Age Related Cognitive Decline and Regionally Specific Changes In White Matter Integrity

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Introduction

There is growing interest in the importance of white matter changes in the ageing brain, and the relationship between this degeneration and cognitive decline. Cognitive changes have been largely ascribed to grey matter atrophy, but a number of methodological flaws place doubt on these findings (1). Moreover, a postmortem study (2) demonstrated loss of small myelinated fibres in white matter of healthy elderly compared to younger subjects. The aim of this study is to use diffusion tensor imaging (DTI) to investigate white matter changes that occur with aging, and the relationship between these changes and cognitive decline.

Methods

Participants

Ninety healthy adults between fifty and ninety years with no prior neurological or psychiatric disorders were recruited. Equal numbers of males and females were recruited to each decade.

MRI Data Acquisition

Whole brain DTI data was acquired on a 1.5T General Electric Signa MRI system as described by Clark et al (3). The in-plane resolution was 2.5 mm, and through plane resolution was 2.8 mm. FA and MD maps were derived from the DTI sequence (see Figure 1 for FA maps by age). Tissue segmentation (probability) images for grey matter, white matter and cerebrospinal fluid (CSF) were generated using the algorithm of Ashburner and Friston (4) from the EPI-T2 image, including correction for intensity non-uniformity. A hard segmentation was computed, with each image voxel being assigned to the tissue type with greatest probability at that voxel. Ten consecutive slices were selected for analysis (5 slices above and 5 slices through the ventricles). Using *dispunc* (David Plummer, University College London, U.K.) automatic contour function, the outer edge of the white matter was selected on segmented images. Using the same technique the ventricles were outlined on EPI-T2 images. A mask was generated for the white matter with the ventricles removed for the ten slices. The mask was then overlaid onto the FA and MD maps. The white matter area was divided into three sub-regions (Anterior, Middle, Posterior) using *mricro* (Chris Rorden, University of Nottingham, U.K.). Sub-region markers were drawn on the EPI-T2 image at the point where the genu of the corpus callosum (CC) was at it's most anterior, and the splenium of the CC was at it's most posterior. FA and MD values were calculated for each area.

Neuropsychology

A detailed neuropsychological assessment was conducted with each participant individually. Standardised assessments were used to assess current IQ, estimated premorbid IQ, information processing speed, memory and executive function abilities.

Results

Age related white matter changes

Progressive increase in MD and decrease in FA (ANOVA, $p < .001$) was apparent over the four decades studied. These results remained consistent when divided into anterior, middle, and posterior brain areas ($p < .001$), see Figure 2. The results also suggest that after the sixtieth year the variability of white matter integrity increases within each decade (demonstrated in Figure 3). Although the rate of decline of brain regions differs across the decades, there was no evidence of a selective decline in the white matter of the anterior part of the brain, as suggested by other studies (5).

White matter changes and neuropsychology

A significant relationship was present between regional white matter changes and cognition, even when age was used as a covariate in the analysis. Both FA and MD showed varying patterns of correlation with cognitive tasks across brain areas.

Discussion

Using DTI we have demonstrated significant and gradual reduction in fractional anisotropy, and a rise in mean diffusivity measures with increasing age, and these parameters correlated with neuropsychological test performance. By selecting more specific brain areas, which are thought to correspond to neural networks it may be possible to investigate in more detail the effect that white matter degeneration has on specific aspects of cognition.

References

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Figure 1

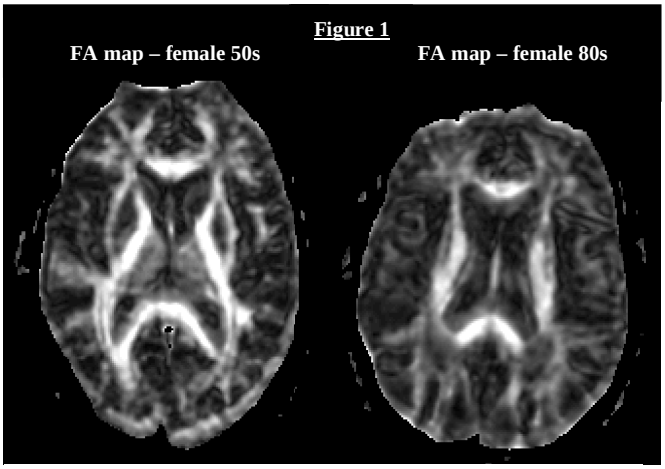

Figure 2: Mean FA values by decade and brain area

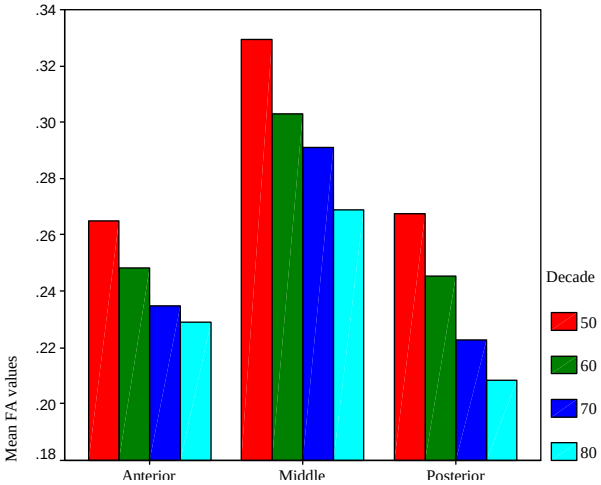

Figure 3: Mean MD by age in all white matter