Fiber tracking of the Arcuate Fasciculus in Autism using High Angular Resolution Diffusion Imaging

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Introduction The visualization of white matter (WM) pathways in the human brain is one of the most promising applications of diffusion imaging. Diffusion Tensor Imaging (DTI) is now widely acquired for clinical studies due to its short scan times and our understanding of tensor properties for WM tissue. DTI based indices of WM integrity are becoming increasingly prominent in studies of neurological and neuropsychiatric disorders like Autism and Schizophrenia. However DTI suffers from one major disadvantage: its inability to accurately track bundles across regions of complex WM with crossing fibers. This severely limits both accurate fiber tracking and tract based statistics. High Angular Resolution Diffusion Imaging (HARDI) is a new form of diffusion imaging that better characterizes complex WM and hence is better able to track across areas where multiple fiber bundles are present. To date, however, there has not been a systematic study of the fiber tracking differences between HARDI and DTI in a clinical population. In this study, we illustrate such differences by tracing the Arcuate Fasciculus in a mixed population of patients with an Autism Spectrum Disorder (ASD) and typically developing controls. The Arcuate Fasciculus is an important WM tract for language, a domain that can be detrimentally affected in ASD [2].

Methods Whole brain HARDI was acquired on 50 subjects (21 Controls and 29 ASD Patients; Ages 8-18 years) using a Siemens 3T Verio MRI scanner with the following parameters: TR/TE=14.7s/110ms, b= $(2mm)^3$, voxel resolution=3000 s/mm^2, number of diffusion gradients=64. Total acquisition time was 18 minutes per subject. In addition to HARDI, DTI was acquired on all subjects with the following parameters: TR/TE=11.5s/73ms, b=1000 s/mm^2, voxel resolution= $(2mm)^3$, number of diffusion gradients =30, with an acquisition time of 8.5 minutes. The Fiber Orientation Distribution function (FOD) was calculated at each voxel in the HARDI acquisition using the constrained spherical deconvolution approach as implemented in MRtrix [1]. For every subject, the DWI volumes of the DTI acquisition were aligned to the HARDI DWIs using an affine transformation. We traced the left and right Arcuate Fasciculus (AF) using MRtrix. The AF is traced by placing a seed region of interest lateral to the projection fibers of the corona radiata, anterior to the tempo-parietal junction in the coronal slice. An inclusion ROI is then placed in the axial slice lateral to the sagittal stratum. Deterministic fiber tracking is performed in HARDI as well as DTI acquisition using these seed regions using MRTRIX software on all subjects. We used a curvature threshold of 2mm and a scalar cutoff threshold of 0.25(FA value in DTI and FOD amplitude in HARDI).

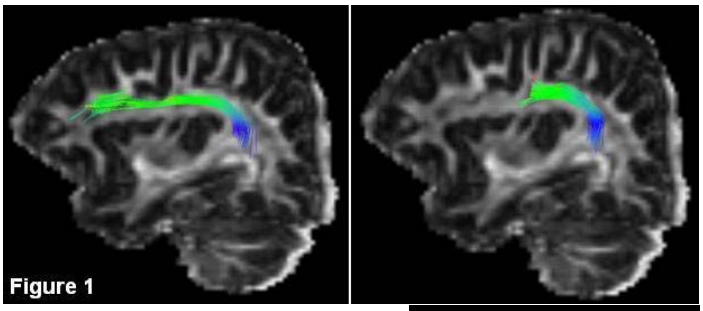

Figure 1

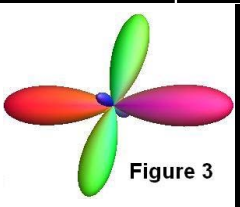

Figure 3

Results Figure 1 shows the AF as seen in one of the HARDI datasets of a TDC subject (left) vs. the DTI dataset of the same subject(right) in the sagittal plane. While the AF clearly extends into the frontal lobe in HARDI, ending at the inferior frontal gyrus(Figure 2 top), DTI based fiber tracking stops close to the precentral gyrus(Figure 2 bottom). This is probably due to the presence of lateral fibers going into the precentral gyrus which intersect the anterior-posterior (green) limb of the AF. The diffusion tensor changes from very prolate to oblate in the area of the fiber crossing; the resulting drop in FA value leads to the truncation of DTI tracks. The HARDI FOD, on the other hand, is capable of effectively modeling multiple fiber-crossings (Figure 3) and therefore, is able to extend the AF into the frontal lobe, consistent with postmortem anatomy that shows that the AF connects Broca's area (Inferior Frontal Gyrus) to Wernicke's area (Posterior Superior Temporal Gyrus).

Table 1	HARDI	DTI	p value
Average Length of Fibers(Arcuate R)	84 mm	44 mm	10^-9
Average FA value(Arcuate R)	0.262	0.226	10^-6
Average Length of Fibers(Arcuate L)	85 mm	76 mm	0.0323
Average FA value(Arcuate L)	0.238	0.202	10^-6

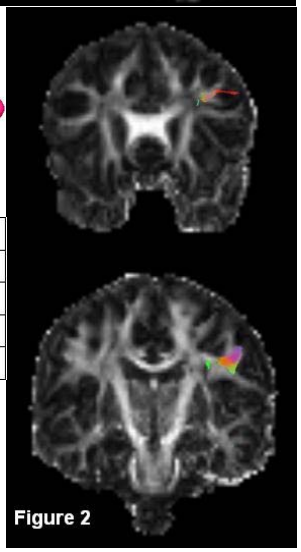

Figure 2

We analyzed the resulting fiber tracks in all subjects for average track length and average FA value along the whole tract. Paired t-tests indicated that the average length of the AF fibers as well as average FA value was significantly higher in HARDI tracking than in DTI in both left and right AF (p value < 0.05), showing that the difference in the localization of the AF is consistent across subjects. Table 1 summarizes all results.

Conclusions Arcuate Fasciculus can be localized significantly better(closer to the anatomical definition of the tract) using HARDI due to a better characterization of complex white matter(relative to DTI) in patient and control populations. This establishes the importance and feasibility of HARDI acquisitions and tracking in children and in clinical populations. It also paves the way for future tract-based population studies in a larger sample size (to account for the population heterogeneity) using HARDI-based measures.

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[2] Fletcher et al, Microstructural connectivity of the arcuate fasciculus in adolescents with high-functioning autism, NeuroImage, 51(3), 1117-25