Diffusion Tensor Tractography in Schizophrenia

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Introduction

The nature of schizophrenia makes it a particularly difficult disease to study. The symptoms range from simply having a flat affect or difficulty concentrating to having full-blown auditory hallucinations and psychotic behavior. While clinicians have struggled with documenting and categorizing these symptoms, researchers have similarly been struggling to find new and better ways to identify the potential causes of the disease. Recently, diffusion tensor imaging (DTI), a new variation of MRI, has emerged as an effective modality for penetrating the previously hidden patterns of neural connectivity. This study utilizes a novel fiber tracking algorithm called GTRACT (Guided Tensor Restore Anatomical Connectivity Tractography) to test the hypothesis that individuals with schizophrenia may have reduced anisotropic diffusion indices in the cortical-thalamic-cerebellar-cortical circuit (CCTCC). The GTRACT algorithm was developed in order to solve the fiber crossing problem that has plagued previous tractography algorithms[1-2].

Methods

Subject recruitment was performed at the University of New Mexico, the University of Minnesota, Massachusetts General Hospital, and The University of Iowa in accordance with the Institutional Review Boards at these institutions. Twelve male patients having a DSM-IV diagnosis of schizophrenia with formal thought disorder (age 32±9.5 years) and 10 normal controls (5 males and 5 females, age 43.5±9.0 years) were enrolled into this study. MR imaging was performed on either a Siemens Symphony or Sonata 1.5T scanner. The subjects were imaged using an imaging protocol to acquiring a structural MR scan and diffusion tensor images. The structural imaging protocol acquired multimodal scans consisting of T1 and T2 weighted sequences. Diffusion tensor images were obtained with the following protocol: TE=80ms, TR=9500ms, flip angle=90, FOV=256x256, Matrix=128x128, slice thickness=2.0, slice gap = 0.2mm, number of slices=65, NEX=4, B values=1000, bandwidth=1346Hz/pixel, number of diffusion directions=6.

A standard image analysis pipeline in the BRAINS[3-5] software was utilized to analyze the structural MR images. This included 1) spatial alignment of the T1 weighted scan along the AC-PC line and the interhemispheric fissure; 2) co-registration of the T2 images to the spatially aligned T1; 3) tissue classification; 4) brain extraction; and 5) neural network regional brain labeling. The neural network defined regions of interest for the thalamus and the cerebellar white matter (corpus medullary) were verified by an expert anatomical rater and manually edited if required. The diffusion weighted images were co-registered to the b=0 image. A 3x3x3 voxel neighborhood median filter was applied to the DWI first, and then the tensor field was calculated using a background suppression threshold of 100 on the b=0 image. The resulting tensor image was resampled into 2x2x2mm isotropic voxel size. A fractional anisotropy (FA) image was then calculated. The diffusion weighted images were co-registered to the AC-PC aligned T1 image using the b=0 image from the DWI series. This registration was then inverted to place the thalamus and cerebellar regions of interest defined on the T1 weighted images into the native space of the diffusion tensor images. For the tract tracing, we focused on one major pathway that represents the connection between the cerebellum and the thalamus in the CCTCC circuit. The defined regions of interest were used as starting and ending regions for the GTRACT software. Separate tracts between the left cerebellum and right thalamus and right cerebellum and left thalamus were generated and compared between patients with schizophrenia and normal controls.

Results

In both the right and left thalamus we found significant lower anisotropy values in the white matter tracts connecting the cerebellum to contralateral thalamus ($p<0.05$) in subjects with schizophrenia as compared to normal controls. The average tracts for the two groups are shown in Figure 1. Comparing each of the sample points along the fiber tracts revealed that the effect was not overall a general reduction in the anisotropy, but instead was a distinct regional deficit in the anisotropy values as shown in Figure 1.

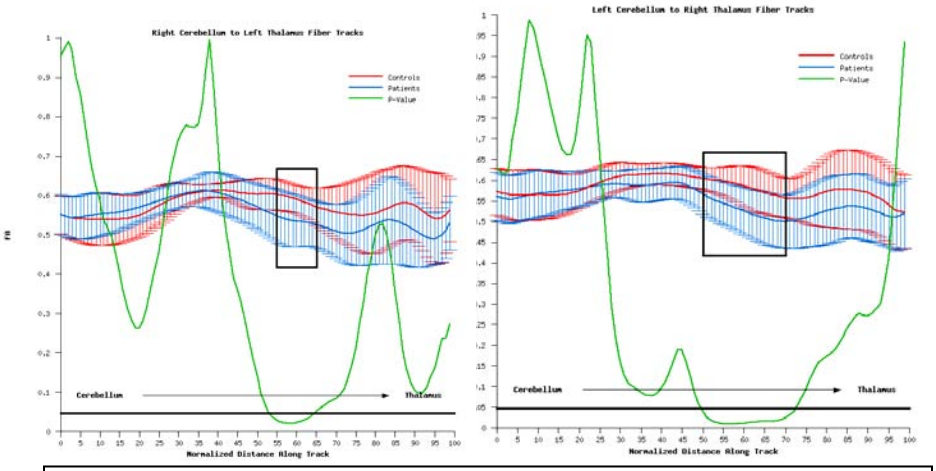

Figure 1. Fractional Anisotropy values along the generated fiber tracts between the cerebellum and thalamus. The regions enclosed within the black box are significantly lower in patients with schizophrenia as compared to normal controls.

References

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