Fornix shows a unique pattern of microstructural alteration and a relationship to network efficiency in healthy ageing

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Target audience

Clinical neuroscientists with interest in ageing and age-related diseases, diffusion MRI and connectomics specialists

Purpose

Healthy ageing is characterised by degradation of white matter microstructure and reduced structural network efficiency, which both relate to a decline in cognitive function. Studies often describe microstructural and topological alterations at a global scale or report age associations for individual tracts. It remains unclear to what extent age-related alterations of individual tracts are driven by a global process and how individual tracts relate to network efficiency changes. We explored age-related microstructural alterations for selected temporal lobe association tracts, known to be involved in memory and/or affected in healthy ageing, and linked these changes to measures of microstructural integrity for whole white matter. Additionally, we linked microstructural variation in single tracts to network global efficiency.

Methods

39 healthy elderly (aged 53-93 yrs.) underwent diffusion-weighted MRI (3T GE HDx system, twice refocused spin-echo echo planar imaging sequence, 2.4 mm isotropic voxels, TE = 87 ms, b = 1,200 s/mm^2, 30 isotropically distributed directions, 3 non-diffusion-weighted scans, acquisition time approx. 13 min). A two-compartment model using Free Water Elimination was fitted and values of fractional anisotropy (FA) and mean diffusivity (MD), corrected for cerebrospinal fluid-contamination, were computed.
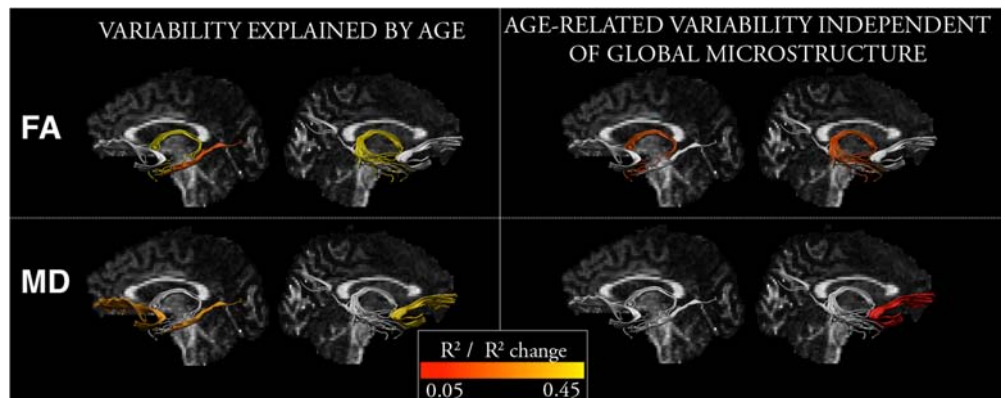
The fornix, uncinate fasciculus (UF) and parahippocampal cingulum (PHC) were reconstructed by region of interest based deterministic tractography. Whole white matter mean FA and MD values were calculated by applying white matter masks. White matter structural networks were constructed by parcellating whole-brain tract reconstructions using 90 cortical and subcortical regions in the automated anatomical labeling atlas. Edges between nodes were weighted by the number of reconstructed streamlines between any two regions of the template.

Contribution of age to microstructural variation of individual tracts was assessed using linear regression modelling and repeated using mean white matter FA and MD in the model to assess the contribution of age independent of global microstructural variation. The values of global efficiency of white matter structural networks were correlated with participant age. Linear regression was used to assess the contribution of individual temporal pathways to age-related changes in network efficiency.

Results

Fornix FA and MD of both UF and left PHC show significant relationships with age (Fig, left). Only fornix FA shows a significant contribution of age independent of global white matter microstructural variation (Fig, right).

White matter structural networks exhibit a decrease in global efficiency with increasing age (r = -.435, p = .006). When fornix FA is additionally included in the model, fornix FA is a significant predictor

of global efficiency (t = 3.30, p = .002), while age is not a significant predictor (t = -0.37, p = .71). This is not the case for regression models in which other microstructural measures (fornix MD, FA and MD of both UF and PHC) were included as independent predictors of global efficiency in addition to participant age. Only participant age is a significant factor in these models.

Discussion

Microstructural alterations in temporal association tracts partly reflect global alterations in white matter. Only the fornix manifests significant age-related microstructural variation not shared with the rest of the brain. White matter structural networks show an age-related decrease in global efficiency. This relationship is mediated by fornix microstructure, in contrast to microstructural measures of other temporal association tracts, which do not show an age-independent relationship with global efficiency.

Conclusion

The fornix stands out in demonstrating age-related microstructural variation not shared with the rest of the brain. It also has a unique relationship to structural network topology by mediating the age-related decline in global efficiency.