White matter atrophy and lesion formation explain the loss of structural integrity of white matter in aging

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Introduction

The importance of macrostructural white matter changes, including white matter lesions and atrophy, in intact brain functioning is increasingly being recognized. Diffusion tensor imaging (DTI) enables measurement of the microstructural integrity of white matter. Loss of white matter integrity in aging has been reported, but whether this is inherent to the aging process itself or results from specific white matter pathology is unknown. Using DTI in persons aged 60 years and older, we studied whether and how white matter atrophy and white matter lesions related to microstructural integrity in normal-appearing white matter and whether this was independent from age.

Materials and methods

In 813 persons (mean age 67.3 years) from the population-based Rotterdam Study, we derived fractional anisotropy (FA) measurements from DTI scans. FA values of the central voxels in the major white matter tracts of all subjects were projected onto a common white matter skeleton using Tract Based Spatial Statistics [3], an automated robust mapping technique that prepares data for direct voxelwise comparison. Separately, automated tissue segmentation [2] identified voxels originating in white matter lesions. These voxels were excluded from the analysis to allow a specific focus on the normal-appearing white matter. Statistical analysis was performed with multiple linear regressions, adjusting for age, sex and white matter atrophy or white matter lesion load and corrected for multiple comparisons.

Results

With increasing age, multiple regions showed significant decreases in FA in normal-appearing white matter. However, nearly all of these regional decreases in FA were explained by either white matter atrophy or by white matter lesions as depicted below and in [3]. Both processes were found to be related to distinct brain regions: white matter atrophy was primarily related to FA decrease in the body of the corpus callosum and in the limbic system (cingulate tract and hippocampal region), while white matter lesion load related mainly to periventricular integrity loss.

Conclusions

Loss of white matter integrity in aging is primarily explained by atrophy and lesion formation and not by the aging process itself. Furthermore, white matter atrophy and white matter lesion formation relate to loss of integrity in distinct brain regions, indicating the two processes are pathophysiologically different.

References