**Research Activity:**

**Extrinsic and intrinsic brain network connectivity maintains cognition across the lifespan despite accelerated decay of regional brain activity**

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**Introduction**

Maintaining cognitive function is critical to successful ageing\(^1\), although the factors that support cognitive performance in older age are poorly understood. Cognitive performance is associated with communication between brain regions that is intrinsic to large-scale functional networks, as well as extrinsic interactions between such networks\(^2\). These interactions have been examined previously in resting-state fMRI\(^3\), but not in relation to a broad range of cognitive measures obtained from large-scale, population-representative cohort (n = 602, 18 to 88 years, www.cam-can.com). Moreover, previous studies have only measured functional connectivity at the level of fMRI signals, which are limited to correlational inferences and are potentially confounded by age-related changes in the neurovascular coupling. Here, we used generative models that allow us to distinguish between neural connectivity and neurovascular coupling. We tested the hypothesis that interactions within and between large-scale functional networks determine neurocognitive health, and that these interactions are increasingly important for maintaining cognitive function with age.

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**Methods**

Sample selection
- CC700 resting state fMRI dataset
- Low head movement (<2SD MRD)

ROI extraction
- 81 voxels per node

Data processing
- Wavelet despiking
- Spatial smoothing (8mm)
- Regression (inc. 1st and 2nd derivatives)
- WM and CSF signal
- motion parameters
- Temporal filtering (0.01 - 0.08Hz)

Node location priors using group-ICA
- 20 ICs
- Match ICs to existing RSN
- Identify nodes within DMN, DAN & SN

Model space selection
- between network within network

Model space estimation
- \( \beta = (x_i, \mathbf{x}) = \mathbf{w} + \varepsilon \)
- \( \mathbf{y} = (\mathbf{y}_i, \mathbf{y}) = \mathbf{w}' + \varepsilon \)
- \( \mathbf{w} = \mathbf{A} \mathbf{w} + \mathbf{A} \mathbf{w} \)
- \( \mathbf{x} = \mathbf{A} \mathbf{x} + \mathbf{A} \mathbf{x} \)

Predictive analysis
- Multiple linear regression of age and spDCM parameters
- CCA of effective connectivity and cognitive performance

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**Results**

**Group-ICA and functional connectivity**

<table>
<thead>
<tr>
<th>Default Mode Network</th>
<th>Dorsal Attention Network</th>
<th>Salience Network</th>
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<tbody>
<tr>
<td>r = 0.46</td>
<td>r = 0.64</td>
<td>r = 0.52</td>
</tr>
<tr>
<td>r = 0.96</td>
<td>r = 0.96</td>
<td>r = 0.91</td>
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Spatial overlap of three ICs with previously reported SN, DAN & DMN templates. Nodes within each network were highly correlated, while DAN and SN were partially correlated.

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**Summary**

- Changes in coupling of just three major resting-state networks were sufficient to account for 30% of the variance in age, and 20% of the age-related variance in cognitive performance.
- Another widespread feature of ageing was changes in regional, inhibitory self-connections, resulting in reduced stability of neural states.

**Conclusions**

- Using generative models to dissociate neural from vascular components of the fMRI signal, we discovered behaviourally-relevant and age-dependent differences in resting-state effective connectivity.
- These were manifest both within and between large scale networks, and were associated with faster decay of local neural activity.
- Maintaining resting connectivity profile is increasingly relevant for older adults in order to maintain cognitive function across many domains.

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**References**

1. Tsvetanov K et al. (2013) Cognitively healthy older adults have better brain health. Neurobiol Aging 34: 1823–1833
2. Tsvetanov K et al. (2014) Cognitively healthy older adults have better brain health. Neurobiol Aging 34: 1823–1833
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