Reduced lateralization in early onset schizophrenia: a DTI study using TBSS

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Introduction

It has been proposed earlier, that schizophrenia could result from failure of correct lateralization [1] and lead to misconnectivity in white matter architecture [2]. Along with other papers in the literature, our previous imaging studies have described white matter alterations in the cerebellum, the posterior aspects of the visual system and in the corpus callosum in patients with schizophrenia [3,4].

Here, we investigated these regions in more detail using Tract-Based Spatial Statistics (TBSS) [5]. Additionally, we evaluated potential changes in lateralization of the optic radiation and the superior cerebellar peduncle.

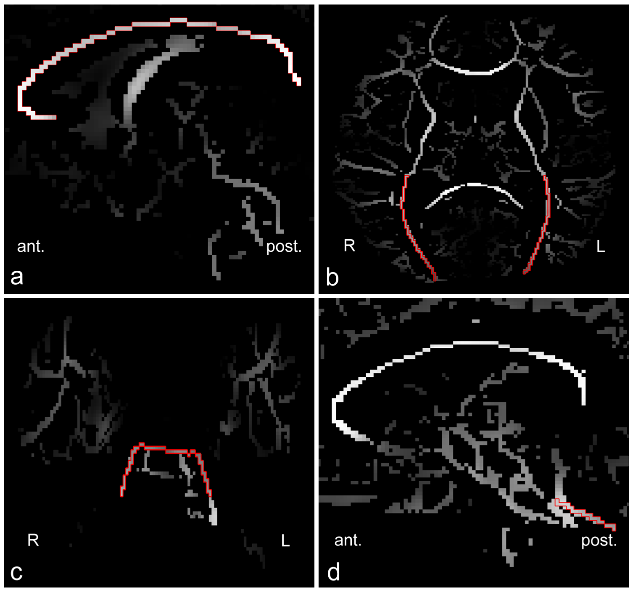

Figure 1: Segmentations in MITK3M3 of tract based spatial statistics (TBSS)-based mean fractional anisotropy (FA) skeleton. Red squares represent the segmented region of interest. Grey scale of the skeleton is analogue to FA values whereas light grey colors indicate higher FA values and dark grey colors illustrate lower FA values. A) corpus callosum (sagittal); B) bilateral optic radiation (axial); C) middle cerebellar peduncles (axial); D) right superior cerebellar peduncle (sagittal); Ant.: anterior; Post.: posterior; R: right; L: left.

Materials and Methods

The study was approved by the local ethics committee and performed in accordance to the declaration of Helsinki. Twelve adolescent inpatients with a diagnosis of early onset schizophrenia and 13 healthy controls matched for age, gender, school type and handedness were examined. The diffusion tensor imaging data were preprocessed using tract-based spatial statistics and the obtained white matter skeleton was used to perform a regional analysis of fractional anisotropy in the corpus callosum, the optic radiation, and the superior and middle cerebellar peduncles. Imaging was performed on a 1.5T whole-body clinical scanner and a quadrature head coil (Avanto, Siemens, Erlangen, Germany) with a gradient strength of 40 mT/m. A transversal single shot echoplanar imaging technique with a dual bipolar diffusion gradient and a double spin echo was utilized for reduction of eddy currents using the following parameters: TR/TE 6600/88ms, field of view 240 mm, data matrix of 96x96 yielding an in plane resolution of 2.5 mm. Fifty axial slices with a thickness of 2.5 mm and no gap, 6 gradient directions, two b-values (0 and 1000 s/mm^2) and 10 subsequent complete DTI datasets were acquired. The DTI data were preprocessed in order to obtain FA images that were registered using the FSL toolkit [6]. Registration was performed by non-linearly warping all images to one image from the set that had been identified as most representative for the whole group of subjects. Then, that image was affine-aligned into MNI152 standard space. A binary mask of the skeleton was obtained after setting the threshold of the mean FA skeleton to 0.2. Then, a mean FA skeleton was created for all individuals by using the TBSS skeletonization and projection method. Next, a manual segmentation of the CC, the OR, the MCP and the SCP (Fig. 1) was applied on the acquired binary skeleton mask using MITK diffusion Version 3M3 [7] (http://www.mitk.org/DiffusionImaging). Then, the FA from all individual voxels within the respective region of interest was extracted and a statistical analysis between groups was performed as described below.

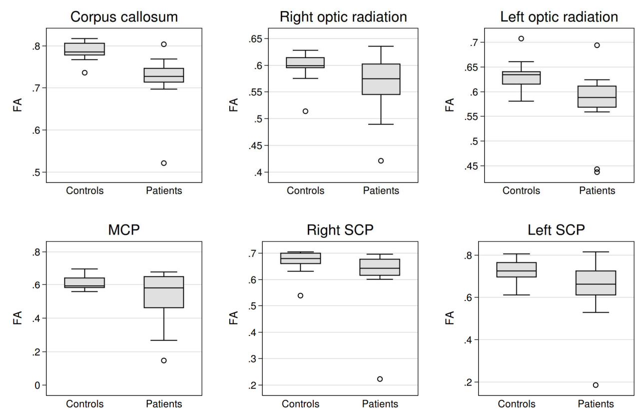

Figure 2: Boxplot analysis of mean fractional anisotropy (FA) value distribution in corpus callosum, optic radiation, middle and superior cerebellar peduncles. Y-axis: FA. The lower segment of the rectangle represents the second quartile whereas the upper segment corresponds to the third quartile. The horizontal line dividing the two segments represents the median. Outliers are signified by circles (distance from median is at least twice as high as the box).

Results

There were no significant differences between patients with schizophrenia and healthy controls in age ($t(23) = 1.24$, $p = .23$), sex ($\chi^2(1) = 0.03$, $p = .87$), or type of school ($\chi^2(2) = 3.88$, $p = .14$). Using TBSS, a significant reduction of fractional anisotropy in the whole corpus callosum ($p < .001$) and the optic radiation ($p= .016$) but not in the middle ($p= .076$) and superior cerebellar peduncles ($p= .062$) was found. Furthermore, a significantly decreased lateralization of the optic radiation ($p= .016$) and the superior cerebellar peduncles ($p= .014$) in patients was observed (for box plot distribution see Fig. 2).

Discussion

Using TBSS, our findings substantiate the concept that schizophrenia is a neurodevelopmental disorder which affects fiber connectivity of selected regions. Moreover, our results support the thesis that changes in lateralization may play a key role in the pathogenesis of this disease.

References

[1] Crow, 2000; Brain research [2] Inocennti et al.; Mol Psychiatry 2003; [3] Henze et al., 2012, J Neuroimaging [4] Henze et al., 2012 Neurosci Lett [5] Smith et al., 2006; Neuroimage [6] Jenkinson et al., 2011; Neuroimage [7] Fritzsche et al., 2012; Methods Inf Med