

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



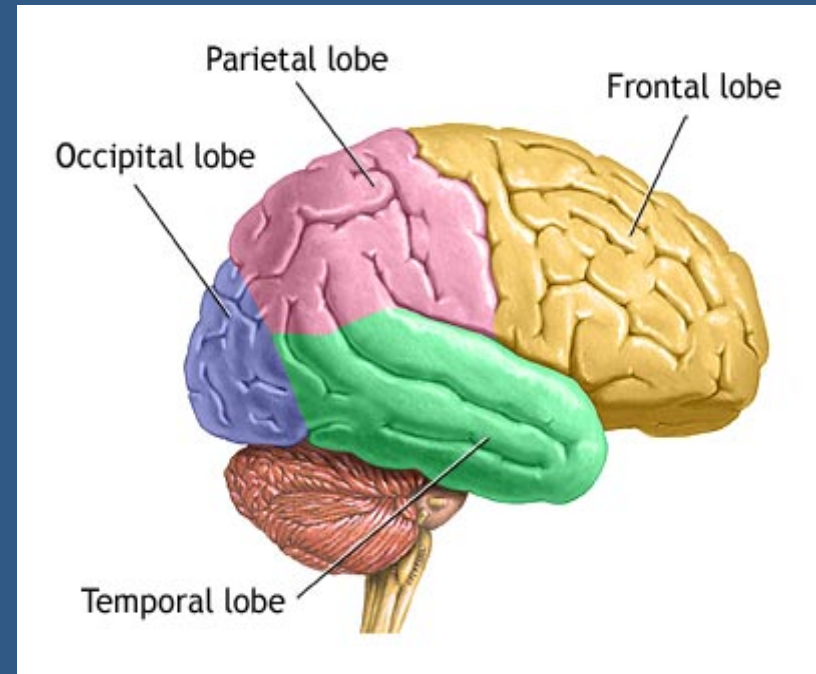
Cognitive & Brain Ageing

- 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



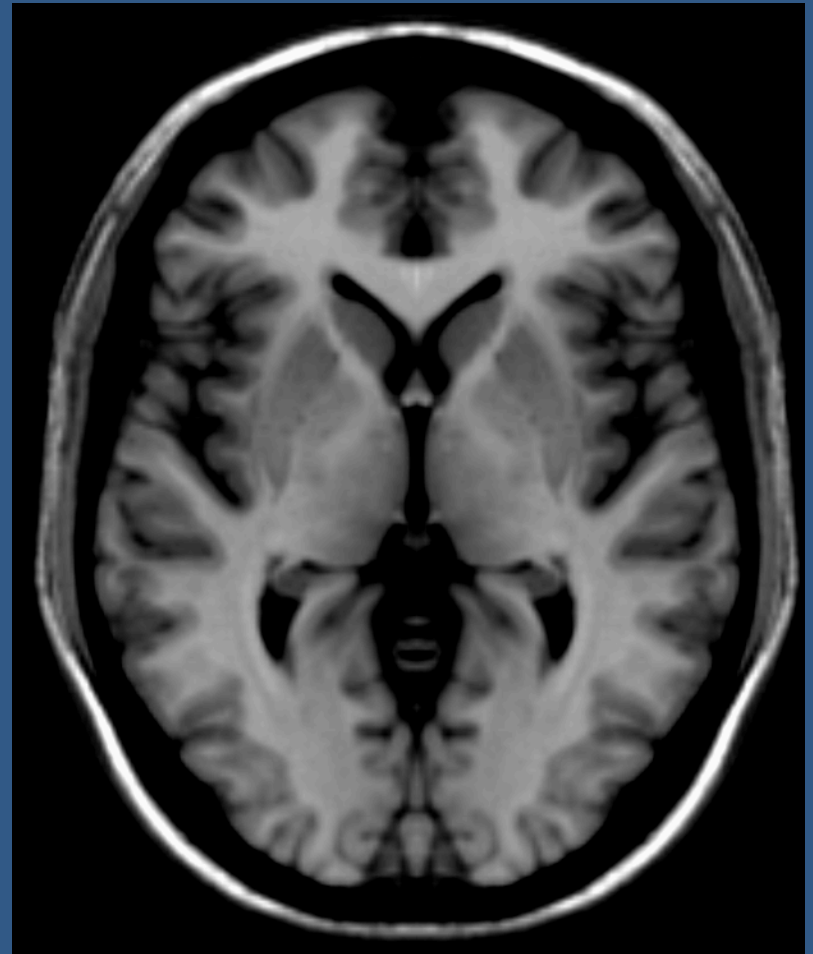
Frontal-Executive hypothesis

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



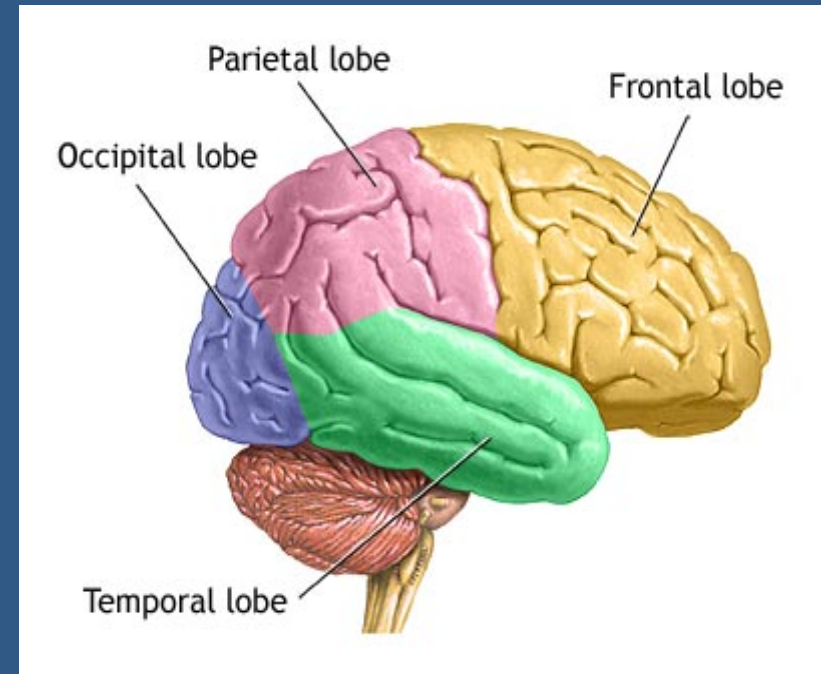
Disconnection hypothesis

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

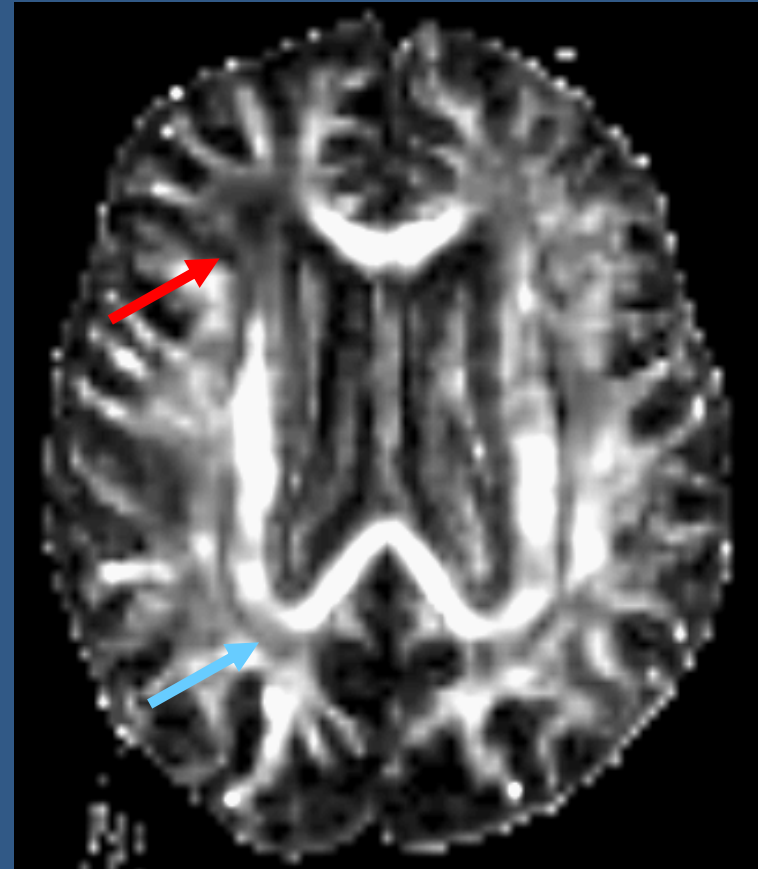
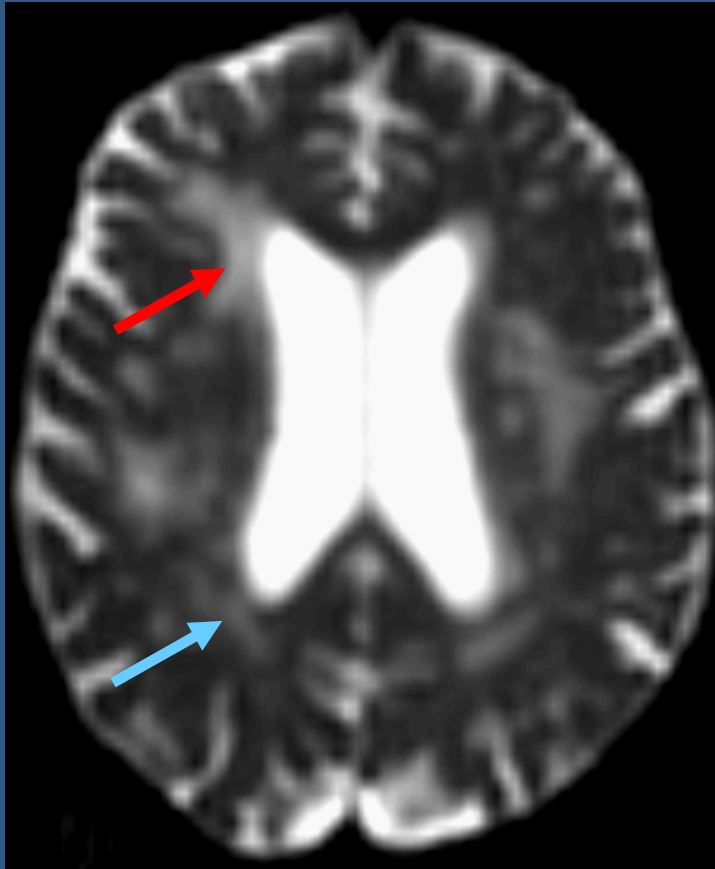


Disconnection hypothesis

- Previous studies showing correlations between white matter and working memory
- Working memory & executive function: evidence for distributed neural networks



Tract Disruption due to Ischaemia



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

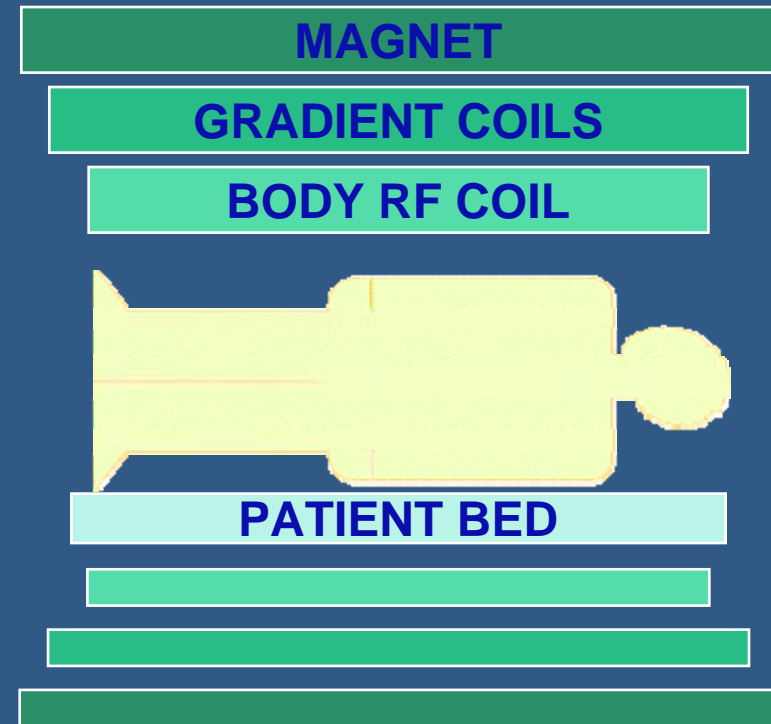


Participants

- 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

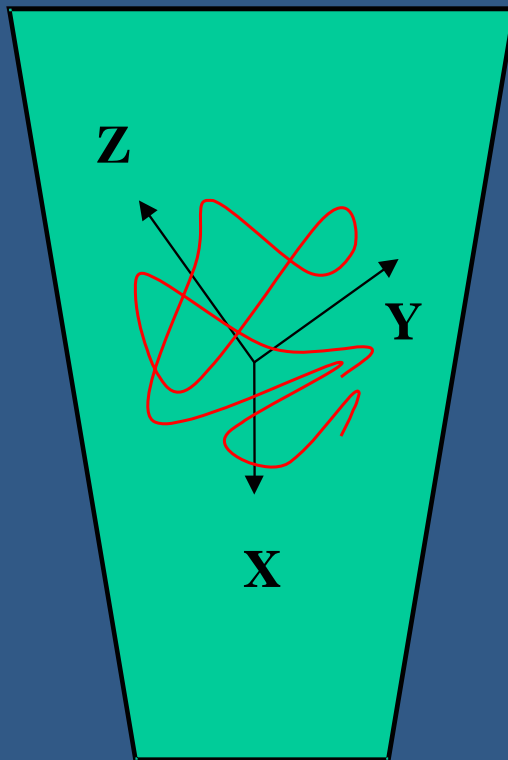


Methods: MRI

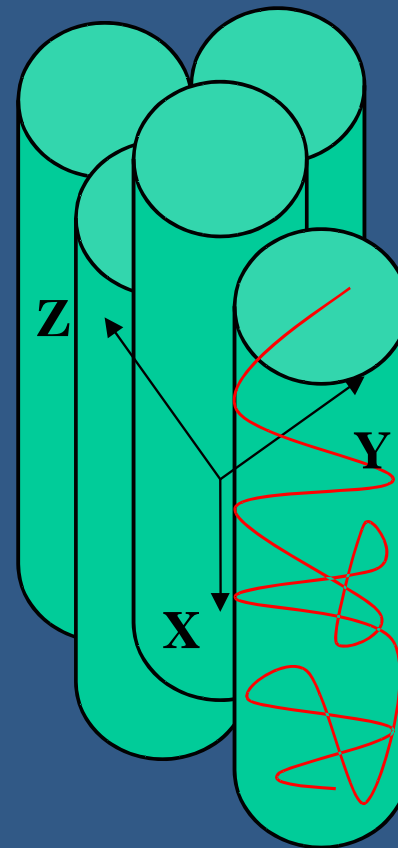


Diffusion

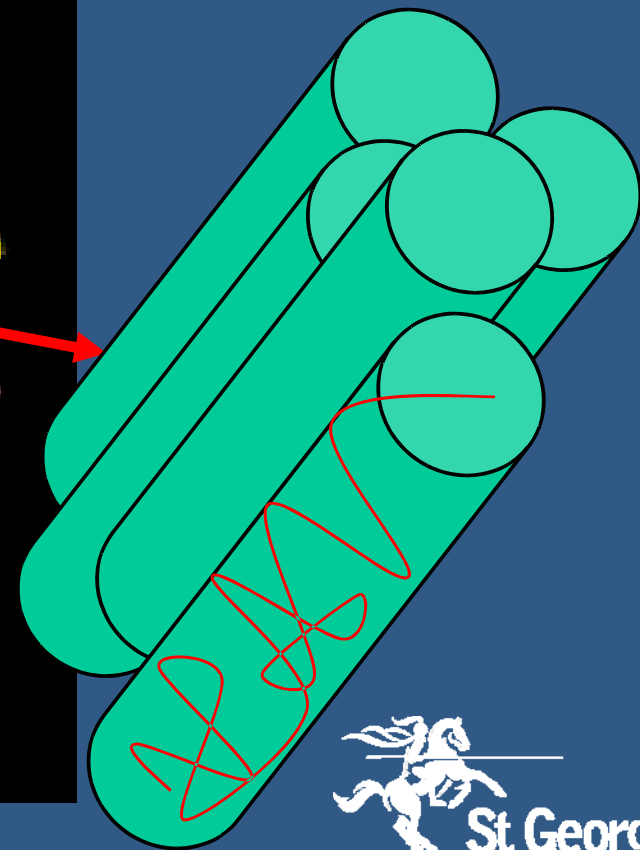
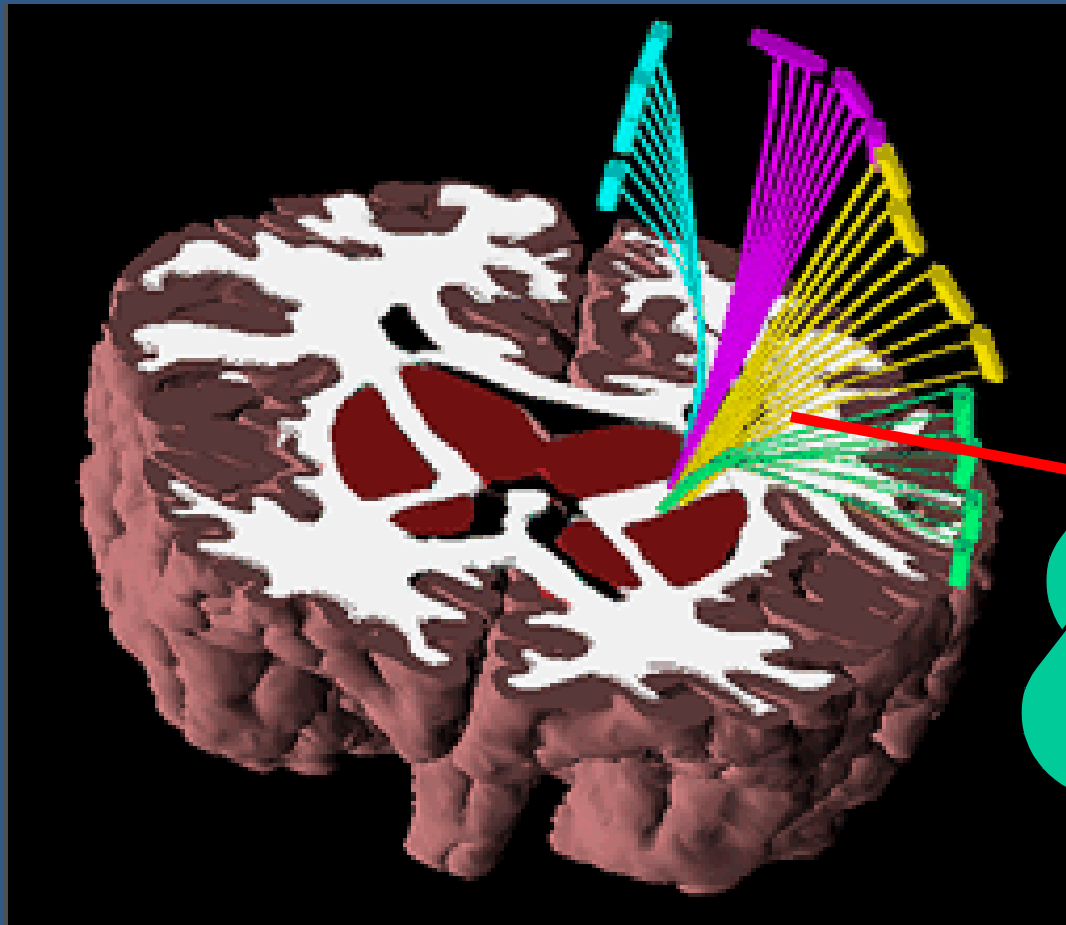
Isotropic diffusion



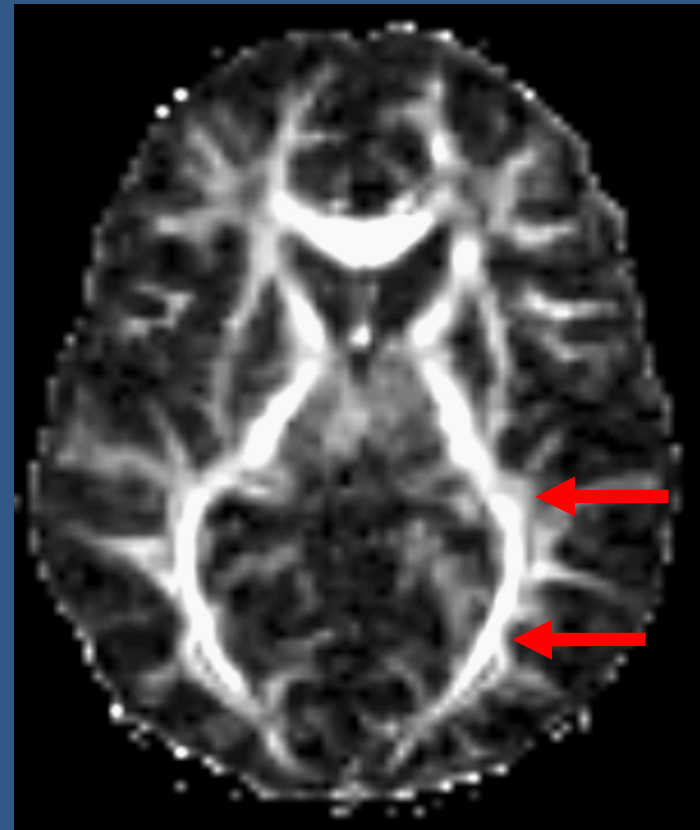
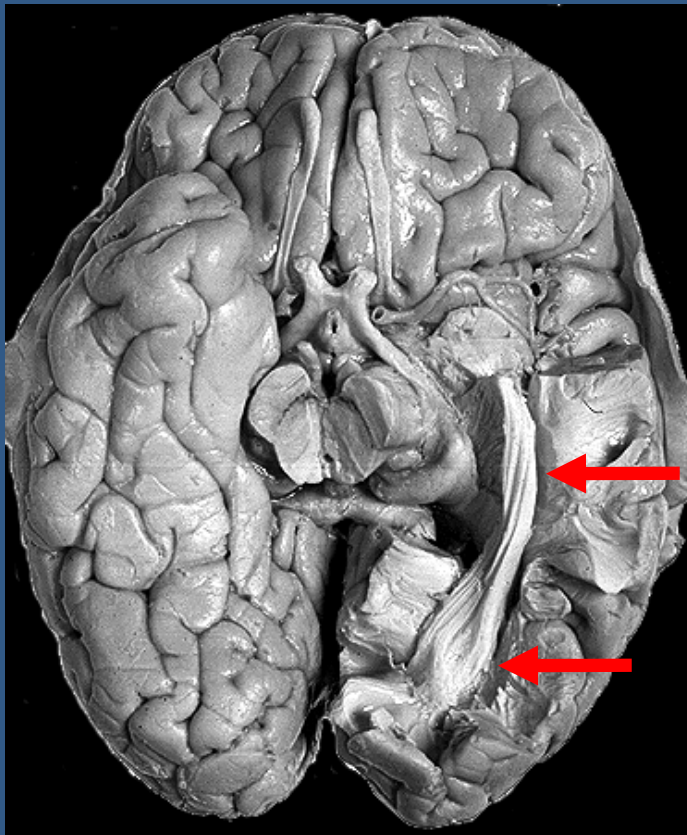
Anisotropic diffusion



Diffusion Tensor Imaging



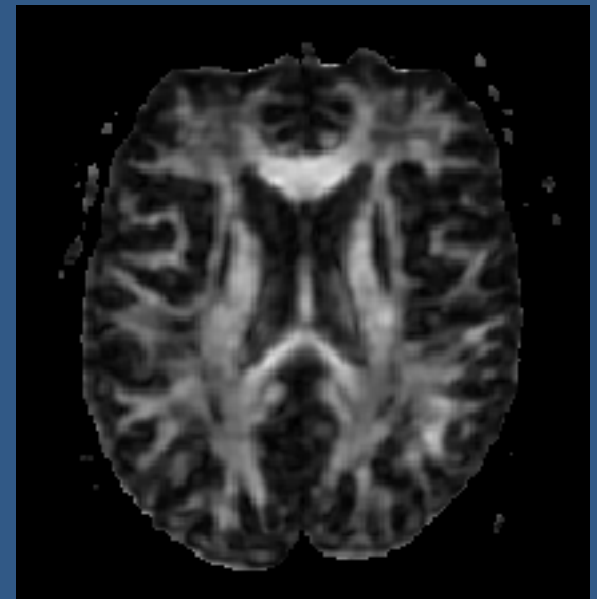
White Matter Tracts



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

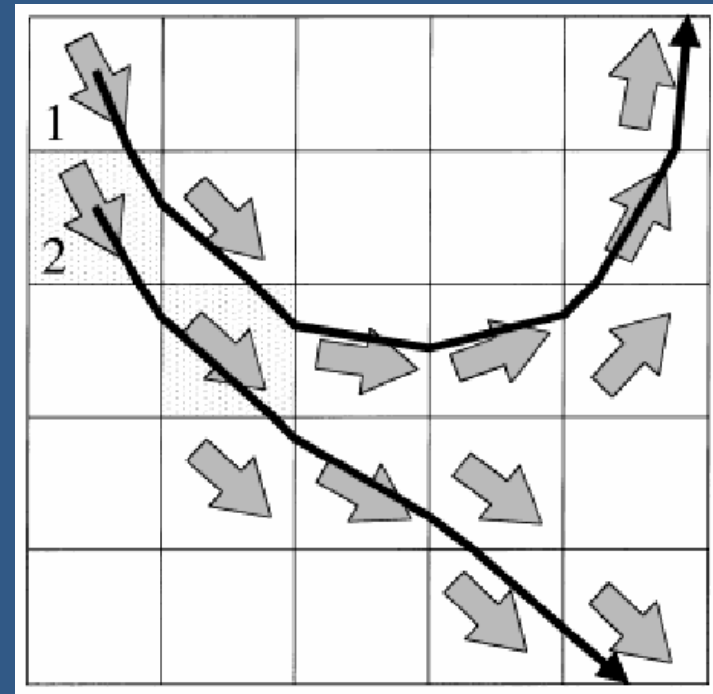
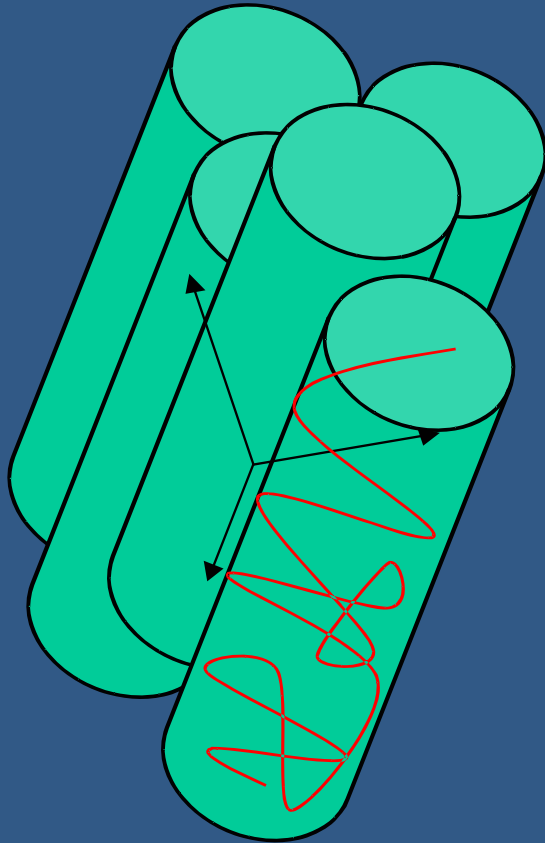


DTI – Voxel based statistics

- 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



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

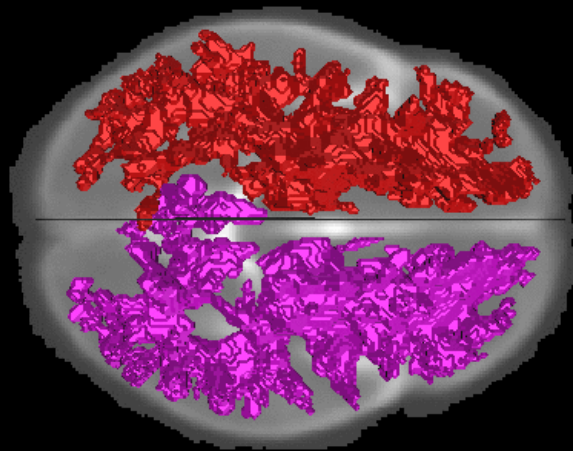
Experiment 1: Age effects



Significant 3D Voxel Clusters

Mean Diffusivity

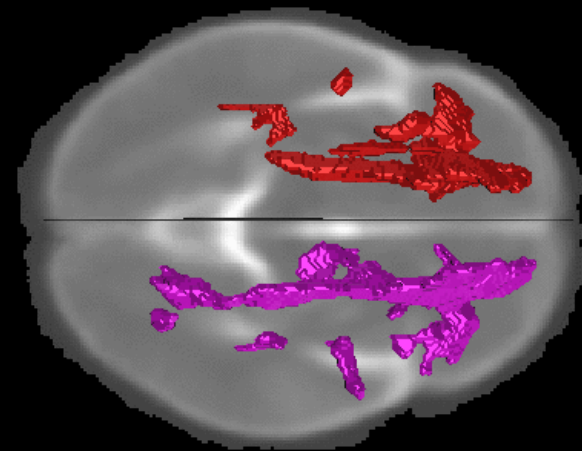
Fractional Anisotropy



Left



Right



Methods – Tractography

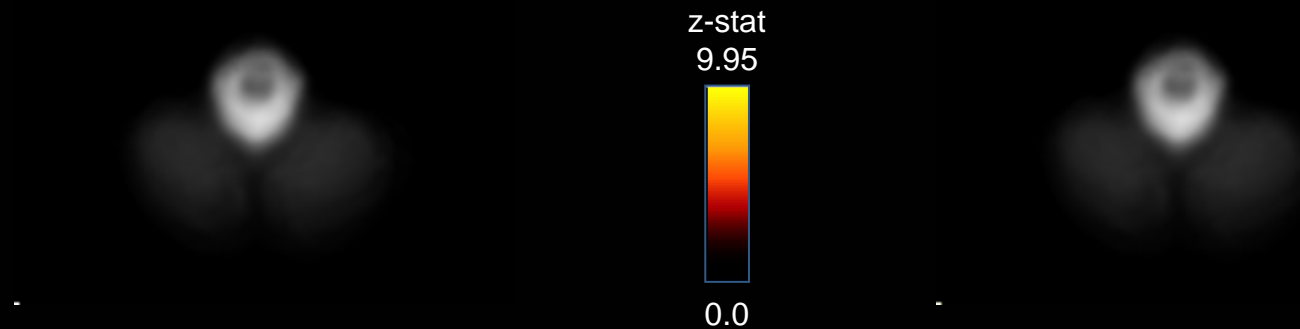
- Tracts initiated from each voxel centre throughout the entire brain
- Tracts retained that passed through significant clusters
- Step vector length, e.g. $t = 1.0$ mm
- Tract termination criteria
 - Fractional anisotropy ($FA < 0.08$)
 - No angle termination criterion



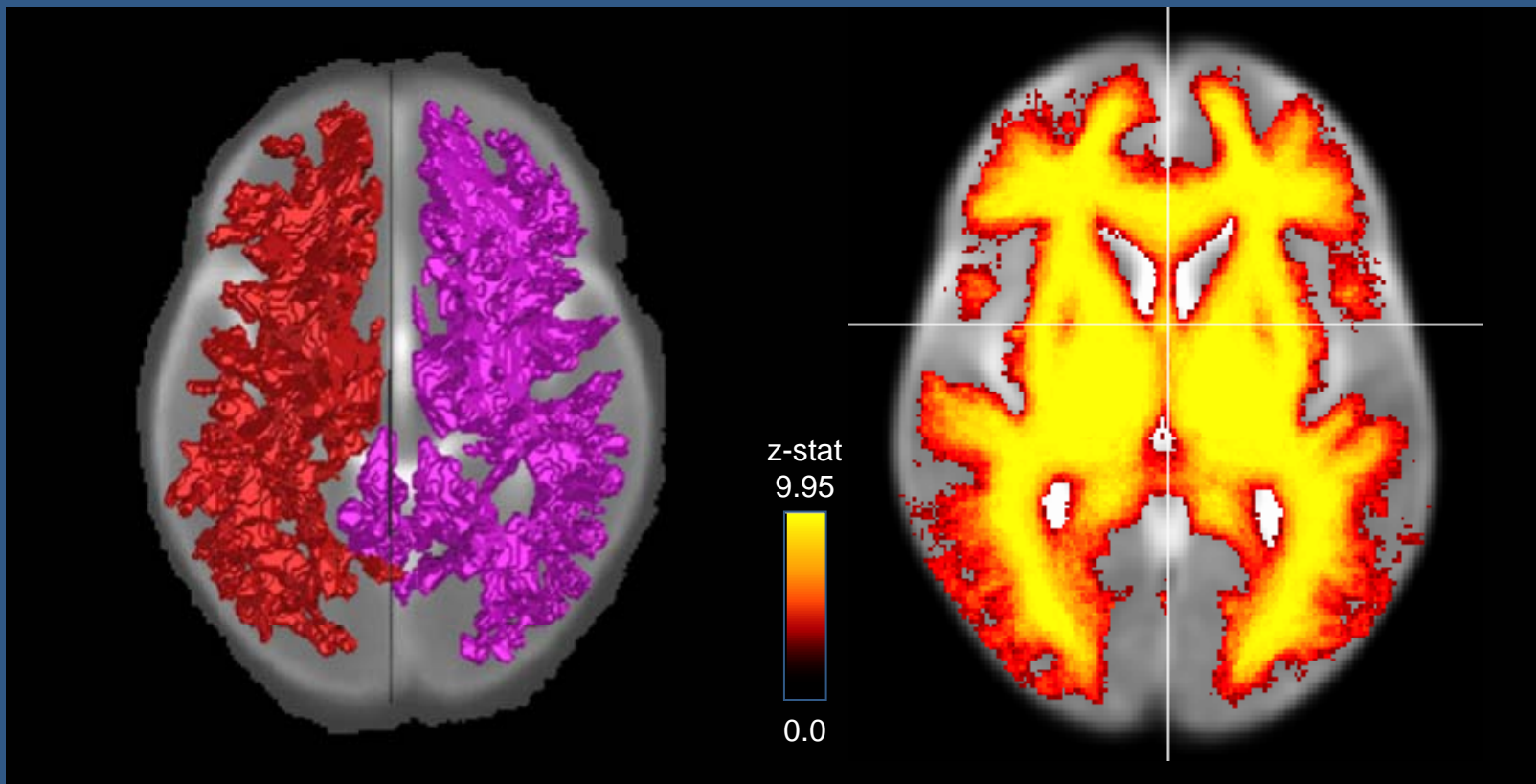
MD & FA Tracts

Mean Diffusivity

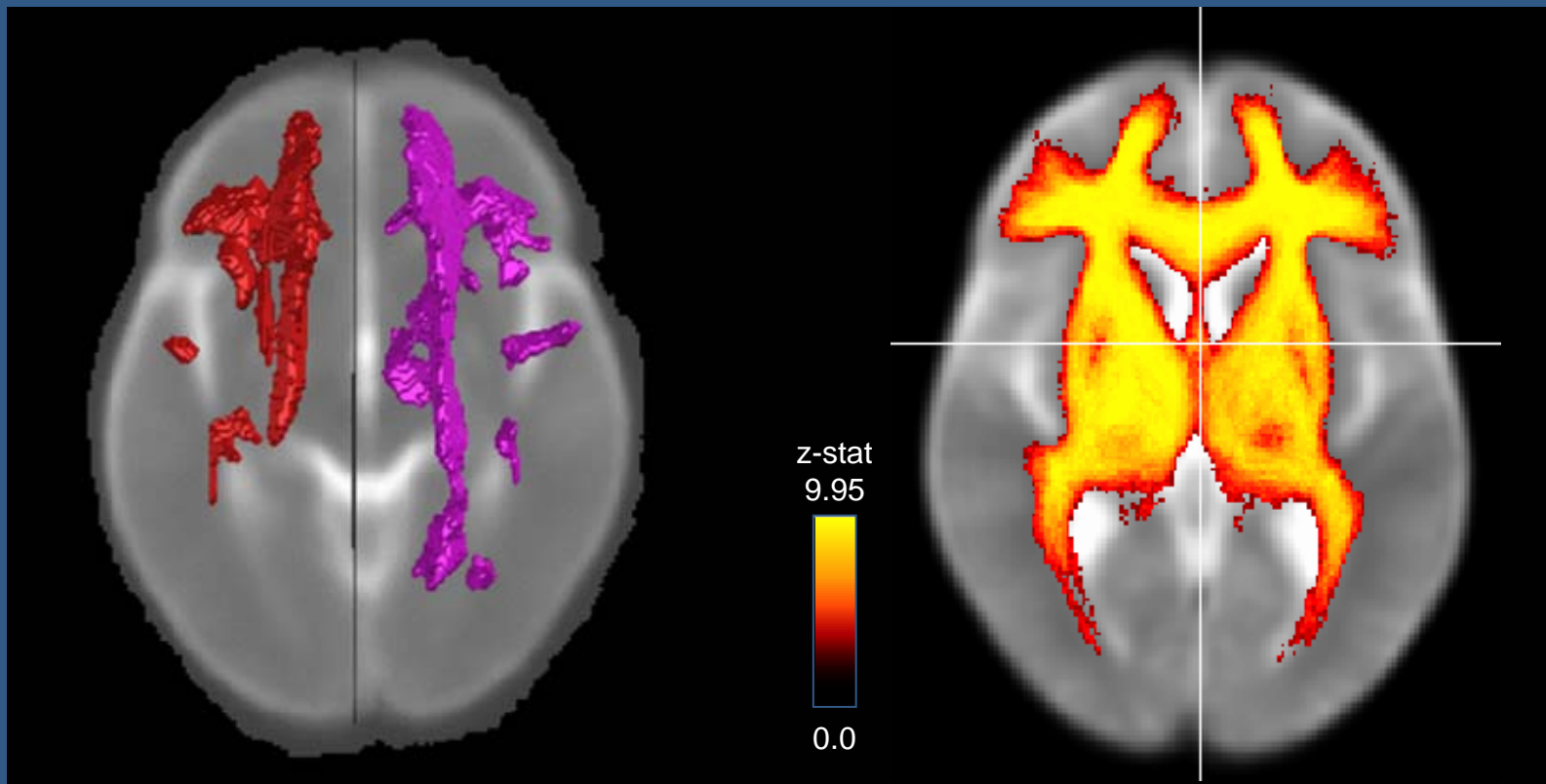
Fractional Anisotropy



MD Tracts



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 pericallosal 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.

Auditory Presentation

L – 2

R – 4 – D

M – 4 – E – 7 – Q – 2

Reply

2 – L

4 – D – R

2 – 4 – 7 – E – M – Q



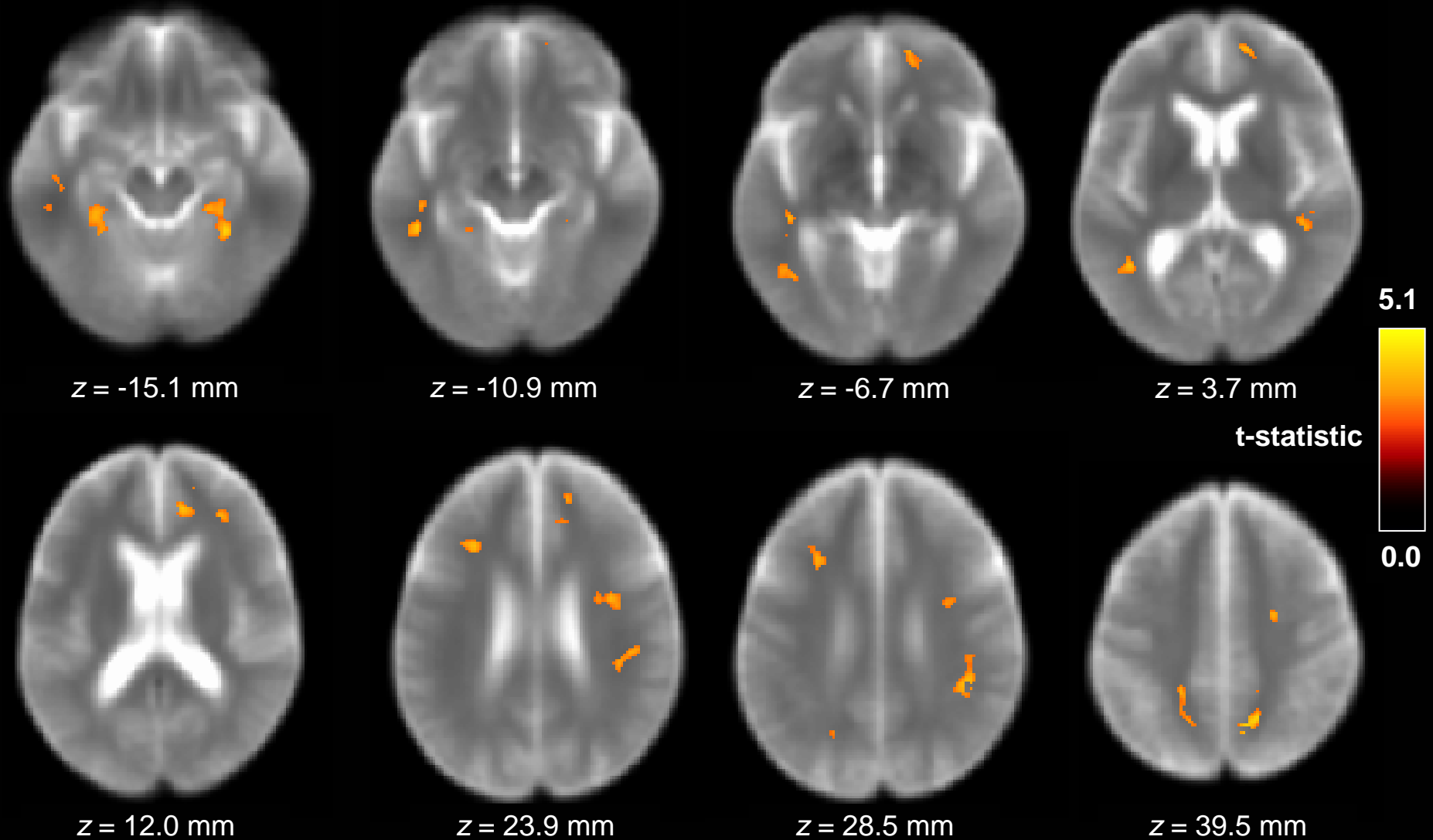
Analysis methods

Experiment 2: Working Memory

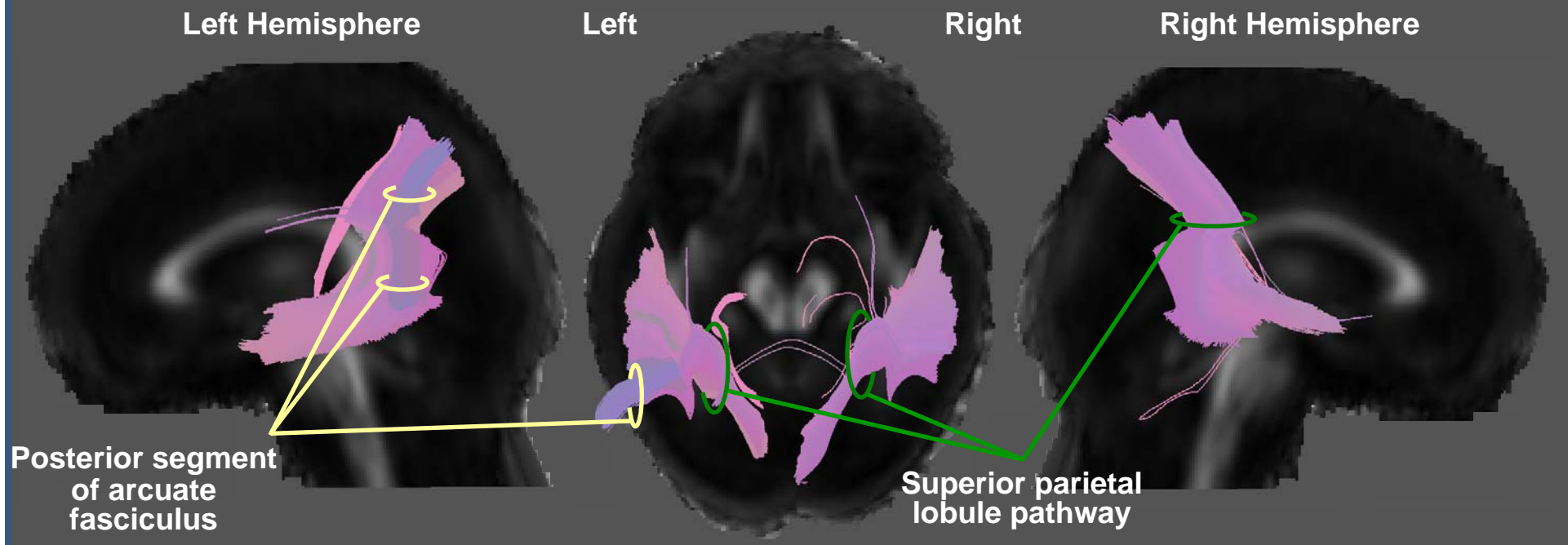
- Voxels significantly associated with working memory significant at $p < .01$
- Voxel clusters significant at $p < .05$
- Multiple comparison correction applied
- Tracts retained that passed:
 - through significant clusters
 - between temporal, parietal & frontal lobes.



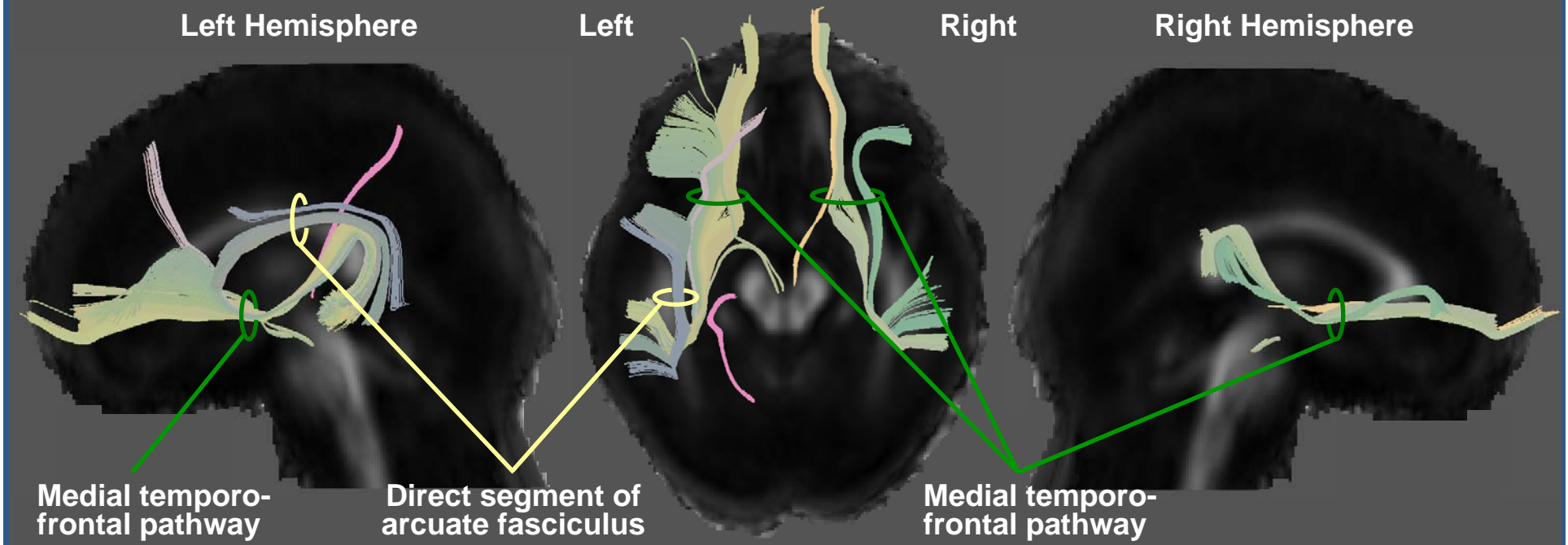
Working Memory Clusters



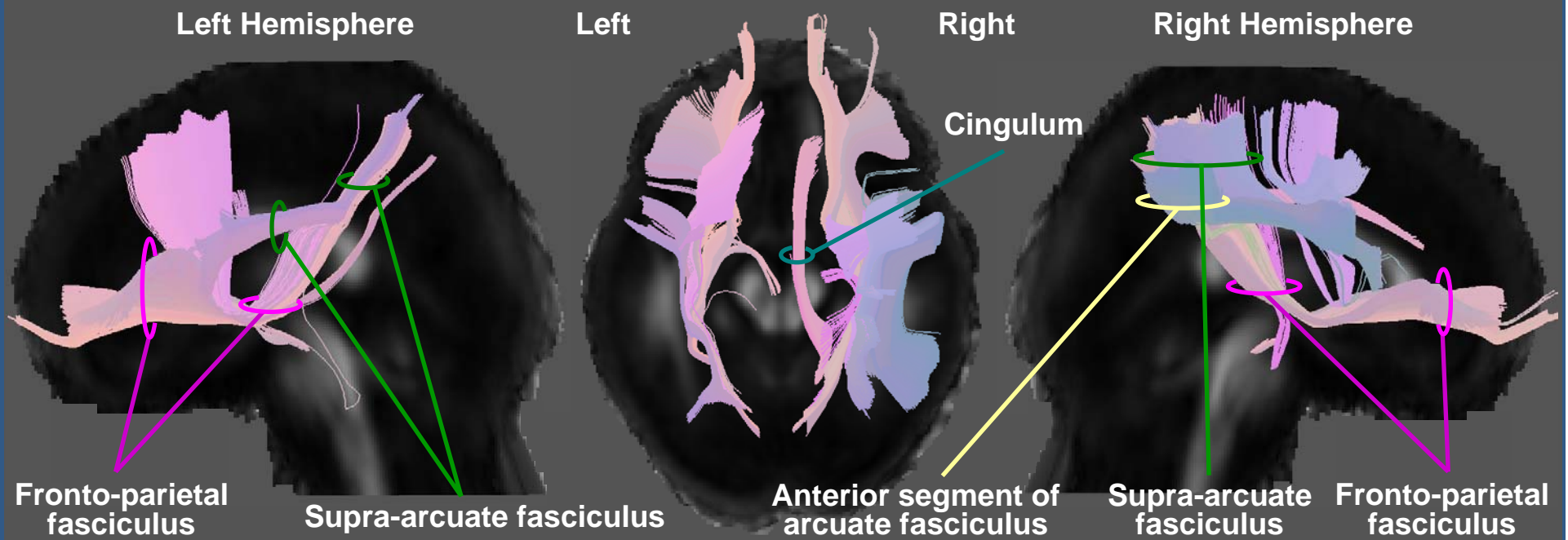
Working Memory Tracts - Temporo-parietal paths



Working Memory Tracts - Temporo-frontal paths



Working Memory Tracts - Fronto-parietal paths



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



General Conclusions

- 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



Acknowledgements

- Church Lane Practice, Wimbledon, for their help with recruitment, and all participants.
- Tom Barrick, Francesca Schiavone, Hugh Markus, Robin Morris.
- Research into Ageing for funding the project

