Tract-Based Spatial Statistics (TBSS) of Diffusion Tensor Imaging Data in Bipolar Disorder: Abnormalities of the Neurocircuitry

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Introduction:

Previous research indicated microstructural disruption of white matter (WM) [1,2] and neurocircuitry abnormalities [3] in bipolar disorder (BD). The present study used Tract-Based Spatial Statistics (TBSS) [4] of diffusion-weighted imaging (DWI) measure to investigate the microstructure in neurocircuitry affected by BD.

Methods:

Participants included 17 unmedicated bipolar disorder (BD, M/F=2/15, 31.4 \pm 9.2 years) and 18 healthy controls (HC, M/F=4/14, 30.9 \pm 8.6 years). 3T Diffusion-weighted imaging data (Siemens Trio MR scanner, EP2D_DIFF, TR/TE=8000/88ms, 1.7x1.7x3mm³, FOV= 220x220mm², matrix=128x128mm, 51 slices, 1 average) were acquired by using diffusion sensitizing gradients along 86 non-colinear uniformly distributed directions (b-value=800s/mm²), together with additional acquisition of three non-diffusion weighted (b=0). A simple least squares fit of the tensor model and fractional anisotropy (FA) were calculated [5]. TBSS used three major analysis steps: 1) All FA images were nonlinearly co-registered to the target image (FMRIB58_FA, http://www.fmrib.ox.ac.uk/fsl/tbss/FMRIB58_FA.html) and transformed to standard MNI152 space, 2) Creating the mean FA image and its skeleton and projecting all individual FA values onto the mean FA skeleton, 3) Voxelwise statistics analysis on both the skeletonized FA and FA data (thresholded to FA=0.2) separately. General linear model analysis evaluated the local group difference (HC *vs* BD) across the whole WM skeleton and WM. A permutation-based non-parametric approach [4] tested voxel t value (t > 3, p < 0.001), and threshold-free cluster enhancement (TFCE) was utilized for cluster-like correction of multiple comparisons with controlled family-wise error rate (p < 0.05).

Results:

Fig. 1 shows the regions characterized by low fractional anisotropy in BD (red) (t > 3, p < 0.001) overlaid on the mean FA skeleton (green) and mean FA (gray) images. These included the bodies of bilateral corpus callosum (*CC*), bilateral anterior cingulum (*acg*), superior longitudinal fasciculus, sagittal striatum (include inferior longitudinal fasciculus and inferior fronto-occipital fasciculus), and left cerebral peduncle (*cpd*). Fig. 2a shows the significant clusters (red-yellow) at the regions of *acg*, the bodies of corpus callosum, right superior branch of corona radiata (*scr*) and anterior limb of internal capsule (*alic*) after correcting for multiple comparisons using TFCE. Fig. 2b shows the 3-D view of significant clusters (orange) overlaid on the 3-D rendering of mean FA skeleton image.

Conclusions:

The study findings of diffusion abnormalities in commissural fibers (the bodies of *CC*), *acg*, *scr/alic* and cerebral peduncle provide direct evidence of compromised integrity of the inter-hemispheric connections, fronto-limbic and cortico-striatal circuits and motor control in BD. These abnormalities could be partially responsible for deficiencies in executive functions, behavioral regulation, impulse control and motor physiology commonly described in BD.

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