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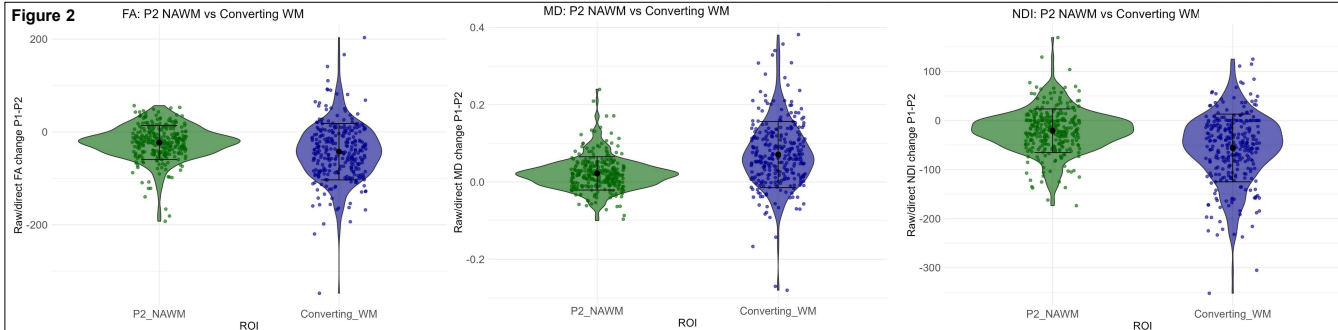
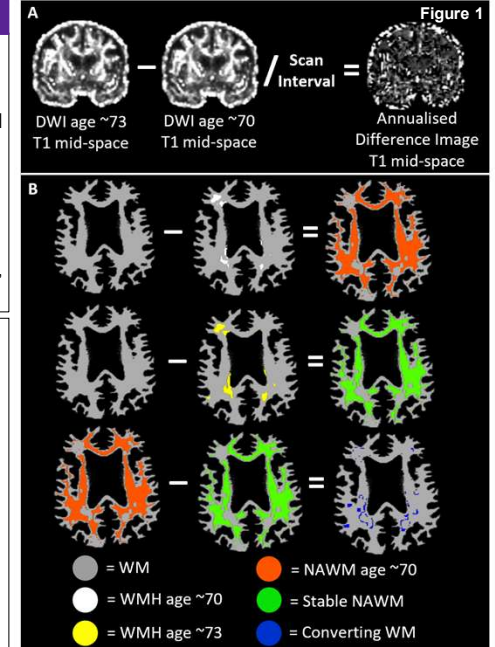
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Background

- Diffusion weighted imaging (DWI) measures white matter (WM) microstructure (WMMS).
- Poorer WMMS integrity is seen in Alzheimer's disease (AD).
- Aims: determine how blood pressure (BP), beta-Amyloid (A β) and apolipoprotein-E (APOE) -e4 status influence changes in WMMS between ages ~70-73 in "stable" normal-appearing WM (NAWM) that remained NAWM at age ~73 and "converting WM" (NAWM that converted to WM hyperintensity (WMH) between ages ~70 and ~73).

Methods

- Cohort: Insight46 participants without neurological conditions born in the same week of 1946 in Great Britain and studied throughout life.
- Calculation of fractional anisotropy (FA), mean diffusivity (MD), neurite density index (NDI) and orientation dispersion index (ODI) changes (A) and regions of interest (ROI) (B) are shown in Figure 1.
- Mean change for each metric was calculated in stable NAWM and converting WM.
- Separate linear regression models tested the effects of life-course BP measures, A β age ~70, and APOE-e4 status on annualised change in each DWI metric between ages ~70-73 in the stable NAWM and converting WM, adjusted for sex, age and head size.



Results

- N=292
- Each DWI change metric was multiplied by 10,000 to aid interpretation.
- Violin plots (Figure 2) show the means and distributions of FA, MD and NDI changes in stable NAWM and converting WM and forest plots (Figure 3, P1 = age ~70, P2 = age ~73) show coefficients and 95% confidence intervals for associations between independent variables (per 10 centiloids or 10 mmHg) and WMMS changes in both ROIs.
- Higher BP in the 30s and 40s is associated with decline in stable NAWM microstructure from age ~70-73.
- Higher BP in the 50s and 60s and higher A β age ~70 contribute to changes in WMMS in the converting WM from age ~70-73.
- APOE-e4 carriers show greater increases in MD in both ROIs than non-carriers.
- Effects of A β and APOE were attenuated when included in the same model.

Conclusions

- Higher BP across adulthood influences later life changes in WMMS in both stable NAWM and converting WM regions.
- Therefore, controlling BP as early as the 30s and in following decades could potentially slow decline of WMMS integrity later in life before the development of overt WMH.
- This would be clinically meaningful as WMH are associated with cognitive impairment and AD.

