Distinct gender and age related changes in the functional connectome during development from adolescence to adulthood

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Introduction

Does healthy developmental act as a proxy for brain repair? That is, does restoration of brain function after injury utilise similar mechanisms to those used to in its formation?

Hypothesis: synaptic pruning in adolescence creates 'developmental plasticity' of functional brain networks, but in a spatially discrete and gender distinct manner.

Aim: use a large cross-sectional study of currently healthy participants and a data-driven approach to characterize 'developmental plasticity'.

Methods

We recruited 100 healthy participants aged 14 to 24 years (50 female). Functional MRI during wakeful rest was acquired at 3 Tesla. Group-average functional connectivity networks were identified using probabilistic independent component analysis (ICA). Subject specific versions of group-average ICA networks were generated using dual regression. Network modelling between ICA networks was performed with L1-normalised regression without thresholding. Gender and age specific changes within and between ICA networks were analysed with a general linear model and permutation testing correcting for family-wise error. All analyses were performed with FSL tools (figures 1 & 2).

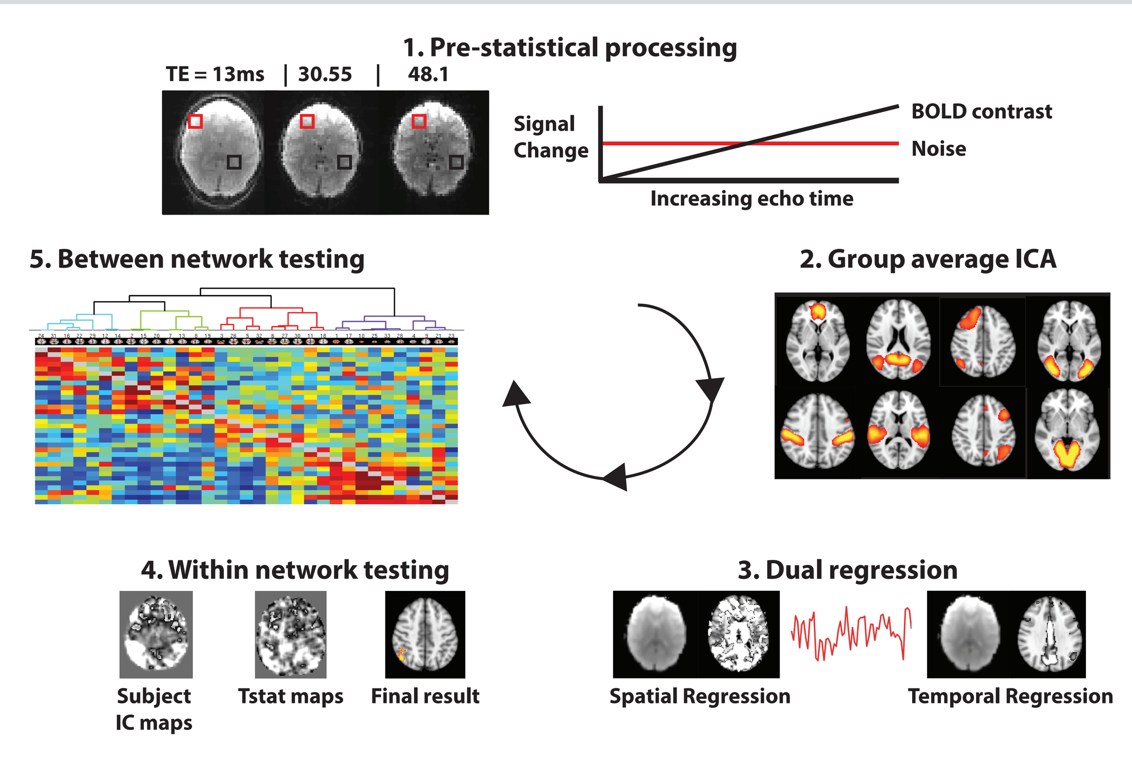


Figure 1: analysis methods. Resting state FMRI data were de-noised. Group ICA was performed and individual subject IC maps were generated with dual regression. Permutation testing was performed on the spatial maps or L1 regression between individual IC time series.

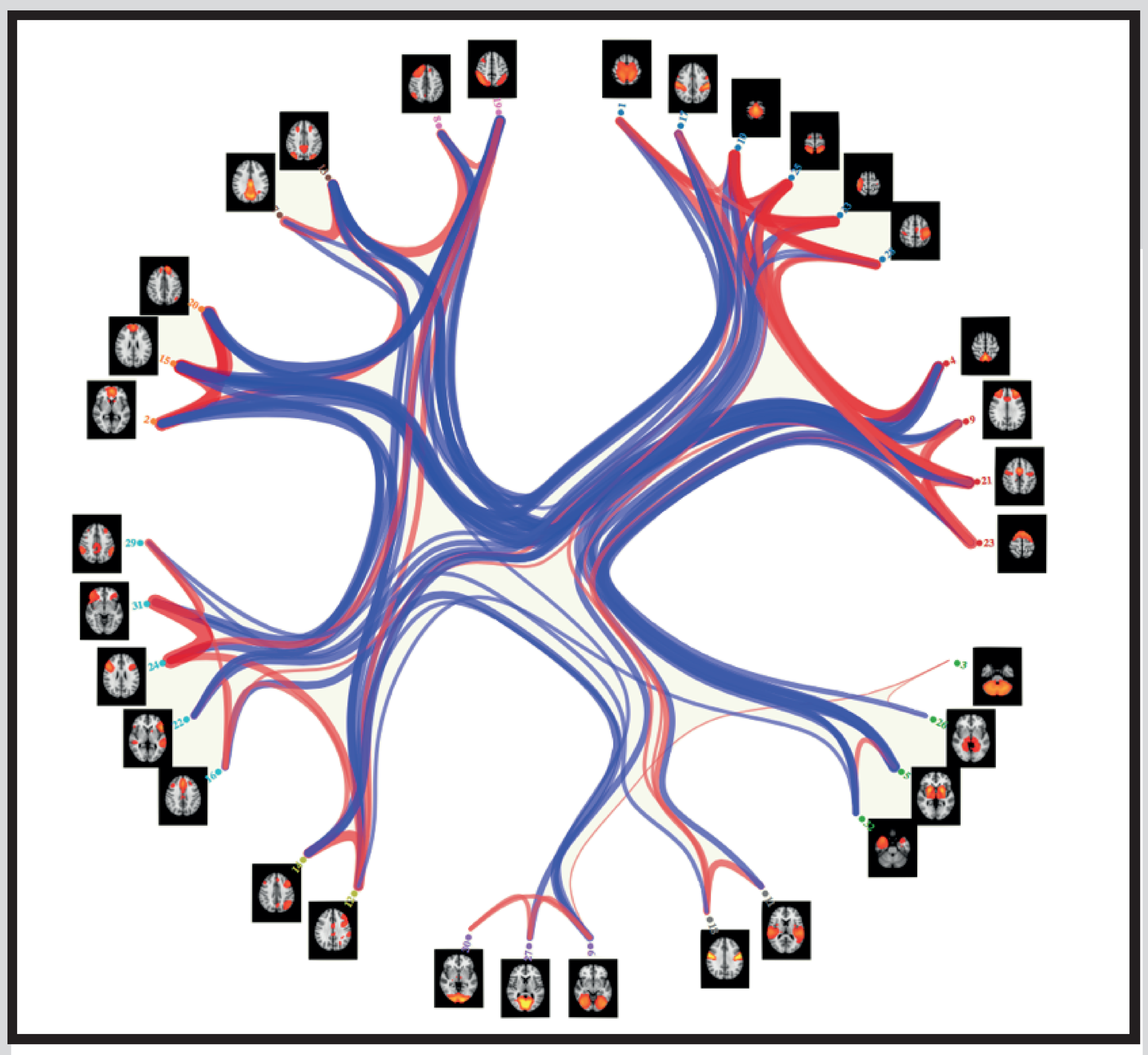


Figure 2: group ICA network. hierarchical clustering of group average ICA networks on the perimeter with 'links' between them defined by Pearson correlations (after R-to-Z transformation).

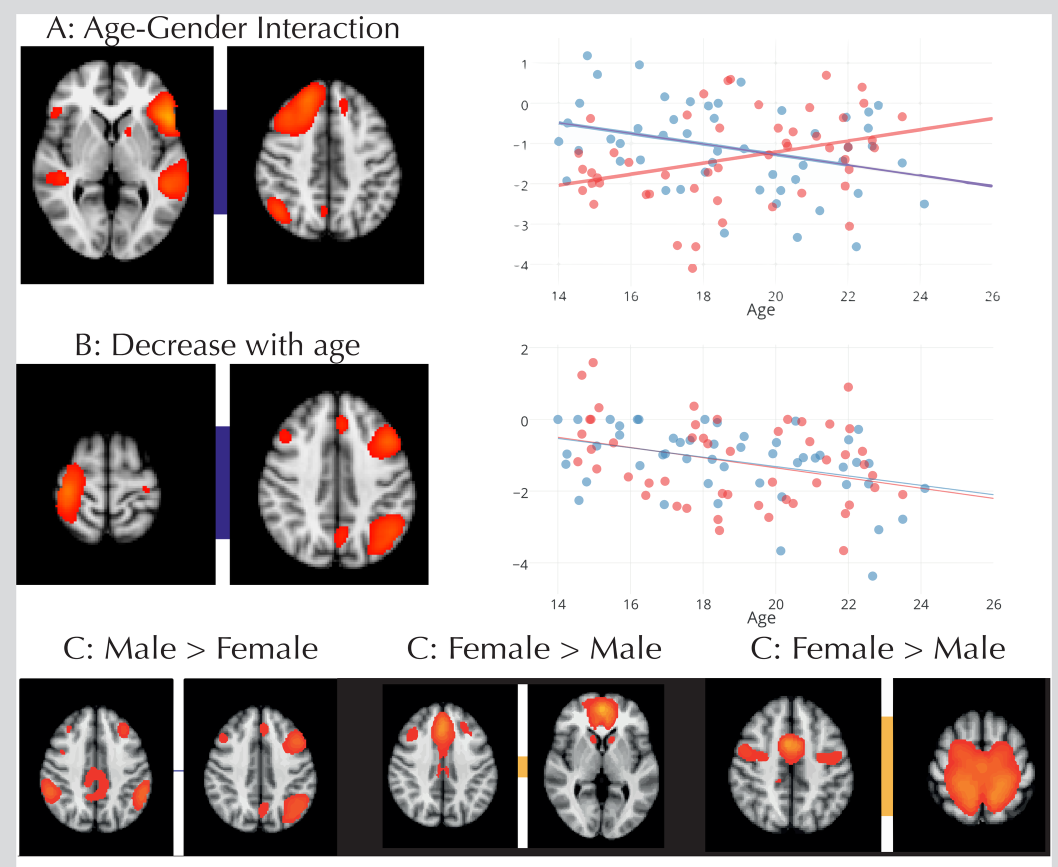


Figure 5: between network changes. A: age-gender interaction B: age dependent decrease in connectivity, C: gender related differences. Link colours represent mean connectivity.

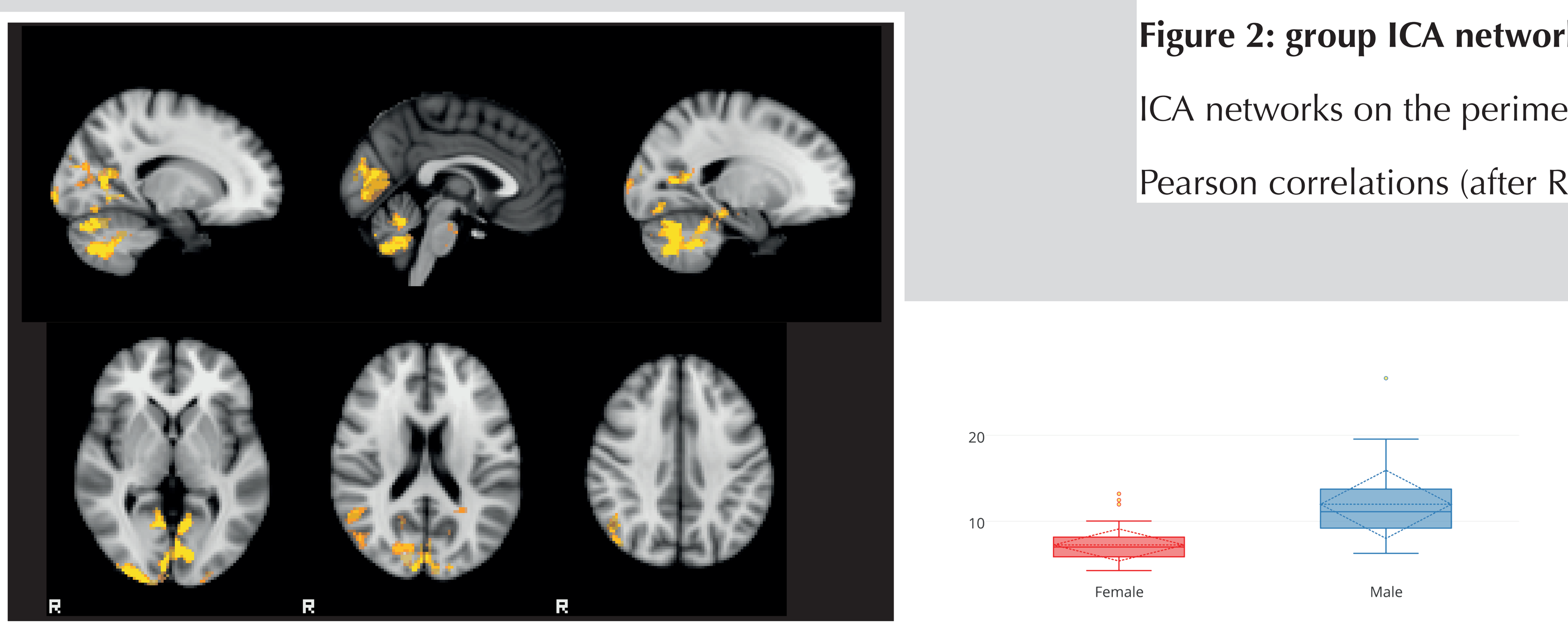
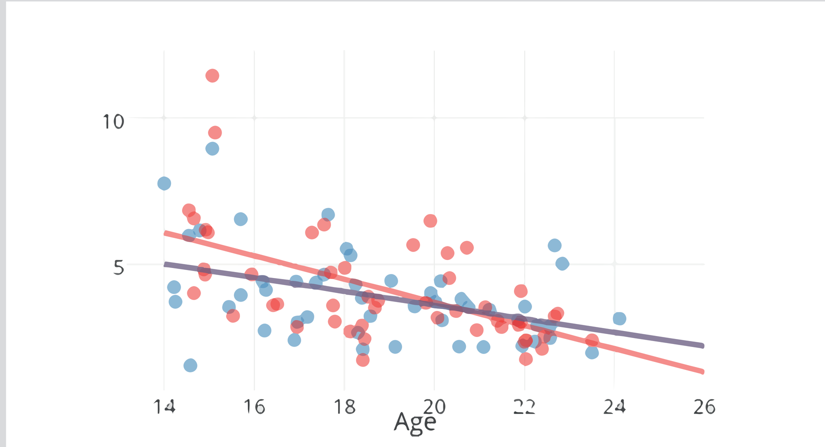


Figure 3: within network gender changes.
A combination of clusters within 7 separate IC maps demonstrating greater within network connectivity in males than females adjusted for age (boxplot, above).



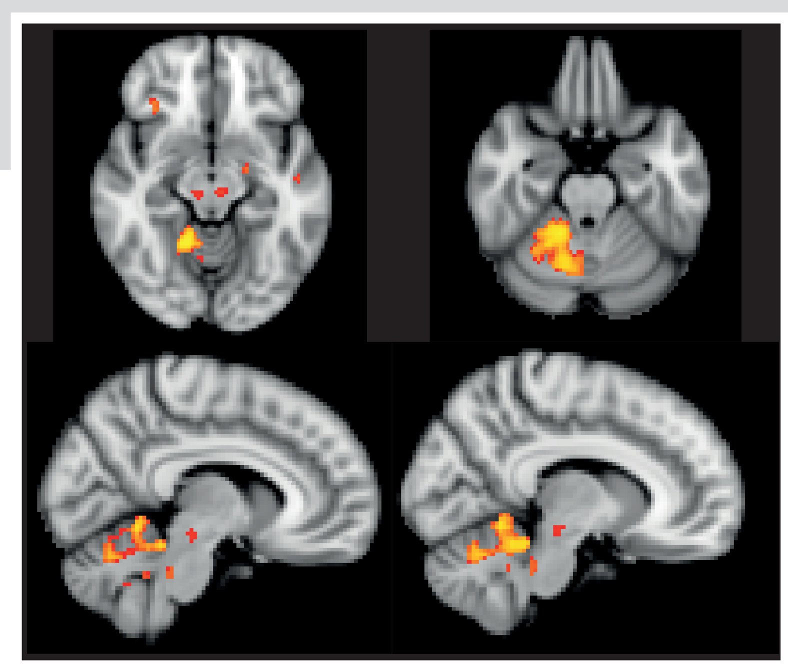


Figure 4: within network age changes.
A cluster of voxels (involving bilateral superior cerebellar hemispheres and red nuclei) demonstrating age related reduced within-network connectivity (scatterplot, above).

Results

Intra-network connectivity

- Higher male than female in right default mode and dorsal visual stream networks (DVS), and bilateral visual networks and thalami (figure 3).
- Reduction with age in the superior cerebellum bilaterally (figure 4).

Inter-network connectivity

- Interaction effect with connectivity in males with age increasing between contralateral fronto-parietal regions (figure 5A).
- Decrease with age between language and contralateal DVS (figure 5B).
- Females had higher inter-network connectivity than males in multiple pre-frontal and fronto-temporal regions (figure 5C).

Conclusions

- Development of functional connectivity in the adolescent to adult period is characterized by reduced connectivity within cerebellar networks and increased connectivity between language and dorsal visual stream networks.
- Distinct gender related profiles in this developmental period are apparent with a propensity towards increased within-network connectivity in males, and between prefrontal networks in females.
- Modelling synaptic refinement (for example with graph theory) in these specific regions could reveal mechanisms applicable to brain repair and plasticity in later life.

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