitofrontal and anterior cingulate cortex following control for treatment with quetiapine. Future studies including medication-free patients would be of interest.

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