Diffusion tensor imaging bootstrap metrics differentially predict memory among older adults

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Purpose

There has been an increasing interest in identifying white matter microstructural abnormalities associated with cognition in aging. Fractional anisotropy (FA), derived by diffusion tensor imaging (DTI), is one of the most popular metrics to quantify fiber integrity. However, FA suffers from measurement error in smaller fiber structures due to the limitations of the tensor model and often fails as a reliable metric to reveal microstructural abnormalities. Bootstrap methods [1] have recently been introduced to DTI to compute measurement error. Here, we used the bootstrap method to estimate uncertainty in the acquired data and to determine whether it can be used to derive new reliable metrics, including the coherence of the dyadic tensor (κ) and the apex angle of the cone of uncertainty (aCU) [2]. Using the fornix as a region-of-interest, we compared these new metrics to FA to determine whether they independently predicted memory performance.

Methods

Whole brain echo-planar diffusion imaging scans were acquired in 253 non-demented older participants (mean age=76.2±5.17) from an ongoing community-based study of aging and dementia [3] with a 3T Philips Achieva MRI scanner (field-of-view=240x240mm^2, matrix reconstructed to 112x112, 81 contiguous slices, slice thickness=2mm, parallel imaging reduction factor=2, echo time=68.56ms). Diffusion-weighted scans were performed along 15 directions with a maximum b-factor of 800s/mm^2, complemented by two scans with b=0s/mm^2.

The wild bootstrap was applied to generate 1000 bootstrap samples of the diffusion data per subject. Tensor calculation and the bootstrap statistics are part of in-house developed software. As bootstrap metrics of interest we chose the aCU, defined as the 95-percentage angle, and the coherence of the dyadic tensor:

$$\kappa = \left(1 - \sqrt{\frac{\beta_2 + \beta_3}{2\beta_1}}\right)$$

with $\beta_{i=1,2,3}$ being the three eigenvalues of the mean dyadic tensor (representing the average of the principal eigenvectors). Atlas based analysis of the fornix was performed with the FMRIB58_FA standard-space FA template (in MNI152 space) and the ICBM-DTI-81 white-matter labels atlas using the FSL software package.

Participants were evaluated clinically with a comprehensive neuropsychological battery and summary measures of cognition, including memory, were derived. We examined the independent association of the average new bootstrap metrics in the fornix, along with FA, participant age, and number of voxels with memory functioning using simultaneously-entry multiple regression analysis.

Results

The coherence κ and the aCU correlated with memory performance (see Table 1). These associations were independent of the covariates in the model, including FA, number of voxels, and subject age. Of the covariates, number of voxels and subject age, but not FA, were associated with memory functioning.

variable of interest	predictor	standardized β	p-value
coherence of dyadic tensor	κ	0.331	0.015
	FA	0.074	0.581
	number of voxels	0.286	0.027
	subject age	-0.207	0.001
angle of cone of uncertainty	aCU	-0.330	0.014
	FA	0.075	0.570
	number of voxels	0.288	0.026
	subject age	-0.207	0.001

Table 1: Results of the multiple regression analysis

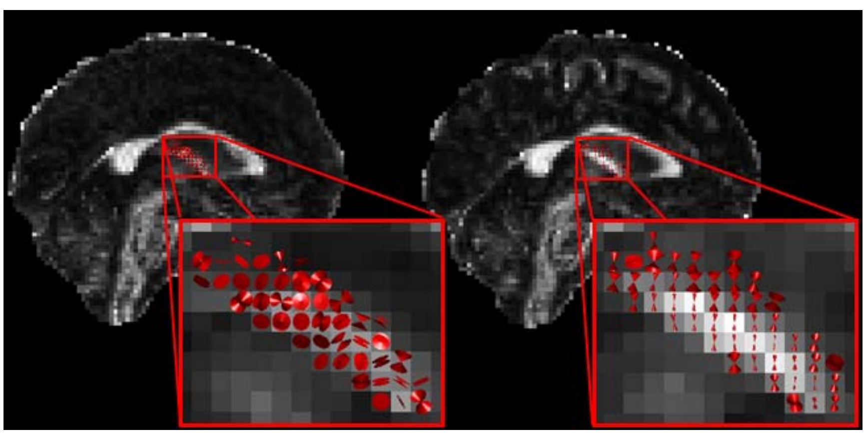

Figure 1: Exemplary cones of uncertainty in the fornix overlaid onto the FA map. The image shows an example of large aCUs (left) and of small aCUs (right).

Discussion

Bootstrap-derived metrics of the principal eigenvector may provide more sensitive measures of fiber integrity for the examination of brain-behavior relationships. Compared with FA, which only takes into account changes in the spatial diffusion distribution, these bootstrap metrics are affected by any diffusion alteration. Our analyses also confirm the role of the fornix in memory functioning among older, non-demented, adults.

Conclusion

Bootstrap analysis of the principal eigenvector provides metrics that are unique and independent of other DTI values. Future work will focus on the relevance of these metrics on other aspects of cognition in aging.

References

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