VOXEL BASED ANALYSIS DERIVED FROM FRACTIONAL ANISOTROPY IMAGES OF WHITE MATTER ATROPHY WITH AGING

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Introduction

Age-related effects on brain volume have been extensively investigated both *postmortem* and *in vivo* using magnetic resonance imaging (MRI). A linear grey matter volume decline with age has been shown using both global and local MR approaches, while regional and temporal patterns of age-related WM loss are still controversial. In this study, a method to measure WM fiber bundles atrophy using diffusion tensor MRI (producing an index of atrophy derived from the transformation between a fractional anisotropy (FA) atlas and single subject FA map) was used.

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 (1) and fractional anisotropy (FA) maps calculated (2). Healthy subjects aged between 21 and 40 years old (N=24) were used as reference group for the creation of an FA atlas resembling the reference morphometry: a single control subject's FA image was chosen randomly as a temporary atlas, and all other FA images were then registered to it using a non-linear deformation algorithm (3). The average of the registered FA images has been re-sampled with the inverse of the average deformation field to achieve a morphological (shape) mean as well as an intensity (FA) mean of the group. The new average image was used as a target atlas during the next iteration. To reduce the influence of the first template on the final atlas, three iterations were used to create the final FA atlas (4).

The non-linear transformation between FA maps of all subjects and the atlas was then calculated and the determinant of the jacobian of the transformation calculated; this scalar summarizes the point-wise volume changes produced by the deformation: values less than unity reflect atrophy, whereas values greater than unity reflect hypertrophy (5). Determinant jacobian maps were smoothed with an 8 mm gaussian filter, before antering the statistical analysis.

To assess correlations between age and volume changes, a general linear model (6) was used to predict at a voxel level the changes from age. We also used a multi-linear regression approach with second-order polynomial expansion, as suggested by Buchel et al., (1996). (7) by using an F statistic and estimating thresholds of statistical significance with False Discovery Rate (FDR) correction (8) for $p<0.05$.

Results

A linear correlation was found between age and WM decline in superior-frontal and parietal fibers, anterior cingulum bundles, fornix, and cerebellar peduncles (F values ranged from 13.9 to 26.1). By contrast, a quadratic regression model best fitted age-related WM loss in the genu of corpus callosum, pons bundles, and inferio-fronto-occipital/uncinate fasciculi (F values ranged from 9.3 to 15.5), as well as the increase of CSF with age in third and lateral ventricles (F values ranged from 11.3 to 27.1).

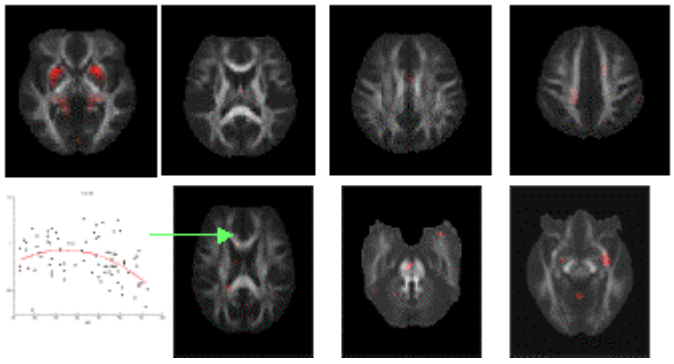

Figure. Brain regions showing an inverse linear (top) and a quadratic (bottom) relation between volume changes and age. Supra-threshold F values ($p<0.05$ corrected with False Discovery Rate) mapped over the FA template using a red lookup table. Regression plot for the non-linear model is reported for the genu of the corpus callosum.

Conclusions

WM volume decline with age is unevenly distributed across brain regions. Age-related WM changes have to be taken into account in explaining the steady loss in function in non-diseased elderly. This approach holds promise to gain additional information on the pathological changes associated to neurological disorders of the elderly.

References

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