White matter connections and working memory in normal ageing

Presented to
Understanding the ageing brain

Presented by
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Talk Outline

- Background
- Aims of study
- General Methods
  - Study participants
  - Imaging Methods
- Results for Experiment 1 – age effects
- Experiment 2 – Working memory effects
  - Additional methods
  - Results
- Conclusions
Cognitive & Brain Ageing

- Many cognitive abilities change in normal ageing

- The brain show a variety of changes in normal ageing
  - General reduction in brain volume
  - Appearance of damage over lifespan
Frontal-Executive hypothesis

- Executive function primarily affected in ageing
- Related to decline in frontal brain regions
Disconnection hypothesis

- Disconnection syndromes through damage to white matter
- Effects functions that rely on multiple brain regions
- The importance of white matter for network connectivity
Disconnection hypothesis

- Previous studies showing correlations between white matter and working memory

- Working memory & executive function: evidence for distributed neural networks
Tract Disruption due to Ischaemia

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Aims

- Investigate brain changes in normal ageing
  - White matter clusters associated with ageing
  - Pathways potentially disrupted

- Investigate the networks involved in working memory
  - White matter clusters associated with working memory
  - Pathways potentially disrupted
Participants

- 106 participants (55 males; 51 females)
- Age range 50 – 90; Mean age 69 years
- Inclusion criteria
  - English as first language
  - Suitable for MRI scan
- Exclusion criteria
  - No prior neurological disorders
  - No previous stroke
  - No prior psychiatric disorders
Methods: MRI
Diffusion

Isotropic diffusion

Anisotropic diffusion

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Diffusion Tensor Imaging
White Matter Tracts

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DTI - Acquisition

MRI - GE 1.5 T (22mT/m)
- Diffusion Weighted Imaging
  (FOV = 24; TE = Minimum; TR = 7000; 12 directions)
- Two interleaved series of twenty-five 2.8mm slices, with a gap of 2.8 mm: 4 repeats
  - Series co-registered then averaged
  - 50 contiguous 2.8 mm slices for FA, MD, and EPI-T2
DTI – Voxel based statistics

- Statistically assess which voxels are significantly associated with a given parameter, such as:
  - Age
  - Cognitive abilities such as working memory

- Statistically assess where groups of voxels form clusters in a certain location
DTI – Tractography

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Example of white matter tracts
Methods

- All EPI images without diffusion weighting, co-registered into standard space (T1-NMI305)
  - using an affine transformation
    (FLIRT; www.fmrib.ox.ac.uk/fsl)

- Map from EPI co-registration applied to DTI

- MD and FA calculated in standard space
Methods – Voxel based statistics

- Linear regression between DTI parameters and age using SPM2
  - Included multiple comparison correction

- Results were considered significant at $p < .05$ level
  - Corrected for multiple comparisons using family-wise error
Results

Experiment 1: Age effects
Methods – Tractography

- Tracts initiated from each voxel centre throughout the entire brain

- Tracts retained that passed through significant clusters

- Step vector length, e.g. $t = 1.0\ \text{mm}$

- Tract termination criteria
  - Fractional anisotropy (FA < 0.08)
  - No angle termination criterion
MD & FA Tracts

Mean Diffusivity

Fractional Anisotropy

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MD Tracts

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FA Tracts
Summary

- Voxel based statistics reveal age-associated changes in MD & FA
- MD clusters are large & include white matter from all lobes of the brain
- FA clusters are large & are primarily in peri-callosal regions between frontal & parietal lobes
- Tractography reveals that pathways throughout the brain are potentially affected by changes to white matter integrity
  - True for both MD & FA
Working Memory

- Temporary storage of information with manipulation of stored information

- Supported by complex cortical networks including connections between deep grey matter structures, frontal, parietal and temporal lobes.
Working Memory Methods

- Tests from the Wechsler Memory Scale:
  - Digit Span Backwards
  - Letter-number sequencing

- Z-scores created for whole sample

- Scores from tests combined to create a mean score for working memory
  - Cronbach’s alpha to confirm latent variable
Example of working memory test

Say the **numbers** first from lowest to highest, then the **letters** in alphabetical order.

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<th>Auditory Presentation</th>
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Analysis methods

Experiment 2: Working Memory

- Voxels significantly associated with working memory significant at \( p < 0.01 \)
- Voxel clusters significant at \( p < 0.05 \)
- Multiple comparison correction applied

- Tracts retained that passed:
  - through significant clusters
  - between temporal, parietal & frontal lobes.
Working Memory Clusters

- z = -15.1 mm
- z = -10.9 mm
- z = -6.7 mm
- z = 3.7 mm
- z = 12.0 mm
- z = 23.9 mm
- z = 28.5 mm
- z = 39.5 mm
Working Memory Tracts - Temporo-parietal paths

- Superior parietal lobule pathway
- Posterior segment of arcuate fasciculus

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Working Memory Tracts - Temporo-frontal paths

Left Hemisphere

Medial temporo-frontal pathway

Direct segment of arcuate fasciculus

Right Hemisphere

Medial temporo-frontal pathway
Working Memory Tracts - Fronto-parietal paths

- Fronto-parietal fasciculus
- Supra-arcuate fasciculus
- Anterior segment of arcuate fasciculus
- Cingulum
- Supra-arcuate fasciculus
- Fronto-parietal fasciculus

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Summary

- Voxel based statistics reveal clusters significantly associated with working memory in temporal, frontal and parietal lobes.

- Pathways through these clusters connected grey matter areas known to be involved in working memory including:
  - the fronto-parietal fasciculus
  - the medial pathways
  - the superior parietal lobule pathway
  - portions of the arcuate fasciculus
The integrity of white matter is affected in normal ageing.

Small areas of damage may have disproportionate effects, by disrupting white matter pathways.

White matter integrity is important for working memory in normal ageing.

Cognitive abilities that rely on multiple brain regions may be affected by white matter damage.

Loss of white matter integrity may explain age-related cognitive decline.
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