Abnormal white matter microstructure in prefrontal cortex in euthymic bipolar patients revealed with diffusion tensor imaging

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Introduction: Diffusion tensor imaging (DTI) studies have reported various abnormalities in white matter tracts in patients with bipolar (BP) type I disorder. Previous findings have varied, perhaps because no study has controlled for the effects of Lithium, a medication which may have osmotic effects on brain structure (Moore et al., 2000).

Methods: Diffusion weighted images were acquired from 25 lithium-free euthymic subjects with BP I disorder (9f; 37.2±13.2yrs) and 25 age- and gender-matched healthy control subjects (10f; 36.8±13.0yrs) on a 1.5T scanner (55 2.5mm thick slices, 30 diffusion directions). Following correction for eddy current distortion and simple head motion, a diffusion tensor was fitted at each voxel to compute fractional anisotropy (FA). Each subject's non-diffusion weighted (B0) image was aligned to a T1-weighted structural image using a six-parameter linear registration and T1-weighted structural images were normalized to a standard template in Talairach space (Colin27, Holmes et al., 1998) using a nonlinear fluid registration (Lepore et al., 2008). Both linear and nonlinear transformations were applied to subjects' FA maps. To exclude gray matter and CSF voxels, spatially normalized FA images were thresholded and masked using segmented T1-weighted structural scans. Preprocessed images were entered into a voxel-wise t-test in SPM2 (www.fil.ion.ucl.ac.uk/spm) and thresholded at $p<0.001$ uncorrected, with an extent (k) threshold of 5 voxels to resolve group differences in WM microstructure.

Results: Relative to healthy subjects, bipolar-euthymic subjects had significant decreases in FA in WM of the left frontal (x/y/z=-22,32,1; k=5) and temporal lobe (x/y/z=-38,-45,1; k=17). Increases in FA were also found in patients in WM adjacent to the inferior portion of the right thalamus (x/y/z=25,-28,0; k=5).

Conclusions: Decreased FA in frontal lobe WM in lithium-free patients likely represents disruptions in WM tracts of fronto-subcortical circuits involved in the modulation of limbic structures and regulation of mood. Increased FA in thalamic regions in patients are harder to interpret, but may relate to abnormalities in thalamo-cortical circuits.

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