Diffusion Tensor Spectroscopy and Imaging of Arcuate Fasciculus

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Introduction

The arcuate fasciculus (AF) is a white matter pathway important for language processes; it projects between Wernicke's area (left posterior superior temporal gyrus on the Sylvian fissure) and Broca's Area (opercular and triangular regions of the left inferior frontal gyrus). Multiple groups have utilized diffusion tensor imaging (DTI) in humans to characterize the left and right AF and have reported leftward asymmetries in volume, fractional anisotropy (FA) or density (1-3). However, because DTI is unable to separately measure intra- and extracellular molecular water diffusion in white matter, it is not possible to determine whether leftward asymmetries are caused by intra- and/or extracellular factors. Additionally, a histological study of the fiber composition of the left and right AF has not been carried out because a gross dissection of this pathway is very difficult. As a result, a concise histological explanation for the leftward asymmetries found using DTI is unknown.

N-acetyl-aspartate (NAA) is a neurometabolite confined to the intracellular space. Past studies have measured the diffusion properties of NAA in humans, and have found it is an excellent probe of tissue properties (5-6). Furthermore, we have performed Diffusion Tensor Spectroscopy (DTS) of NAA and water in human corpus callosum (CC), and have found that the diffusion properties of the two molecules are reflective of the known histology of the CC (work submitted). In this preliminary study, diffusion tensor fiber tracking and probabilistic mapping was performed to accurately segment the left and right AF from neighboring fasciculi. Once the locations of the left and right AF were known, DTS measurements of NAA and water were made in both fasciculi to compare, contrast and relate the diffusion properties of the intracellular space (NAA diffusion) with the diffusion properties of the combined intra- and extracellular space (water diffusion).

Materials and Methods

DTI, DTS and anatomical imaging were performed using a 3 Tesla Philips Intera scanner on a healthy right-handed 26 year old male. **DTI**: Pulse sequence=Single Shot SE-EPI, TR/TE=10646ms/91ms, b-value=1069sec/mm^2, Resolutions=1.8x1.8x2.0mm^3, # of Diffusion Directions=15, # of axial slices=73. Three DTI datasets were acquired, corrected for motion, coregistered and averaged within and between acquisitions. Left and right Wernicke's and Broca's area were identified on T1-weighted anatomical images and used as regions of interests (ROI) for probabilistic mapping. ROI constrained probabilistic mapping was achieved with the probabilistic mapping method proposed by Parker et al. (7). **DTS**: In separate scanning sessions, DTS was performed in the left and right AF (*Horizontal Section of AF not included in VOI*). Single voxel (40x10x8 mm^3) NAA and water diffusion measurements were obtained by incorporating diffusion gradients within a standard PRESS sequence (TR/TE=2500ms/135ms). Water suppression was performed such that a substantial residual water peak was still present, thus allowing zero-order phase correction to be performed on individual spectra prior to averaging. In each VOI, NAA and water diffusion measurement were made using three distinct b-values: 1) 161.02 sec/mm^2, 2) 779.38 sec/mm^2 and 3) 1648.90 sec/mm^2. For each b-value diffusion weighting was applied in the following six directions: [1 0 1] [1 1 0] [0 1 1] [0 1 -1] [-1 0 1] [1 -1 0]. 48 measurements were acquired for NAA diffusion characterization, while only 8 measurements were necessary for water diffusion characterization. For each spectrum 2048 data points per scan were collected with a spectral window of 2.5 KHz.

Results and Discussion

Figure 1 shows the AF projecting between Wernicke's and Broca's area in the left hemisphere, while **Figure 2** depicts 2D probabilistic maps of the left and right hemisphere AF. Probabilistic mapping allowed for fiber density estimation within each white matter voxel. Those regions colored in light blue-green have higher fiber density than the blue voxels. We observed a leftward asymmetry in FA(NAA), FA(Water) and fiber density (**Table 1**), while the ADC(water), measured by both DTI and DTS, and ADC(NAA) were similar in left and right AF and in agreement with past studies (5,6,8). The FA(water) as measured by DTI was higher than FA(water) measured by DTS. This is likely a result of the much smaller voxel size implemented in DTI, and thus a far less susceptibility to the macroscopic curvature of the AF which decreases the calculated FA value. We found that the FA(NAA) was significantly higher in the left AF in comparison to FA(water). The highly anisotropic nature of FA(NAA), particularly in the left AF, is a result of a relatively small radial diffusivity component (*RD - diffusion occurring perpendicular to the main fiber axis*), in comparison to the axial diffusivity component (*AD - diffusion occurring parallel to the main fiber axis*); a diffusion behavior reflective of small diameter axons. In left AF, the RD(NAA) was 32% of the AD(NAA), while in the other NAA and water measurements, the RD was between ~45% to ~60% of the AD. Given the relatively lower RD and higher fiber density in the left AF, we believe that the higher FA values or stronger connectivity observed in the left AF in present and previous studies is perhaps caused by a higher density of small diameter axons in left AF. However, additional DTS and DTI in right and left AF will be performed on more right-handed male subjects in order to validate the initial findings.

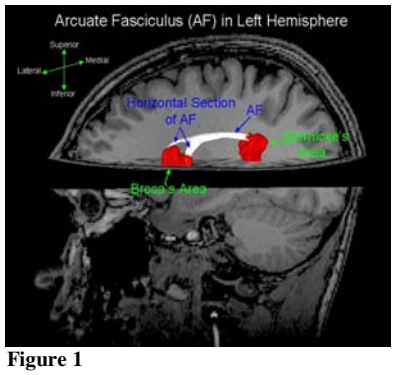

Figure 1

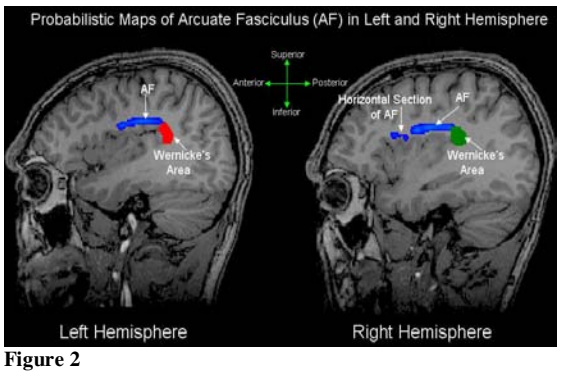

Figure 2

Table1		Left AF	Right AF
ADC ($\times 10^{-3}$ mm^2/sec)	Water(DTI)	0.642	0.627
	Water(DTS)	0.601	0.668
	NAA	0.150	0.157
FA	Water(DTI)	0.56	0.51
	Water(DTS)	0.42	0.38
	NAA	0.69	0.57
RD ($(\lambda_2+\lambda_3)/2$) ($\times 10^{-3}$ mm^2/sec)	Water(DTI)	0.479	0.447
	Water(DTS)	0.423	0.551
	NAA	0.0887	0.120
AD (λ_1) ($\times 10^{-3}$ mm^2/sec)	Water(DTI)	1.08	0.989
	Water(DTS)	0.843	0.902
	NAA	0.274	0.230
Probability(%)	Water(DTI)	13.03	11.28

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