AGE-RELATED DIFFUSIVITY CHANGES IN BRAIN WHITE MATTER FIBER BUNDLES

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Introduction

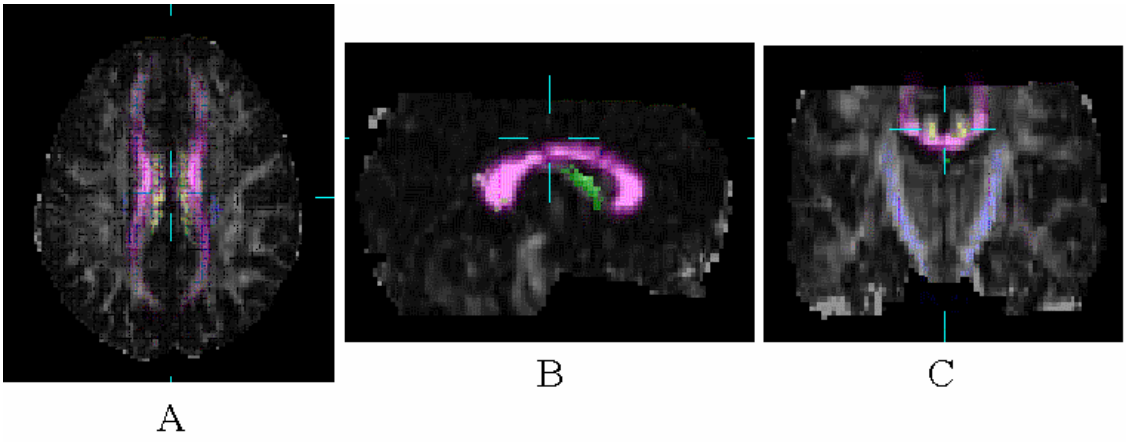
Several diffusion tensor (DT) magnetic resonance imaging (MRI) studies have demonstrated that in the normal appearing brain tissue, mean diffusivity (MD) increases and fractional anisotropy (FA) decreases with age, suggesting tissue deterioration over time, which goes undetected when using conventional MRI (1,2). Reduced white matter (WM) integrity in elderly people, expecially in the frontal lobes, was also revealed (2). In this study, we investigated the influence of normal aging on selected brain pathways. To this aim DT derived metrics were obtained from several brain WM tracts.

Methods

We studied 84 healthy subjects, spanning seven decades of life (mean age=44 years, range=13-73 years). The following brain scans were performed using a 1.5 Tesla scanner (Avanto, Siemens, Erlangen, Germany): a) pulsed-gradient spin-echo single shot echo-planar sequence (PGSE-SS-EPI) (inter-echo spacing=0.77, TR=2900, TE=84), with diffusion-encoding gradients applied in 12 non collinear directions (b factor=900 s/mm^2). Eighteen contiguous axial slices, with 4 mm slice thickness, 128x128 matrix and 240[mm]x240[mm] field of view; b) dual-echo turbo spin echo (TSE) (TR=3460, first echo TE=27, second echo TE=109, echo train length [ETL]=5). Forty-four contiguous axial slices, with 4 mm slice thickness, 512x512 matrix and 250[mm]x250[mm] field of view.

DW images were first corrected for distortion induced by eddy currents; then the diffusion tensor was estimated by linear regression (3) and fractional anisotropy (FA) and mean diffusivity (MD) maps calculated (4). Healthy subjects aged between 21 and 40 years old (N=24) were used as reference group. Subsequent steps consisted in the creation of tract probability maps from the reference group and their application to entire cohort of subjects as described in (5). To make the selection of the starting region of interest for tractography more reproducible and easier, an atlas of the FA was created from the reference group. After coregistration between PGSE and dual echo scans, the dual-echo T2-weighted images were used to calculate the affine transformation to the standard Montreal Neurological Institute (MNI) space. The atlas was then obtained by averaging the transformed FA maps. The following tract probability maps were obtained: corpus callosum (CC) (5), corticospinal tract (CST) (5), cingulum (CYN) (8), fornix (FORN) (9), uncinate fasciculus (UNC) (10), occipito-frontal fasciculus (FO) (10), optic radiation (OR) (11). Because of the presence of atrophy, a non-linear deformation algorithm (6) was used to calculate the transformation between FA maps of all subjects and the atlas. The probability maps were then applied to the transformed MD and FA and their histograms obtained. The correlation of histogram metrics with age were assessed using the Spearman Rank correlation coefficient.

Figure. Transformed FA map (A axial, B, sagittal, C coronal) from a 73 years old subject. Probability maps of corpus callosum (violet), corticospinal tract (blue), cyngulum (yellow), and fornix (green) are superimposed.



Results

Univariate correlations between age and DT MRI metrics from the considered WM fiber bundles are reported in the Table.

Table. Correlations between age and WM tracts diffusivity metrics (r value, p value)

		CC	CST	CYN	FORN	UNC	FO	OR
Age	MD	0.46, <0.0001	0.31, 0.004	0.29, 0.007	0.59, <0.0001	n.s.	0.45, <0.0001	0.53, <0.0001
	FA	-0.64, <0.0001	-0.67, <0.0001	-0.44, <0.0001	-0.63, <0.0001	-0.22, 0.04	-0.55, <0.0001	-0.70, <0.0001

Conclusions

Our study demonstrates that regional measures of brain tissue diffusivity may improve our understanding of the pathobiology of aging. These findings also provide direct evidence that WM tract disruption occurs in normal aging. The interruption of the normal neural networks, subserving cognitive and motor performance, by age-related structural changes might underlie decline in function.

References

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