

Compromised frontal callosal connectivity in unmedicated obsessive-compulsive disorder: a quantitative diffusion tractography study

J. S. Oh^{1,2}, J. Jang², W. Jung³, C-H. Choi⁴, J-S. Choi⁵, D-H. Kang⁵, and J. Kwon²

¹Brain Korea 21 Division of Human Life Science, Seoul National University, Seoul, Seoul, Korea, Republic of, ²Psychiatry, Seoul National University College of Medicine, Seoul, Seoul, Korea, Republic of, ³Interdisciplinary Program in Brain Science, Seoul National University, Seoul, Seoul, Korea, Republic of, ⁴Radiology, National Medical Center, Seoul, Seoul, Korea, Republic of, ⁵Neuropsychiatry, Seoul National University Hospital, Seoul, Seoul, Korea, Republic of

Objective: The delineation of frontostriatal circuitry-related white matter tracts into dorsal and ventral pathways using diffusion tractography has been of particular interest in obsessive-compulsive disorder (OCD) studies, since abnormalities of these pathways involve with the pathophysiology and etiology of the OCD. In this study, we aim to investigate fractional anisotropy (FA), which is diffusion property that can render voxelwise fiber integrity information, of dorsal and ventral projections of callosal fibers in the OCD patients on the basis of quantitative diffusion tractography analysis using Brodmann area region-of-interest (ROI) approach and tract parameterization technique.

Methods: Twenty unmedicated OCD patients diagnosed by DSM-IV (15 drug-naïve and 5 unmedicated) and 19 demographically similar healthy normal controls were recruited for this study. Using Brodmann area (BA) atlas-based ROI selection in conjunction with tract-specific coordinated system termed “tract parameterization”, we conducted a function-specific (guaranteed by BA ROI) and location-specific (guaranteed by tract parameterization) analysis of white matter tracts.

We used whole brain tractography and two-ROI approach in order to extract callosal fibers interconnecting bilateral dorsolateral prefrontal cortices (DLPFCs) and orbitofrontal cortices (OFCs). First, the midsagittal corpus callosum (CC) was automatically extracted using color-coded diffusion tensor image (DTI) maps. Second, we used BA atlas-based ROI selection methods. BAs 9 and 46 were used as the DLPFC ROI, and BAs 11(12) and 47 as the OFC ROI.

Finally, we used a tract-oriented DTI analysis by defining tract-specific coordinates using arc-length parameterization of the constructed fiber tract (tract parameterization - see **Figure 1** for the details. In brief, this method divides the entire length of each tract interconnecting bilateral cortical areas into the same number of segments (e.g., 100 segments for a percentile division). Similar method was used in our previous study of thalamo-frontal pathway analysis in chronic schizophrenia (Oh et al., 2009). Using our quantitative methods of tractography analysis, we were able to analyze fiber integrity levels (i.e., FA values) on the entire length of tract, as well as on length-parameterized tracts for both DLPFC- and OFC-specific callosal fibers.

Results: Our analysis revealed FA decreases [$p < 0.001$, false discovery rate (FDR)-corrected] in callosal fiber of OCD patients in both DLPFC and OFC projections (see **Figure 2** for the details).

Conclusions: Our findings, which benefits from a more quantitative tractography analysis (i.e., function-specific analysis by Brodmann ROI approach and region-specific analysis by tract parameterization approach) than previous studies, have validated well-known abnormalities in dorsal and ventral networks in the pathophysiology of obsessive-compulsive disorder in terms of hemispheric integration. In particular, DLPFC-specific callosal fiber integrity was first revealed by the function- and region-sensitivity of the present methods, and not found by previous available methods.

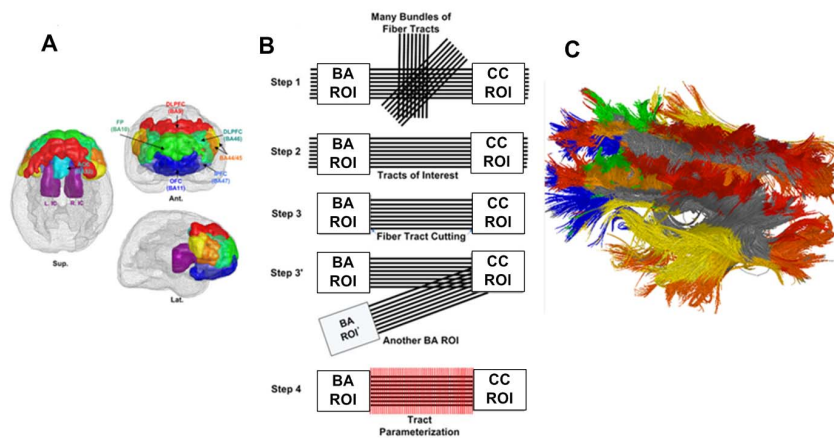


Fig.1. Tracts of interest selection. A) frontal Brodmann area (BA) ROI approach; B) pipeline for selecting Brodmann area-specific callosal fibers; C) resulting callosal fiber parcels color-coded per corresponding BA (A and B are adapted from Oh et al., 2009)

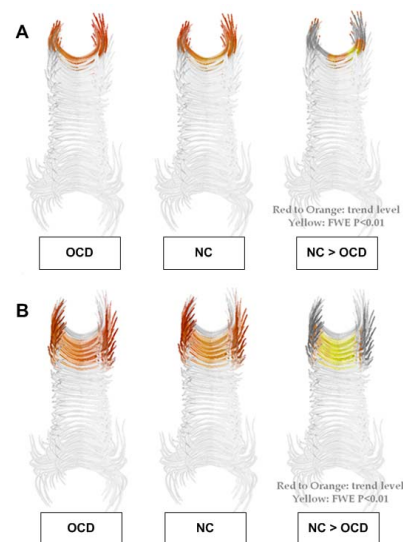


Fig.2. Mean values and group differences of fiber integrity on the ventral and dorsal fronto-striatal network-specific and region-specific definition of callosal fibers. A) FA values of OCD and NC groups and significant NC-greater-than-OCD group difference of FA value of the DLPFC-specific CC (orange to yellow, as FA values/statistical significance get high); B) the same of the OFC-specific CC