White matter microstructure in a healthy population aged 50-65; automated tractography method and TBSS.

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*Introduction: W*hite matter (WM) microstructure has to a large extent remained unmapped in general human populations. Only one large population study, the Rotterdam Study, has used DTI in participants (n=832) > 60 years (Vernooij et al, 2008). In this project we aim to study WM microstructure at the population level in a cohort of 1006 participants between 50 and 65 years participating in the MRI substudy of the Health Survey of Northern Norway 3 (HUNT MRI). Our first approach will be to explore WM using a new automated tractography method to segment WM tracts and tract-based spatial statistics (TBSS) to investigate voxelwise statistics in the core of the WM tracts. In these preliminary data the effects of sex and age are examined. There are ample questionnaire data and clinical measures available for the HUNT MRI participants which will be used in future studies.

Materials and Methods: DTI was performed in 1006 healthy participants (50-65 yrs) from the HUNT MRI substudy. A total of 812 successful DTI scans were obtained (n=65 were removed due to pathology and n=129 were removed due to artefacts) on a 1.5 T GE scanner (Signa HDx) with a single-shot balanced-echo EPI sequence acquired in 40 non-collinear directions with b = 1000 s/mm^2 and 5 b=0 images using the following parameters: TR = 13500 ms, TE = 104 ms, FOV 240 x 240 mm, slice thickness 2.5 mm, acquisition matrix 96 x 96. A new partition-based clustering method for automatic segmentation of WM tracts was used to visualize and calculate mean fractional anisotropy (FA) and volume of corpus callosum, corticospinal tract, cingulum, inferior longitudinal fasciculus, superior longitudinal fasciculus and inferior fronto-occipital fasciculus (Visser et al, 2011). TBSS was carried out to analyze the effects of age and sex on FA.

Results: Individual results from the automated tractography segmentation of corpus callosum from a random sample of 14 HUNT MRI individuals are shown in figure 1A, and for corticospinal tract, cingulum, inferior longitudinal fasciculus, superior longitudinal fasciculus and inferior fronto-occipital fasciculus in one of the subjects in figure 1B. The segmentation results demonstrated that both mean FA and volume of corpus callosum was higher in males compared to females. TBSS showed decreased FA in large areas of the white matter skeleton with increasing age in the HUNT MRI population (Figure 1C). In females FA was higher than males in the occipital lobe, while in males FA was higher than females in the deep central WM structures and in association tracts in the frontal and temporal lobes (Figure 1D).

Discusssion: The automated tractography segmentation method demonstrated that it is possible to derive automatic segmentation, quantitative information and identification of WM tracts that are consistent across a large number of individuals (n=812). We will further exploit this method to investigate the relationship between FA and questionnaire data and clinical measures available for the HUNT MRI participants.

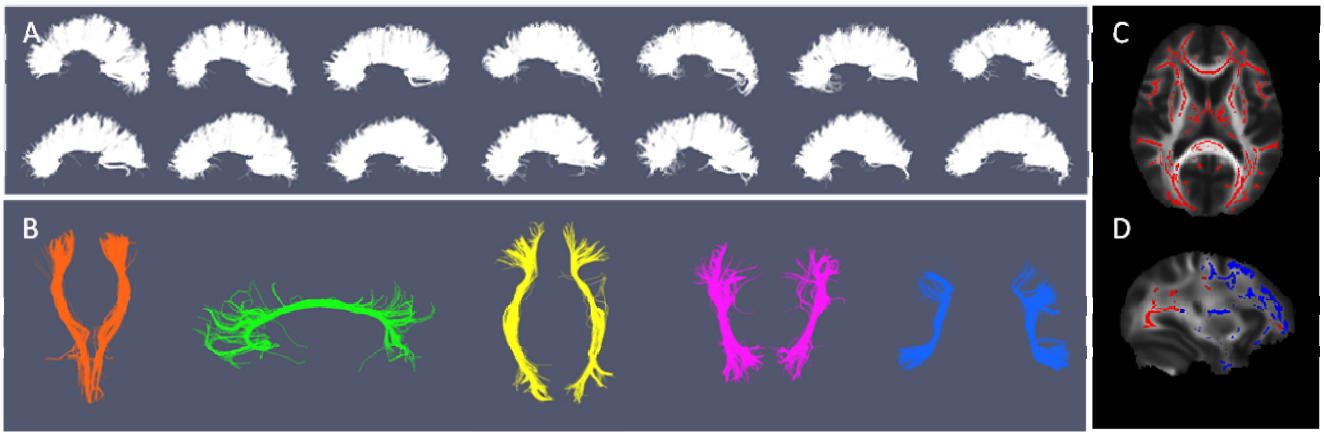

Figure 1. Automated tractography results of corpus callosum from a subpopulation of n=14 individuals from the HUNT MRI population (A) and corticospinal tract, cingulum, inferior longitudinal fasciculus, superior longitudinal fasciculus and inferior fronto-occipital fasciculus in one of the subjects (B). TBSS analysis demonstrated areas with significantly decreased FA (RED) with increasing age (C) and significantly higher FA in female than males (RED), and significantly higher FA in males than females (BLUE) (D) ($p<0.05$, nonparametric permutation test, corrected for multiple comparisons).

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Vernooij MW, de Groot M, van der Lugt A, Ikram MA, Krestin GP, Hofman A, Niessen WJ, Breteler MMB. White matter atrophy and lesion formation explain the loss of structural integrity of white matter in aging. Neuroimage 43 (2008) 470-477.