The Association between Poor Sleep and Accelerated Brain Ageing in Older Adults

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INTRODUCTION

The ageing brain undergoes widespread gray (GM) and white matter (WM) degeneration leading to cognitive decline. Numerous studies indicate large heterogeneity in the age-related brain changes **[1-3]**. Growing body of evidence links this striking heterogeneity to modifiable lifestyle factors such as sleep, diet and physical activity **[4]**. As we get older overall sleep quality deteriorates. Up to half of elderly population experiences various sleep problems and sleep disruptions, including difficulties in maintaining or initiating sleep, and fragmentation of sleep **[5,6]**. Short sleep duration and poor sleep quality in healthy older adults have been previously associated with grey matter atrophy and microstructural white matter changes, putting them at increased risk of dementia. Here, we used measures derived from structural and diffusion magnetic resonance imaging (MRI) to examine interlinked GM and WM changes in healthy ageing. We subsequently investigated the associations of age-related brain changes with sleep quality and sleep disturbance, hypothesising that poor sleep accelerates brain ageing. Accelerated brain ageing, i.e. the deviation from normative ageing can be computed as the difference (δ) between chronological estimated from date of birth and "brain age" estimated from neuroimaging datasets **[7]**. Here, we used a novel technique **[8]** to estimate δ and study its associations with sleep quality and sleep disturbance.

METHODS

DATA & PRE-PROCESSING

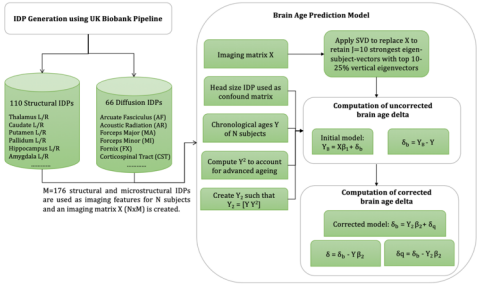
Elderly participants (n=50; mean ± SD age 73.5±4.7) were scanned on a 3T Philips Achieva MRI system. T1-w MPRAGE (spatial resolution 1x1x1mm) and multi-shell diffusion MRI (single-shot EPI, 2x2x2mm, b=1000 & 2000s/mm, 55 directions per shell) scans were acquired. Subjective sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI;**[9]**) and sleep fragmentation was measured as actigraphy derived wakefulness after sleep onset (WASO; **[10]**). Data pre-processing and distortion correction were performed using the UK Biobank pipeline **[11]**. 110 subject-specific T1 image-derived phenotypes (IDPs), reflecting GM volumetric features and 66 diffusion derived, tract-specific microstructural IDPs **[12]** were extracted.

VOXEL-WISE AGE-RELATED BRAIN CHANGES

Tract-based spatial statistics (TBSS) analysis **[13]** was employed to explore changes in FA (fractional anisotropy) and MD (mean diffusivity) associated with age. Linked independent component analysis (FSL FLICA; **[14]**) was used to investigate modes of simultaneous covariation of GM structure and WM microstructure. FLICA decomposition into 10 independent components (ICs) was run on the skeletonised FA/MD and GM density maps following FSL voxel-based morphometry pipeline **[1]**.

METHODS (cont.)

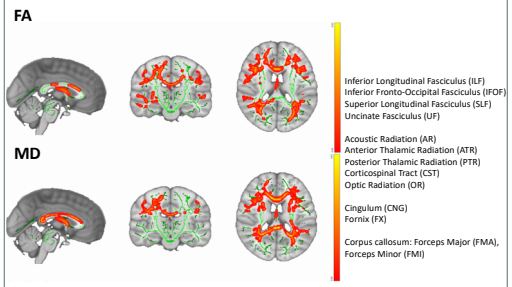
BRAIN AGE PREDICTION



Overview of the employed here "brain age" prediction model. We used a recently published approach [8] to predict "brain age" from the set of M=176 structural and microstructural IDPs in an unbiased manner. A matrix X (NxM) was created to represent the IDPs. Singular value decomposition was applied to reduce the feature dimensionality of X. We retained the J=10 strongest eigen-subject-vectors with the top 10-25% vertical eigenvectors. Using the matrix X as predictors, we estimated δ and δ_q, accounting for linear and quadratic age effects respectively.

RESULTS

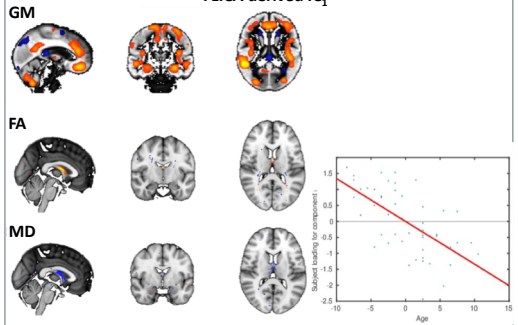
AGE-RELATED MICROSTRUCTURAL BRAIN CHANGES



TBSS analyses showed significant widespread changes in the WM microstructure. Age was a significant predictor of reduction in FA and increase in MD (p<0.05 FDR) within the association (ILF, IFOF, SLF, UF), projection (AR, ATR, PTR,CST, OR), limbic (CNG, FX) and commissural (FMA and FMI) fibre bundles in healthy older adults.

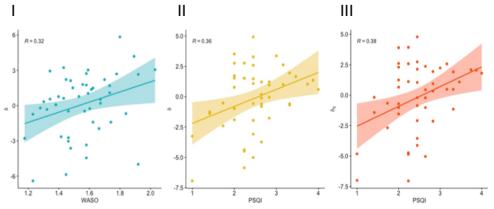
RESULTS (cont.)

INTERLINKED GM AND WM CHANGES IN HEALTHY AGEING



FLICA indicated two modes of covariation in GM and WM in healthy older adults (IC_1 and IC_2). The independent component IC_1 showed a significant linear decrease of the global GM and WM microstructure with increasing age. Age explained 40% of the variance within IC_1 (R2=0.40, p<0.001 FDR). The linear relationship between the IC_1 loading and age was driven by FA (44%), GM volumetric information (30%) and MD (25%).
The IC_2 showed a linear (R2=0.15) and U-shape (R2=0.23) relationship with PSQI, which did not survive FDR correction. The relationship between IC_2 and loading and PSQI was driven by FA (37%) followed by GM (33%) and MD (27%).

RELATIONSHIPS BETWEEN BRAIN AGE DELTA AND SLEEP



Poor sleep as a predictor of accelerated brain ageing computed as δ and δ_q ($|\overline{\delta}|$=2.0; $|\overline{\delta_q}|$=2.1 years) in healthy older adults. The corrected linear estimate of delta (δ) was significantly correlated with WASO (**I**; R=0.32, p=0.05 FDR) and PSQI (**II**; R=0.36, p=0.044 FDR) using the T1 IDPs. There was also a significant relationship between the corrected quadratic estimate of delta (δ_q) and PSQI using the multimodal (T1+WM) IDPs (**III,** R=0.38, p=0.037 FDR).

CONCLUSIONS

- Healthy (neurotypical) ageing is associated with interlinked GM and WM changes accelerated by poor sleep, indexed by low subjective sleep quality and increased sleep fragmentation.
- Based on recent research showing that deviation from normative brain ageing is one of the hallmarks of dementia **[15]**, we conclude that sleep disruptions in healthy older adults should be considered as modifiable risk factor for dementia.

REFERENCES

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