Diffusion Spectrum Imaging of White Matter Abnormalities in Fronto-Striato-Thalamic Circuit in Obsessive-Compulsive Disorder

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Introduction

Obsessive-Compulsive Disorder (OCD) is an anxiety disorder with a prevalence rate of 2% to 3% of the adult population. The clinical manifestations include persistent, intrusive thought and rituals or compulsions. To date, data from different lines of studies including neuronanatomical, neurosurgical, neuropathological and neuroimaging has provided important evidence implicating that the basal ganglia and by extension the striatal-thalamic and thalamic-cortical circuits play a role in the disorder. However, the primary site of pathology remains unclear. Although findings from neuroimaging suggest gray matter abnormality over the fronto-striatal-thalamic circuits, another plausible possibility of pathology of OCD is the involvement of the white matter tracts connecting the gray matter regions of these circuits in addition to gray matter regions per se. In this study, we investigated three potential white matter tracts (cingulum bundles [CB], anterior thalamic radiations [ATR], stria terminalis [ST]) that might serve the neuropsychopathology of patients with OCD inferred from diffusion spectrum imaging (DSI). We hypothesized that white matter abnormalities in patients with OCD might correspond to neuropsychological data.

Materials and Methods

20 right-handed adult patients with OCD (10 males and 10 females) were examined using DSI. Twelve participants with OCD were on different stages of medication. Images were acquired on a 3T MRI system with an eight-channel head coil. DSI was performed using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9100/142 ms, image matrix size = 128 x 128, spatial resolution = 2.9 x 2.9 mm², and slice thickness = 2.9 mm. A total of 203 diffusion encoding gradients with the maximum diffusion sensitivity bmax = 6000s/mm² were sampled on the grid points in the 3D q-space with |q| ≤ 3.6 units [1]. DSI analysis was performed based on the relationship that the echo signal S(q) and the diffusion probability density function P(r) were a Fourier pair, i.e., S(q)=FT{P(r)}. The orientation distribution function (ODF) was determined by computing the second moment of P(r) along each radial direction. The orientations of individual crossing fibers were determined by decomposing the original ODF into several constituent ODFs [2]. The crossing fiber vectors were used for tractography reconstruction. Generalized fraction anisotropy (GFA) at each voxel was quantified based on the shape of the original ODF. Tractography was reconstructed based on a simple algorithm adapted for DSI data and using fiber tracking to define the CB, ST, and ATR. Furthermore, mean path analysis, a method that projected the GFA onto a single mean path of a specific white matter tract bundle, was used to analyze local changes in microstructure coherence along the individual tract bundles. The correlation between GFA values and Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was investigated.

Results

Our findings provided evidence of abnormal white matter microstructures in OCD as inferred from DSI. GFA was positively correlated with Yale-Brown scores, especially obsessive score, over bilateral cingulum bundles and left stria terminalis (Fig. 1) in OCD subjects. GFA was determined by computing the second moment of P(r) along each radial direction. The orientations of individual crossing fibers were determined by decomposing the original ODF into several constituent ODFs [2]. The crossing fiber vectors were used for tractography reconstruction. Generalized fraction anisotropy (GFA) at each voxel was quantified based on the shape of the original ODF. Tractography was reconstructed based on a simple algorithm adapted for DSI data and using fiber tracking to define the CB, ST, and ATR. Furthermore, mean path analysis, a method that projected the GFA onto a single mean path of a specific white matter tract bundle, was used to analyze local changes in microstructure coherence along the individual tract bundles. The correlation between GFA values and Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was investigated.

Discussion

Higher GFA is usually interpreted as increased connectivity in white matter bundles and lower GFA is referred to a defect of white matter integration due to fiber loss or demyelination. Yoo et al. found diminished higher GFA over thalamic radiations with improvement of symptoms after SSRI treatment [3]. Menzies et al. even reported higher GFA in right medial frontal region in both OCD patients and relatives [4]. Therefore, it is intriguing to think that higher GFA might be the original pathology of OCD, which might reflect an increase of connectivity in white matter bundles from development. However, with the improvement of symptoms, the white matter bundles make some compensation process by decreasing the connectivity over the abnormal white matter bundles to cope with the symptoms, resulting in lower GFA. This hypothesis could explain the positive correlation between GFA and Yale-Brown scores in cingulum bundles and stria terminalis in our data. This could be interpreted as a compensation process to deal with biologically inherent abnormal hyper-connectivity. The change of the left-to-right asymmetry, noted in our previous report, was also consistent with this hypothesis and might demonstrate that the compensation process had a complicated influence on bilateral white matter tracts [5]. Furthermore, twelve participants with OCD were on different stages of medication. The decrease of GFA might be possibly due to the interaction of medication effect and the improvement of symptoms. To test the hypothesis, it warrants a longitudinal study on OCD patients before and after medication to investigate the change of GFA and the correlation between the GFA and neuropsychological data.

References


Figure 1 Positive correlation between the YBOCS and GFA values of bilateral cingulum bundles and left stria terminalis.