Symposium: Altered white matter communication in schizophrenia and bipolar disorder: A possible common endophenotype?

S32.01

Uncinate fasciculus and cingulum bundle findings in first episode schizophrenia and first episode bipolar disorder: A diffusion tensor imaging study

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Background and Aims: Fronto-temporal connections have long been thought to be involved in schizophrenia. Two fronto-temporal connections of interest are uncinate fasciculus (UF) and cingulum bundle (CB), which recently have been investigating using Diffusion Tensor Imaging (DTI), a new technique that affords an opportunity to evaluate white matter fiber integrity in vivo. Using this technique, we previously reported abnormalities in UF and CB in chronic patients. Additionally, we noted that schizotypal personality disordered subjects showed UF but not CB abnormalities.

Methods: Here, we sought to determine whether or not UF and CB white matter integrity are altered at initial onset of illness, and are specific to schizophrenia. We evaluated twelve first-episode schizophrenia, 12 first-episode affective psychosis and 12 controls using DTI on a 1.5T magnet. Fractional anisotropy (FA) and mean diffusivity (Dm) were used to quantify water diffusion, and cross-sectional area was defined with a directional threshold method.

Results: Findings showed bilateral reduction of UF FA, but not Dm, in first-episode schizophrenia compared with controls and first-episode affective psychotic patients. For CB, there were no statistically significant group differences for either FA or Dm.

Discussion: These findings suggested that UF white matter integrity, but not CB white matter integrity, is altered at initial onset of schizophrenia and may be specific to schizophrenia. In contrast, CB abnormalities are not present at first episode of schizophrenia and may reflect progressive changes that occur over the course of the illness. The latter will need to be investigated using a longitudinal design.

S32.02

White matter volume in the schizophrenia and bipolar spectrum

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Structural brain imaging abnormalities in schizophrenia-resemble spectrum disorders in many respects. Similar to schizophrenia, cerebrospinal fluid (CSF) is increased and cortical volumes are decreased in schizotypal personality disorder (SPD). In this large sample study, MRI assessed white matter volumes and diffusion tensor anisotropy was assessed in the schizophrenia spectrum. The sample includes 230 schizophrenics (ages 13-78) and an approximately age matched group of 81 patients with schizotypal disorder and 230 normal volunteers. For the bipolar spectrum there were 44 patients with bipolar spectrum disorder. Results in a pilot subsample of patients revealed increases in white matter in the cingulate in SPD and Schizophrenia in comparison to the normal sample. However in prefrontal regions, a schizophrenia spectrum pattern was observed with greater white matter increases in patients with schizophrenia than patients with schizotypal disorder, and greater gray matter decreases in patients with schizophrenia than patients with schizotypal disorder. Anisotropy changes were widely observed across the prefrontal cortex and corpus callosum. Taken together these results suggest that prefrontal change appears associated with a continuous spectrum deficit while some changes in the cingulate and other brain regions may show protective or reactive change in schizotypal patients. Bipolar patients had significantly reduced volume of the white and the gray matter of the frontal cortex. Furthermore, compared with control subjects, BPS patients as a group showed alterations in anisotropy of the internal capsule adjacent to the striatum and thalamus and the frontal white matter.

S32.03

Evidence of shared white matter disruption in bipolar disorder and sschizophrenia

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There is strong qualitative and quantitative evidence of white matter abnormalities in schizophrenia and bipolar disorder from structural magnetic resonance imaging (MRI). There is also good evidence of altered connectivity in schizophrenia using diffusion tensor magnetic resonance imaging, but no study has yet addressed the diagnostic specificity of these findings or whether they are related to specific susceptibility genes.

Methods: Diffusion tensor MRI was used to assess white matter integrity in patients with bipolar I disorder (BD) (n=42), schizophrenia (n=28) and healthy controls (n=38). Clinically stable patients with one other close family member with the same diagnosis were selected. In a second study, we examined white matter associations with Neuregulin I in a sample of healthy controls. Fractional anisotropy (FA) was compared between the groups using voxel-based morphometry, automated region of interest analysis and probabilistic tractography. Results : Patients with BD and those with schizophrenia showed reduced FA in the anterior limb of the internal capsule, anterior thalamic radiation and uncinate fasciculus compared with controls. Results from the second study showed reductions in those carrying a Neuregulin 1 variant previously associated with psychotic symptoms.

Conclusions: Reduced white matter density and integrity is common to both schizophrenia and BD. It is likely that this shared white matter disruption is determined in part by shared genetic risk factors.

S32.04

Cytoarchitecture alterations of white matter in schizophrenia and bipolar disorder

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