Sex disparities in effect of ageing on brain network integrity across the lifespan

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Introduction

- Midlife presents a critical period for the beginning of age-related neuropathology and a unique disease-altering window (Ritchie, et al 2017).
- Age-related reduction in brain network segregation relates to reductions in structural integrity and cognition (Wig, 2017). Therefore, it serves as a proxy for age-related decline in brain health.
- 1) The effect of healthy midlife ageing on network segregation is unknown.
- 2) 60% of people with Alzheimer's Disease (AD) are women. The impact of sex differences on age-related brain changes remains poorly understood.

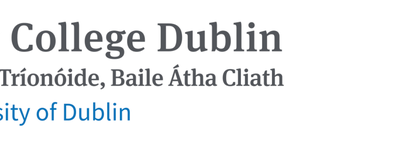
Research questions

- 1) How functional brain network segregation changes in midlife relative to young and older adults?
- 2) Does sex differentially impact functional brain network segregation?

Methods

- Resting state/structural MRI, cognitive data from a healthy lifespan cohort (N=652) from the Cambridge Centre for Ageing and Neuroscience.
- Modular segregation

$$P_i = 1 - \sum_{m \in M} \left(\frac{k_i^w(m)}{k_i^w} \right)^2$$

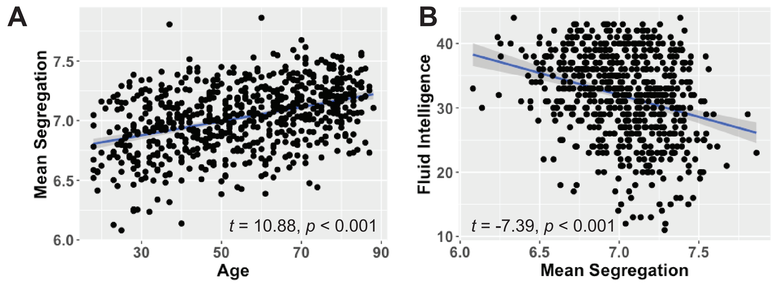


adapted from Power et al., (2011)

- Three age groups: young (18-39 years, 82 M/88 F), midlife (40-59 years, 100 M/104 F), older (60-88 years, 140 M/138 F) adults.
- Sex was included as the second factor. As brain volume differs by sex, we regressed out intracranial volume in this part of the analysis.

Results

Age effects across the cohort



Higher values on Y axis indicate lower segregation

Acknowledgements

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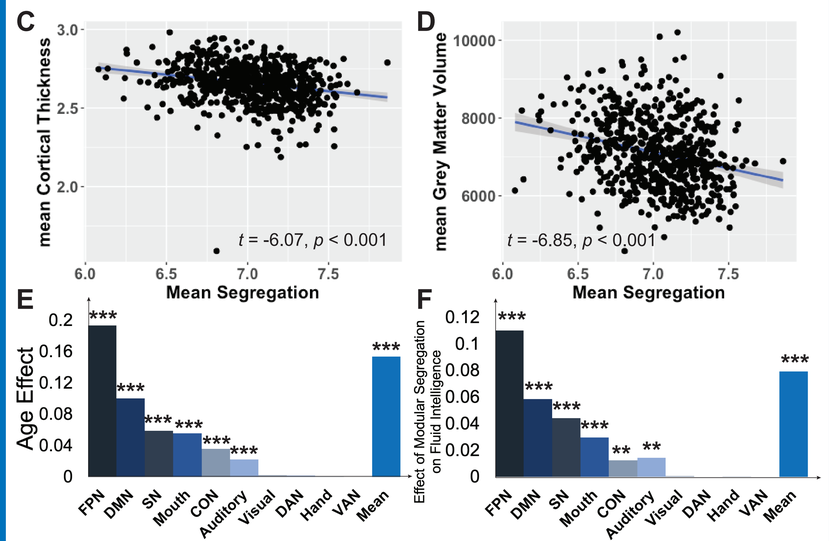

Figure 1. Age effect on functional brain network segregation. Eta-squared as the measure of effect size for (E) and (F). Abbreviations: default mode (DMN), frontal-parietal control (FPN), ventral attention (VAN), cingulo-opercular control(CON), dorsal attention (DAN), and salience (SN) networks.

- Mean segregation across ten networks decreased with age (Fig. 1A), which correlated with age-related reduction in brain structural integrity (Fig. 1C,D), fluid intelligence (Fig. 1B), but not crystallised intelligence.
- 6/10 networks showed the effect of age (Fig. 1E), which also associated with age-related reduction of fluid intelligence in these networks (Fig. 1F).

Age effects in midlife

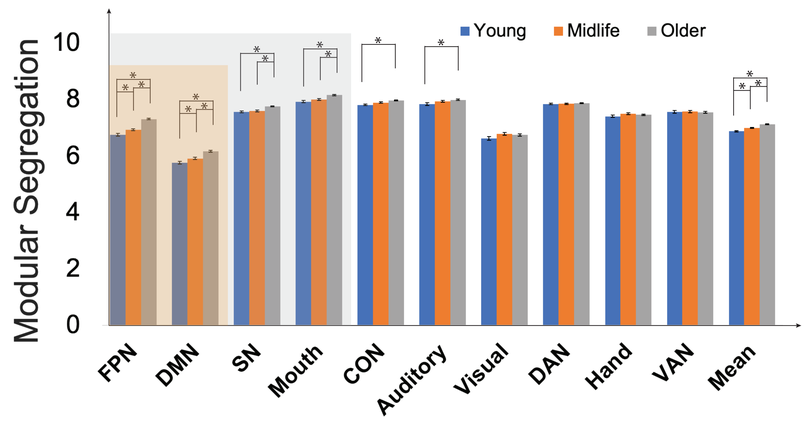

Figure 2. Differences of functional brain network segregation in the three age groups.

- FPN and DMN showed significantly decreased segregation in midlife relative to young adults (Fig. 2 in orange shadow).
- FPN, DMN, SN and Mouth network showed significantly decreased segregation in older relative to midlife adults (Fig. 2 in grey shadow).

Sex effects

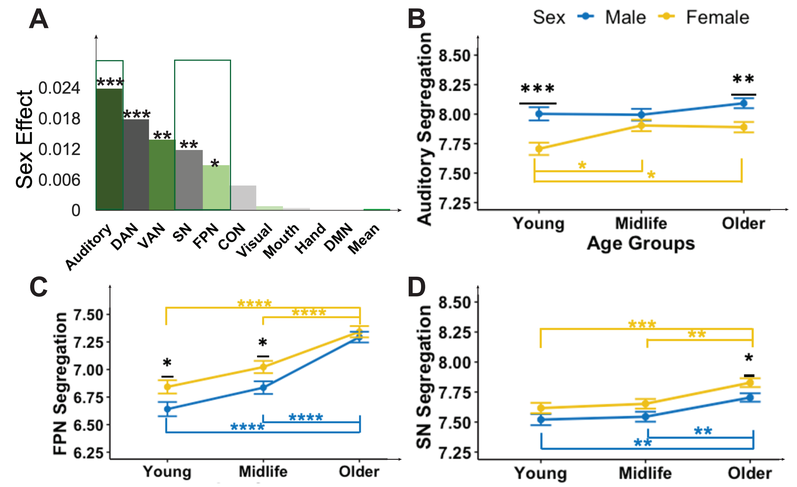

Figure 3. Sex differences in functional brain network segregation. DAV, VAN showed no age effect.

- Among networks affected by age, Auditory, FPN, and SN also showed a main effect of sex (Fig .3A).
- Auditory: females had higher segregation in young/older adults (Fig. 3B).
- FPN: females had lower segregation than males in young/midlife (Fig. 3C),
- SN: females had lower segregation in older life (Fig. 3D). (Effect stands after accounting for education differences between males and females.)

Conclusions

- For the first time, we show significant reductions in key networks segregation from midlife (DMN, FPN).
- These networks may be particularly labile to pathological ageing in midlife.
- Our finding suggest, the first time, that sex differences represent both inherent differences (young adults: FPN, Auditory), and age-related differences on network deterioration (SN).
- Lower segregation in females, from midlife, in key brain networks for cognition, may provide an avenue for understanding in future studies the higher incidence of age-related neurodegenerative disorders, e.g., AD , in females.

References

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