Feasibility of prefronto-caudate pathway tractography using high resolution diffusion tensor tractography data at 3 T

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Introduction. The caudate and putamen (Striatum) are the principal input of the basal ganglia circuit in the human brain (1). The caudate nucleus curves around the ventricular system and receives most of the projections from association areas of the cortex (1). The projections are particularly heavy from prefrontal cortex and frontal pole which project to the head of the caudate (1). The noninvasive mapping of the frontal lobe connections to the thalamus and basal ganglia would help advance our knowledge of brain-behavior relations (2, 3, 4) as a result of natural aging (5), or pathologies such as Huntington's disease (6), bipolar disorders (7), Tourette's syndrome (8), and attention-deficit/hyperactivity disorder (9). Diffusion tensor tractography of white matter connections between the cortex and deep gray matter structures is challenged by the signal-to-noise ratio (SNR) due to overestimation of anisotropy at low SNR (5) and partial volume averaging upon using large voxel volumes (10). This work explored the feasibility of *in vivo* quantification and visualization of white matter connections such as frontostriatal pathway using a high resolution DTI technique and deterministic tractography approach (2,11). In this work we demonstrate, for the first time, the feasibility of *in vivo* delineation and 3D reconstruction of the prefronto-caudate pathway using high resolution DTI data on 3.0 T. We also show the ability to separate and quantify bilaterally the tract volume and corresponding diffusion tensor metrics of anterior thalamic radiation (ATR) and prefronto-caudate pathways.

Methods: *Subjects*: Five healthy men (age range 24-37 years) were studied and written informed consent was obtained from all subjects. *Conventional and DT-MRI Acquisition*: Data were acquired using a Philips 3.0 T Intera system using a SENSE receive head coil. The MRI protocol included conventional MRI (dual echo FSE, phase-sensitive, FLAIR & 3D anatomical) in addition to a matching prescription of DT-MRI. Diffusion-weighted image (DWI) data were acquired axially from the same graphically prescribed cMRI volumes using a single-shot multi-slice 2-D spin-echo diffusion sensitized and fat-suppressed echo planar imaging (EPI) sequence, with the balanced *Icosa21* tensor encoding scheme (5,12). The b-factor = 500 sec mm^{-2}, T_R/T_E = 14460/60 msec, FOV = 256 mm x 256 mm and slice thickness / gap/ #slices = 1 mm / 0 mm / 120. The EPI phase encoding used a SENSE k-space undersampling factor of two, with an effective k-space matrix of 112x112 and an image matrix after zero-filling of 256x256. The acquisition spatial resolution for DTI data was ~ 2.29mm x 2.29mm x 1mm, and the nominal resolution after image construction was 1mm x 1mm x 1mm. To study SNR and partial volume averaging effects we have also repeated the data acquisition from the same subjects and have acquired data at 2mm, 3mm slice thickness with identical in-plane and acquisition parameters to the 1mm experiment. *Fiber Tracts*: anterior thalamic radiation (ATR) pathway originates from thalamus and passes through the anterior limb of internal capsule (ALIC) to the frontal cortex. Prefronto-caudate originates from prefrontal cortex (frontal pole) and traverses through the caudate head and ends in the thalamus and is located parallel and medially to the ATR. *Fiber Tracking*. We have used a brute force and multiple ROI tracking method and the FACT algorithm (2,10,11) (DTIStudio) to reconstruct *prefronto-caudate and the anterior thalamic radiation connections* with a fractional anisotropy (FA) threshold of 0.22 and angle threshold of 60 degrees. Statistical comparisons were made using analysis of variance (student t-test) and the Mann-Whitney tests.

Results: Figure 1 illustrates the construction of the prefronto-caudate (pink) and anterior thalamic radiation (red) and fusion with the T1w data on 3D (a,b) and 2D views(c,d). **Figure 2.** Illustrates the effect that measurable anisotropy can be detected (delineated green fibers passing through the caudate head) using high spatial resolution DTI data. **Table 1** provides a summary of the mean and standard deviations of the tract volumes and corresponding FA and average diffusivity (D_{av}) values of the bilateral FS and ATR fiber tracts on the five subjects. Note that the ATR tract volume and anisotropy are larger than the FS bilaterally ($p < 0.02$; **Table 1**).

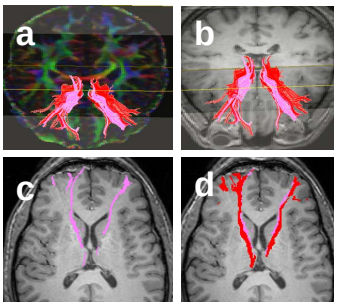

Figure 1. 3D and 2D views of the Prefronto-caudate (pink) and ATR (red) pathways.

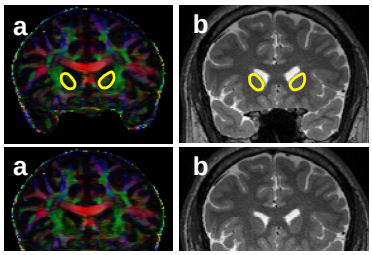

Figure 2. Caudate head cross sectional view o DTI color coded map and T2-weighted images The demarcated area shows the visible green fibers passing through the caudate head.

Table 1. *N=5*	**Tract Volume (mL = cm^3)**	**FA ($\mu \pm \sigma$)**	**D_{av} (x10^{-3} mm^2 sec^{-1})**
ATR Right	5.925 ± 0.902	0.462 ± 0.017	0.847 ± 0.018
ATR Left	5.149 ± 1.248	0.456 ± 0.022	0.833 ± 0.024
p (R vs. L)	0.22	0.49	0.37
FS Right	2.197 ± 0.374	0.414 ± 0.035	0.847 ± 0.038
FS Left	2.248 ± 0.503	0.413 ± 0.031	0.840 ± 0.044
p (R vs. L)	0.64	0.79	0.37
Right p (ATR vs. FS)	**2.8 x 10^{-5}**	**0.02**	1
Left p (ATR vs. FS)	**0.001**	**0.03**	0.77

Discussion and Conclusions: In this report we demonstrated that using higher resolution along with thinner slices reduce the partial volume effect and enabled the tracing of the prefronto-caudate pathway within the gray matter (caudate nuclei) *in vivo*. Using higher resolution combined with higher magnetic field strength improved the detectable anisotropy in gray matter (caudate) along with reducing partial volume effects (5, 10). This allowed us to reveal more anatomical details and to map the prefronto-caudate pathway (12, 13). In our experience, anterior thalamic radiation is traceable using slice thickness ~ 3mm, while the prefronto-caudate pathway was not traceable using the FACT approach at ~ 3mm which is attributable to mixing of fibers in different orientations within the voxel leading to lack of needed anisotropy in gray matter in larger voxel volume which was solved by using thinner slices and smaller voxel volume (12, 13). Extensions of this preliminary work will include the comparison with probabilistic tracking methods (14).

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