Age-dependent response to simulated brain injury in the functional connectome

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Introduction

Brain robustness and recovery from injury is believed to be maximal in infancy and then reduce during development. Despite some corroboration of this theory in animal models, clinical evidence in humans is suggestive of a more complex relationship.

Hypothesis: synaptic pruning in adolescence creates vulnerable hubs and reduced plasticity after brain injury.

Aim: to clarify the relationship between age and response to brain injury using a network model combing functional connectivity, graph theory, and network percolation analysis.

Methods

We recruited 100 healthy participants aged 14 to 24 years (50 female). Functional MRI during wakeful rest was acquired at 3 Tesla. Nodes (167) were based on a group-average independent component analysis parcellation (figure 1) and links were based on L1-regularised regression or Pearson correlations without thresholding (figure 2). Connection weights were performed with signed measures or after transformation to the unit interval. Brain injury was simulated through either removal of nodes individually (delta centrality) or sequentially (in either a random or targetted manner). Gender and age related relationships were tested with a linear model and permutation testing correcting for the false discovery rate or family wise error as appropriate.

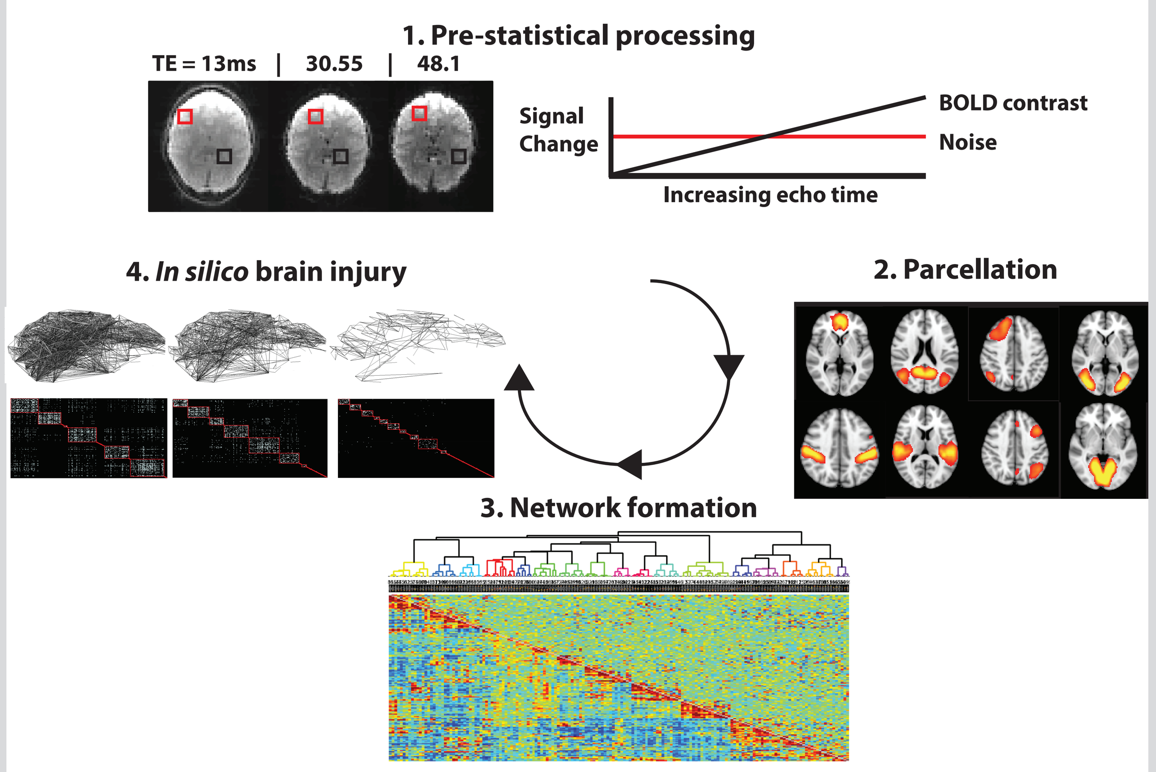

Figure 1: analysis methods. 1. resting state FMRI data were de-noised. 2. Nodes were defined by group ICA (167 nodes). 3. Links were defined by Pearson correlations. 4. Percolation involved targeted or random removal of nodes with consequent dynamics in graph theory measures.

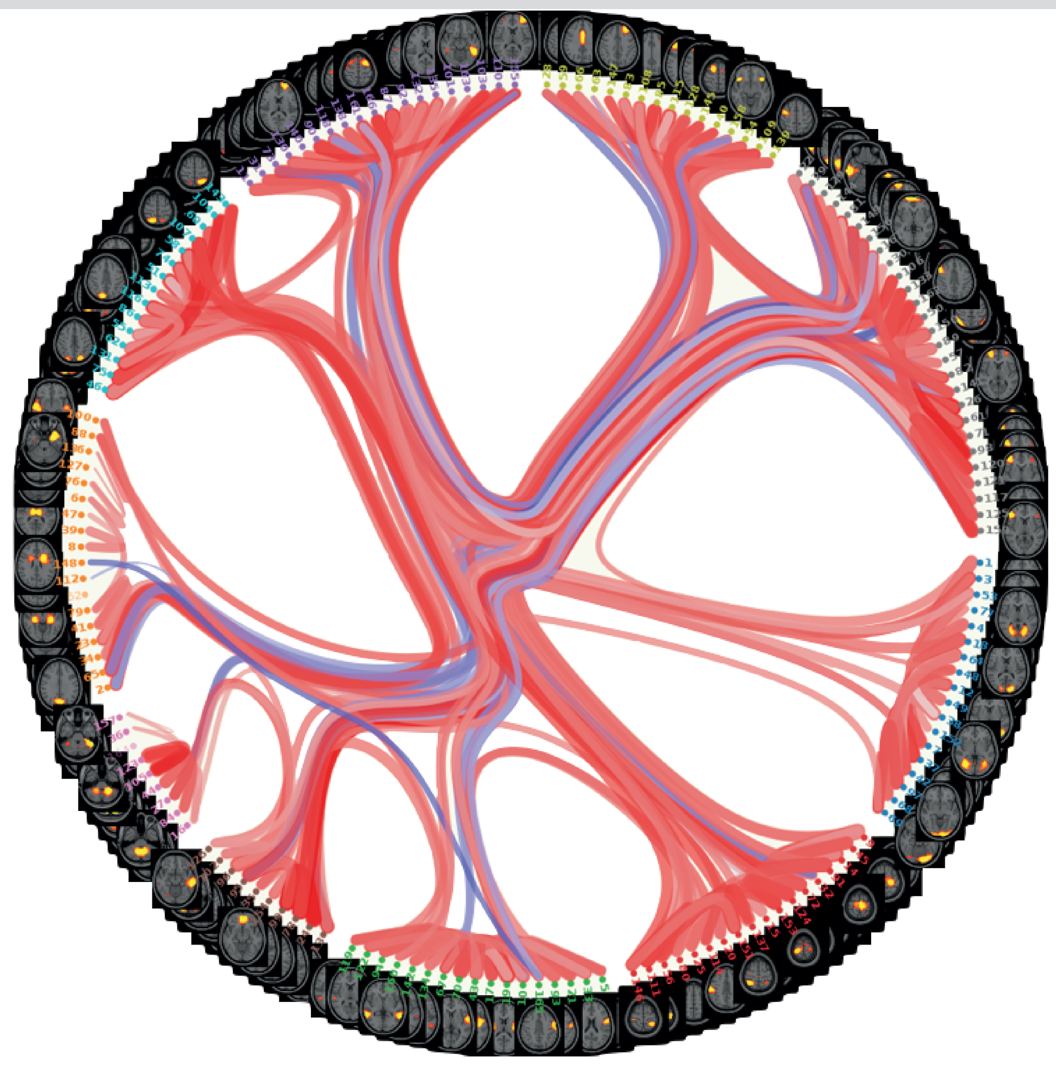

Figure 2: group ICA network. hierarchical clustering of group average ICA networks on the perimeter with 'links' between them defined by L1-regularised regression with R-to-Z transformation (167 nodes).

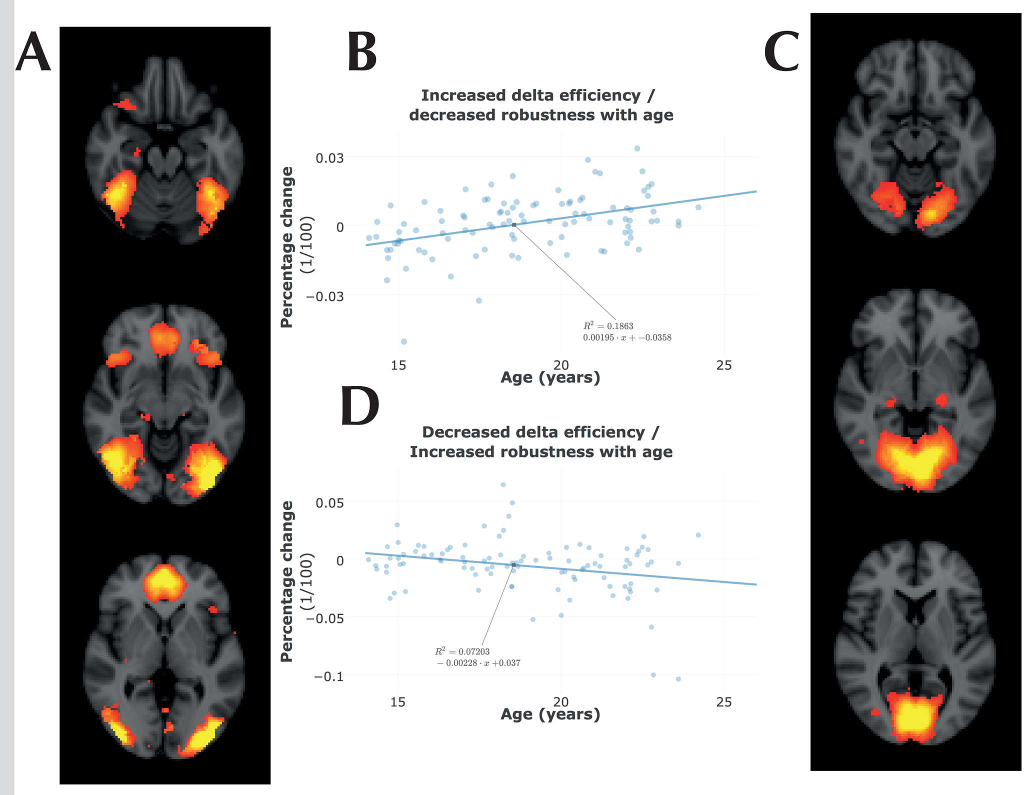

Figure 6: focal vulnerability

Increased vulnerability networks (A) and delta efficiency changes (B). Decreased vulnerability networks (C) and delta efficiency changes (D).

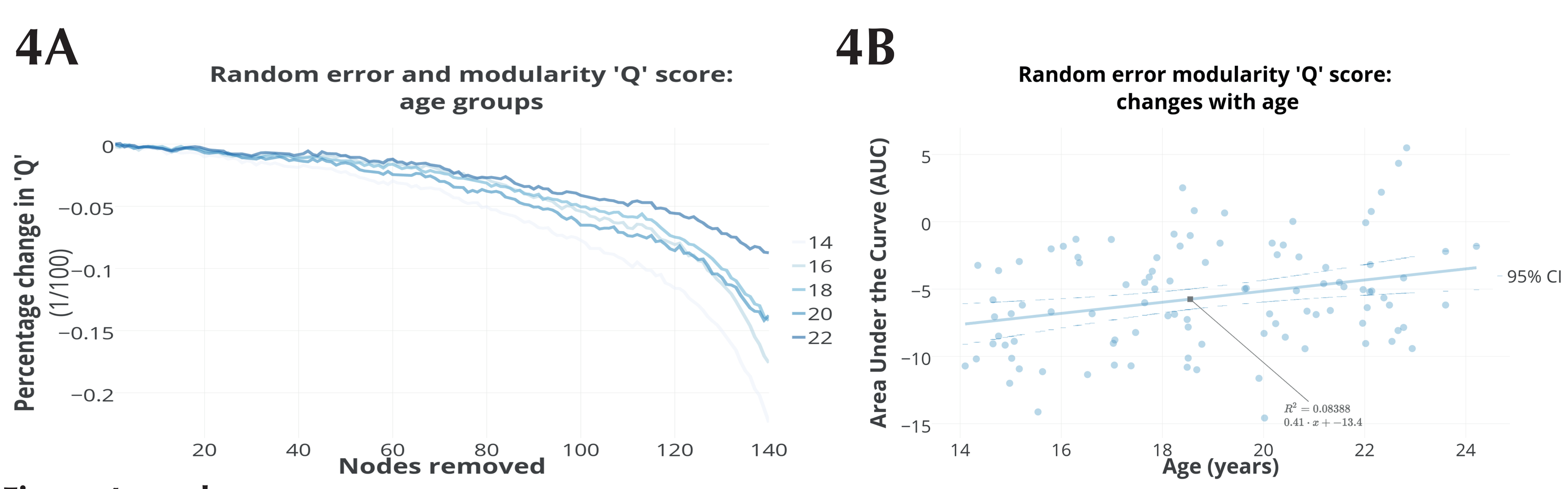

Figure 4: random error

Changes per age group (A) and area under curve over age (B)

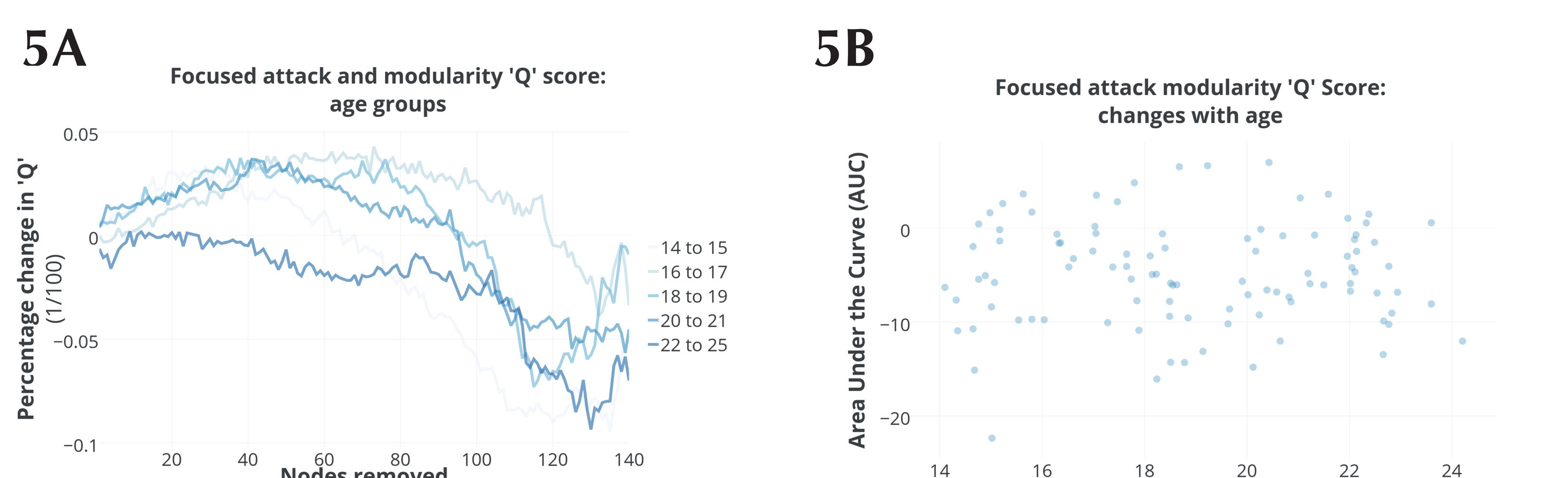

Figure 5: focused attack

Changes per age group (A) and area under curve over age (B)

Results

Random error (figure 4)

- There was increased robustness to random error with age in terms of the ability of brain networks to maintain their modularity.

Focused attack (figure 5)

- There were no age or gender related changes in vulnerability to focussed attack during adolescence using 9 attack measures and 6 outcome measures.

Individual lesioning (figure 6)

- The focal vulnerability of the network reorganised during adolescence from primary cortices and sub-cortical nuclei to higher association cortex locations.

Conclusions

- During adolescence brain networks become increasingly robust to random error without compromising vulnerability to targetted attack.
- This process is driven by re-organisation of 'weak nodes' from primary and subcortical locations to higher association cortices.
- Further work is required to incorporate mechanisms of synaptic pruning and plasticity to the model to encompass resilience.
- Potentially neurosurgeons could tailor procedures to avoid vulnerable regions or those that have limited potential for recovery depending on age and gender.

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