How diffusion model and tract direction growth affects quantitative DTI parameters in Ataxia

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Introduction:

Knowledge of white matter structural organization is essential to have a deeper understanding of the functional consequences of lesions such as stroke or tumors, and the consequences of neurological diseases such as ataxia. Ataxia, or incoordination of movement, is a disorder that can be caused by damage to several motor or sensory regions of the central nervous system[1]. Previous studies demonstrated FA was significantly reduced in corticospinal tract in spinocerebellar ataxia. Several fiber tracking algorithms have emerged in the last few years that provide reproducible visualizations of three-dimensional fiber tracts[2]. One class of these algorithms is probabilistic tractography. As implemented in the FSL software Bayesian Estimation of Diffusion parameters Obtained Using Sampling Techniques (BEDPOST) runs Markov Chain Monte Carlo sampling to build up distributions on diffusion parameters at each voxel[3]. A separate implementation, Qboot is a command line tool embed in FSL that allows estimation of diffusion ODF (Orientation Distribution Function) and fiber orientations via Laplacian sharpening and Laplace-Beltrami regularization [4]. Both models allow one to estimate the white matter connectivity using probabilistic tractography. One can constrain the tractography with anaotmic 'seed and waypoint masks'. Every voxel within the seed mask is used as a start point (sampled 5000 times). In order to be retained, each tract launched from a seed voxel must pass through the waypoint mask to dissect specific tracts based on anatomical priors. The current study compares the effect of (1) different diffusion models (bedpostx vs qboot) and (2) different track growth directions of probabilistic tractography on mean tract FA and fiber volume between ataxia subjects and controls.

Methods:

Five individuals with ataxia and six healthy control subjects participated in the study. The imaging protocol included a sagittal three-dimensional T1-weighted magnetization prepared rapid gradient echo (MPRAGE) sequence and diffusion tensor data acquired using a single shot echo planar imaging (SS-EPI) sequence with diffusion weighting b=1000 s/mm^2 in 64 diffusion directions and b=0 image. Other sequence parameters used were: TR/TE=9400/89ms, matrix=128×128, slice thickness = 2mm, 72 of slices, flip angle=90°, bandwidth =1345Hz/pixel. Using FMRIB's Diffusion Toolbox (FDT), diffusion tensor fitting was performed and voxelwise values for fractional anisotropy (FA) were calculated. Individual masks were drawn on transverse slices of the cerebral peduncle (cp) and posterior limb of internal capsule (plic) separately for the left and right hemisphere, and a midsagittal exclusion mask was used to prevent fibers from crossing the midline. Masks were drawn in diffusion space, guided by a directional colored FA map. In order to obtain the probability of diffusion in each of the measured directions, we applied the BEDPOSTX tool that accounts for 2 crossing fibers per voxel as well as the Qboot method. Probabilistic tractography was completed independently for both hemispheres using three methods: (a) seed at cp and use the plic as the waypoint; (b) use the plic as the seed and the cp as the waypoint; and (c) use both the plic and the cp as seed only points. In order to determine the appropriate threshold for quantification, the voxel with the maximum number of fibers and its nearest six voxels were averaged to generate an average peak number of tracts. A 10% threshold based on this averaged value was then applied to the resulting pathways to remove false connections. From the remaining fibers that make up the desired pathways, we calculated the mean FA of the tract and the tract volume. Two sample t-tests were performed on SPSS 18 to compare the tract-based FA and tract volume between control and ataxia subjects in both hemispheres. P<0.05 is considered statistically significant.

Results:

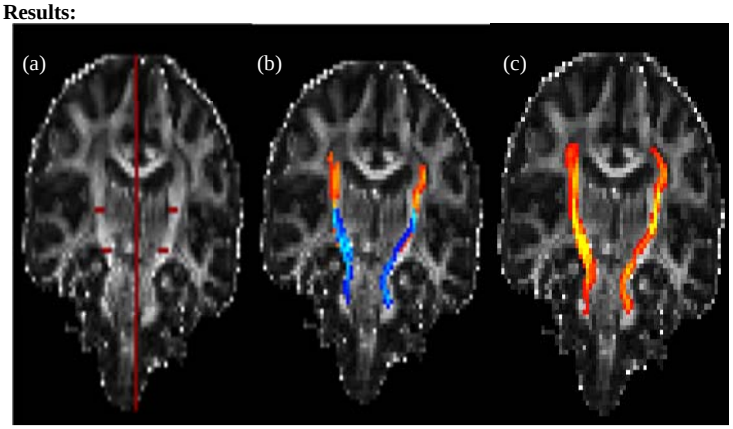

Figure1.(a) Placement of masks (horizontal red bars) in cp and plic for tractography. A midsagittal exclusion mask was placed to exclude fibers that cross to the opposite hemispheres (vertical red bar). Integrated probabilistic tractography images show cerebral peduncles (cp) and posterior limb of internal capsule (plic) fibers. (b) ROI of cp was used as seed and plic was used as waypoint (Red-yellow fibers); ROI of plic was used as seed and cp was used as waypoint (Blue-light blue fibers). (c) Both ROIs of plic and cp were used as seed.

(a)	Seed	Way point	FA			Voxel		
			Ataxia	Control	p-value	Ataxia	Control	p-value
Bedpostx	cpL	plicL	0.445	0.4631	0.056	657	556	**0.015**
	plicL	cpL	0.492	0.5594	0.235	581	380	0.134
	cpR	plicR	0.436	0.4735	0.209	645	467	0.423
	plicR	cpR	0.488	0.5422	0.206	644	352	**0.027**
qboot	cpL	plicL	0.447	0.4603	0.084	640	692	0.947
	plicL	cpL	0.49	0.5329	**0.031**	589	440	0.152
	cpR	plicR	0.457	0.4796	0.248	665	529	0.114
	plicR	cpR	0.519	0.5495	**0.007**	625	378	**0.026**
(b)	Seed		FA			Voxel		
			Ataxia	Control	p-value	Ataxia	Control	p-value
Bedpostx	cpL,plicL		0.461	0.4962	0.727	1019	726	0.309
	cpL,plicL		0.452	0.4902	0.34	1150	659	0.077
qboot	cpR,plicR		0.452	0.4774	0.567	986	869	0.189
	cpR,plicR		0.457	0.5002	0.379	1027	615	**0.047**

Table1. Tract-based mean FA and mean number of voxels in ataxia and control subjects using bedpostx and qboot method. L: Left R: right. (a) One ROI was used as seed and the other was used as waypoint. (b) Both ROIs (plic and cp) were used as seed.

FDT toolbox generates a connectivity distribution from voxels in the seed mask and retains only those paths that pass through all of the waypoint masks. The effect of directional mapping is shown for a single subject in Figure 1. In Fig 1(b), red-yellow represents fibers grown using the peduncle as the seed and the plic as the waypoint, and blue-light blue (overlaid on red-yellow) represents fibers in the reverse direction. Connectivity distributions using both the internal capsule and peduncle as seeds are shown for the same subject in figure 1(c). Table 1 shows that tract-based FA and volume from peduncle (seed) to posterior limb of internal capsule (waypoint) are always respectively smaller and bigger than the one from opposite direction. A consistent trend of FA decrease in ataxia subjects was observed compared to the control group, however only the plic to cp results from qboot were statistically significant. Significant differences between control and ataxia subjects were also observed for volume from plic to cp results in the right hemisphere. Neither Qboot nor BedpostX could distinguish patients from controls when both clip and cp were used as seeds to generate FA values.

Discussion:

FA is commonly used to reflect white matter integrity since it describes the overall degree of coherence in a voxel. Ataxia patients might experience a disruption to membranes and myelin in their motor fibers, which results in a lower FA. In this study, we observed a consistent trend of decreased FA in ataxia patients, but only the plic to cp results calculated with Qboot were statistically significant. Probabilistic tractography from posterior limb to peduncle mainly involves only corticospinal tract, whereas the opposite direction also includes corticofugal and sensory fibers, which contain more crossing fibers resulting in an overall decreased FA. Therefore same masks with different tract growth directions could result in different connectivity measures, leading to different FA values. Using the plic as the seed and the cp as the waypoint may be more sensitive to detect abnormalities in ataxia patients. Although both Qboot and BedpostX are established probalistic tractography algorithms, only the qboot model demonstrated a significant difference of FA between the ataxia and control groups in this study. Our results demonstrate that selection of diffusion algorithm and tract direction is nontrivial in DTI data processing.

References

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