White Matter Properties of Emotion Related Connections in Schizophrenia

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Background

Schizophrenia is associated with abnormal emotional responses such as flat affect, apathy, and anhedonia. Regions of the brain like the amygdala, anterior cingulate cortex (ACC), and orbitofrontal cortex (OFC) are shown to be involved in emotional processing (Phillips et al., 2003) and have been structurally and functionally implicated in schizophrenia (Shenton et al., 2001; Schneider et al., 1998; Fahim et al., 2005). Recent theories suggest white matter (WM) fiber tracts, and their abnormalities, are behind the psychopathology of schizophrenia. We used Diffusion Tensor Imaging (DTI) and a new post-processing method called stochastic tractography to visualize and quantify the WM trajectories between regions involved in emotional processing to determine whether emotional abnormalities observed in schizophrenia are related to WM pathology.

DTI is an in vivo MRI technique that can detect subtle WM abnormalities by assessing the degree to which fiber bundles have lost their normal, organized integrity (**Figure 1**). In the present study, we evaluated WM connections using stochastic tractography , which creates potential WM fibers based on specified regions of interest (ROIs). This method is advantageous compared to "traditional" streamline tractography because it is able to seed from cortical areas that are specific to functional/anatomical deficits and it is able to project beyond areas of crossing fibers where streamline tractography would typically fail (Björnemo et al., 2002). Once connections were extracted, we used Fractional Anisotropy (FA) to measure of WM integrity, which is sensitive to changes in myelination, axonal integrity, and coherence within the emotional network connections.

Methods

• A 3T GE magnet equipped with 8 channel coil was used to obtain scans from 32 male subjects (16 schizophrenic patients, 16 normal controls), who were group-matched on age, handedness, and parental socioeconomic status (**Table 1**).

•Scan Parameters: **Structural-** TR 7.48 ms, TE 3 ms, FOV 256 mm, 1 mm slice thickness, 176 axial slices. **DTI-** Fifty-one directions, TR 17000 ms, TE 78 ms, FOV 24 cm, 144x144 encoding steps, 1.7 mm slice thickness. 85 axial slices.

•Anatomical images were automatically segmented with Freesurfer Software and several ROIs were extracted, including the ACC, amygdala, and OFC bilaterally (**Figure 2**). A white matter mask (WMM) was also extracted and dilated using 3D Slicer (www.slicer.org) to enlarge the WMM volume.

•ROIs were coregistered to DTI space in 3D Slicer and stochastic tractography was performed using tensor information from the diffusion weighted image. Tracts were seeded from two ROIs at a time using 100 seeds/voxel, smoothing, and a step size of 0.5mm and with the WMM as a WM boundary. Connections of the ACC-amygdala, ACC-OFC, and OFC-amygdala connections were extracted and measured.

•Probability maps were generated for each subject based on the number of tracts passing through each voxel, which were analyzed for thresholded mean FA (**Figure 3**).

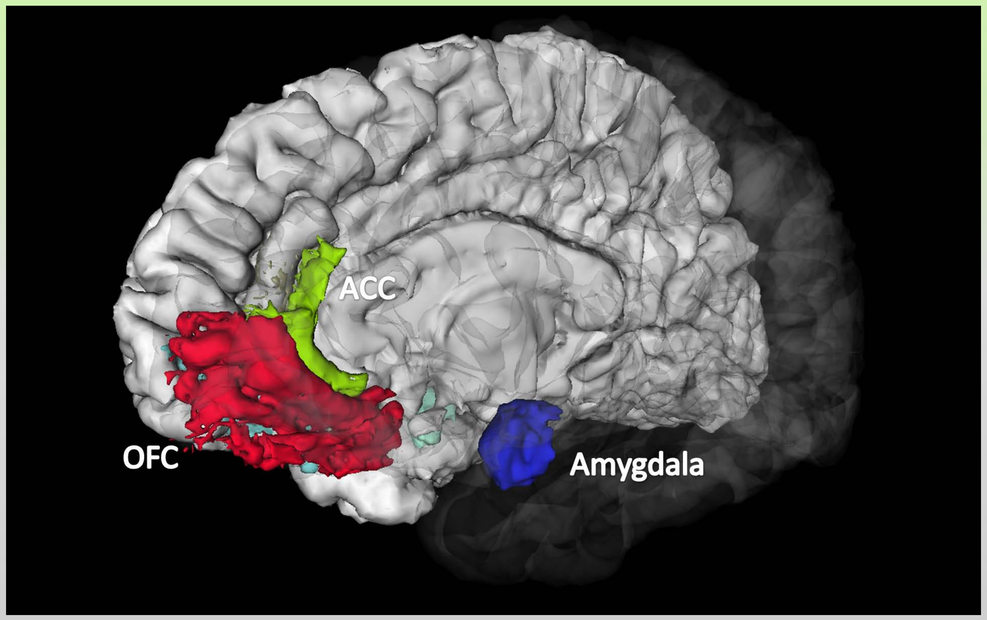

Figure 2. Regions of Interest used in stochastic tractography.

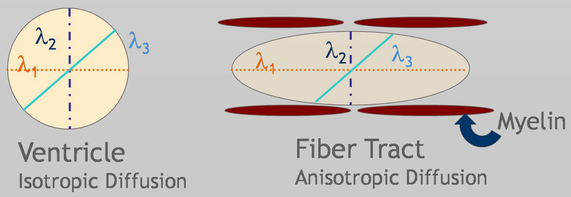

Figure 1. Tensor Estimation.

Group	Schizophrenic (N=16)	Control (N=16)	P value
Age	44.56	43.00	0.65
Handedness	0.70	0.74	0.60
PSES	2.31	2.40	0.84

Table 1. Subject demographics.

Results

Investigated WM connections were thresholded so that connections with less than a 10% probability were filtered out to control for noise. Mean FA among the remaining tracts demonstrated a group effect (t=2.38, p=0.024) where FA of right ACC-OFC connection was decreased in schizophrenic patients when compared to normal controls (**Figure 4**). T-tests did not yield significant result for other connections. Although there were no group differences in the size of the right ACC, there was a significant correlation in patients between ACC-OFC connectivity in the right hemisphere and volume of right ACC (r=-0.71, p=0.002) but not in controls (**Figure 5**). Patients did have a reduced right OFC volume compared to controls (t=2.33, p=0.027), but there were no significant correlations with this measure and WM connectivity.

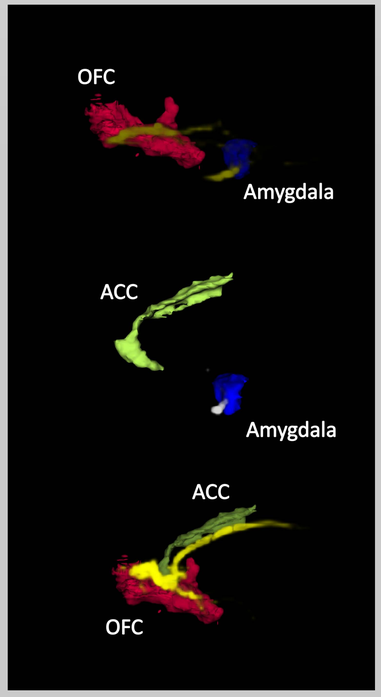

Figure 3. Example tracts connecting the ACC, OFC ,and amygdala

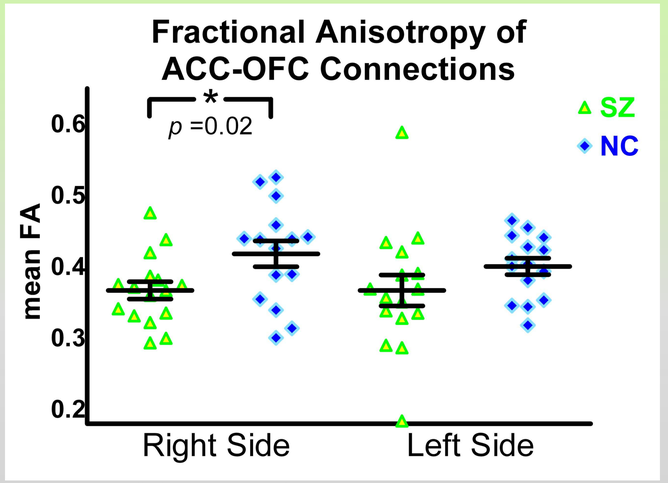

Figure 4. Statistically lower mean FA of right ACC-OFC connection in patients.

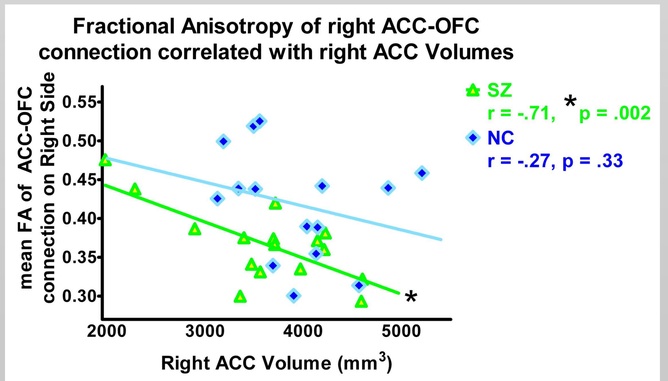

Figure 5. Inverse relationship between right ACC volume and FA of right ACC-OFC connection.

Discussion

Along with WM disruptions, patients with the lowest FA values in the right ACC-OFC connection had the largest right ACC volumes, demonstrating that WM and gray matter abnormalities may be related. Reduced FA in patients implies a loss of axonal and/or myelin integrity. It has previously been proposed that asynchronous neural activity is associated with the degree of synaptic pruning during normal development (Purves, 1998). Since WM plays a large role in modulating neural synchrony, observed WM abnormalities may be related to the gray matter volumes of the connected regions via this mechanism. Further investigation is required to see how these abnormalities are related to emotional deficits in schizophrenia.

References

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