Densely packed white matter regions are less prone to develop white matter hyperintensities

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Purpose

White matter hyperintensity (WMH) maps[1] and diffusion tensor imaging[2] (DTI) parameter maps have been widely used to investigate cerebral white matter (WM) changes of the aging brain, which commonly include damage that is associated with cognitive decline. While the WMH maps provide a macroscopic assessment of the underlying damage, DTI parameter maps provide insight into the microscopic structure. Although the literature comparing the two techniques and their potential to predict cognition is quickly growing, the relationship between the parameters derived from the two techniques is poorly understood. For example, whether regions appearing as WMH are especially prone to microstructural damage or if microstructural damage precedes the formation of WMH is still under investigation. In the present study, DTI parameters in WMH regions and in the remaining normal appearing WM (NAWM) were compared in a sample of elderly subjects. Furthermore, a WMH probability map was derived from the same sample of elderly subjects and a reference DTI dataset was computed from a sample of young and healthy subjects to show, for the first time, a relation between healthy young WM microscopic structure and the probability to develop a WMH.

Methods

Subjects: The elderly subject cohort (C_{old}) consists of 253 non-demented older participants from an ongoing community-based study of aging and dementia[3] and the cohort of young subjects (C_{young}) consists of 222 healthy participants[4].

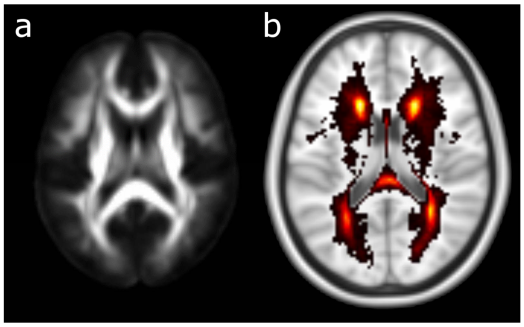

Figure 1: Reference FA map (a) and P_{WMH} map (b).

WMH: T2-weighted fluid attenuated inversion recovery (FLAIR) images for C_{old} were acquired on a 1.5 Philips Intera scanner using the following scan parameters: TE=5500ms, TR=144ms, TI=1900ms, field-of-view: 250x250mm2, matrix reconstructed to 256x256, 47 contiguous slices, slice thickness=3mm. WMH were derived as described previously[5]. Briefly, WMH were selected as voxels with 1.2 standard deviation or greater above the mean intensity value of the FLAIR image. To compute a WMH probability (P_{WMH}) map, the 253 WMH binary masks from C_{old} were transformed into MNI space, additively combined, and normalized with the number of subjects.

DTI: DTI data in C_{old} was acquired with a 1.5T Philips Achieva MRI scanner (field-of-view=240x240mm^2, matrix reconstructed to 112x112, 70 contiguous slices, slice thickness=2mm, parallel imaging reduction factor=2, TE=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. In addition to the most common DTI parameters (MD, AD, RD, and FA) the apex angle of the cone of uncertainty[6] (aCU) was computed. To produce a young and healthy reference map for each of the DTI parameters, the subject based parameter maps derived from the DTI data provided in C_{young} were transformed into MNI space and averaged.

Statistic: DTI parameters were subject-wise averaged for NAWM and regions appearing as WMH, resulting in two samples for each DTI parameter with a common sample size equal to the number of subjects in C_{old}. A t-test was performed to test the difference between the two samples. Furthermore, voxel-based linear regression analysis was conducted treating P_{WMH} derived from C_{old} as the dependent variable and the DTI parameters from C_{young} as the predictors.

Results

Fig 2 depicts the differences of the DTI parameters in the WMH regions and the NAWM. WMH regions show a significantly higher averaged diffusivity in all directions (MD, AD, and RD) than NAWM. In addition, FA as well as aCU are significantly higher in WMH regions. All DTI parameters reveal a significant correlation with P_{WMH} (see Figure 3). The FA value proves to be the most significant predictor. While RD increases with increasing P_{WMH}, the correlation with AD is inverse. Driven by the effect of RD, MD increases also with increasing P_{WMH} despite the decrease of AD.

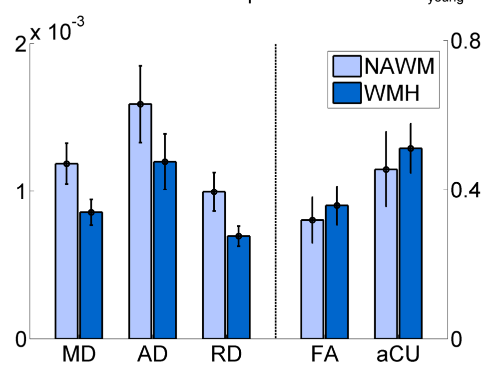

Figure 2: DTI parameters in NAWM and in WMH.

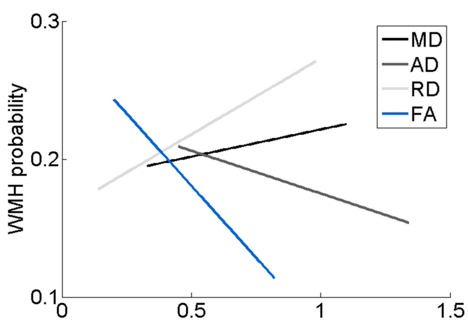

Figure 3: Regression lines for the DTI parameters and P_{WMH}. MD, AD, and RD are normalized with $2 \cdot 10^{-3}$ mm^2/s.

Discussion

The present study makes use of two different subject samples, C_{old} and C_{young}. While C_{old} provided individual DTI parameter maps and WMH maps, C_{young} served only to compute a DTI reference maps. Furthermore, the WMH maps from C_{old} were combined to produce a P_{WMH} map. Two main findings were noted. First, the comparison between DTI parameters in NAWM and WMH regions in C_{old} not only confirms the previous findings of larger diffusivity and smaller FA values in WMH regions but also includes aCU as an additional DTI parameter that shows a significant difference between the two regions. Second, the computation of a P_{WMH} map and of a DTI reference map revealed a higher probability to develop a WMH for regions with normatively less densely packed tracts.

Conclusion

WM regions with less densely packed tracts are more prone to develop a WMH. This relation is best shown using RD and FA.

References

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