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Frontal Lobe Intraconnectivity: Short-range tract characteristics in old age

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The Disconnected Mind
Unlocking secrets of healthy mental ageing

Introduction

- The frontal lobes
  - facilitate our most complex thinking
  - contain multiple cytoarchitecturally and functionally discrete regions[1]
  - regions interact via complex, short-range white matter (WM) connections

- The frontal lobes are particularly prone to age-related structural decline[2]
- This may partially explain age-related cognitive ability decline in the elderly[3]
- Most studies of the frontal lobes focus on various frontal cortical areas.
- Yet, the WM connecting these regions remains relatively under-researched[4]
- It is unclear how individual differences in the number of connections and WM integrity in the frontal lobe vary in older age.

Aims

❶ Measure connectivity among frontal regions in older adults.

❷ Characterise variation in the number, density and integrity of these tracts.

Methods

Subjects & MR Imaging
- Eighty eight males from Lothian Birth Cohort 1936[5], mean age 73.7 ± 1 yr.
- Community-dwelling, MMSE≥24, HADS<11, not on antidepressants.
- T_1W scan (resolution 1x1x1.3 mm), 1.5 T GE scanner
- DTI scan (resolution 2x2x2mm), 1.5T GE scanner

Structural Images
- Seven gyral frontal regions were manually segmented on T_1W with Analyze 8.1 using a protocol published elsewhere[6] with excellent reproducibility (intra-rater ICCs > .96).

- Brain extraction (multi-spectral in Analyze).
  - T_2*-weighted and FLAIR volumes were fused using an image fusion tool
  - Brain extracted using object extractor tool
  - Masks from this processes then applied to T_1W

Diffusion Tensor Images
- Motion & eddy current distortion corrected by registering all diffusion-weighted volumes to the 1st undistorted b0 image[7]

- DT-MRI reconstruction used interpolated streamline and fractional anisotropy (FA) computation in DTI Toolkit.

- Segmented frontal lobe regions then transformed to DT-MRI space (via T_1W) using FLIRT[7]

- Site-to-site connection performed in TrackVis[8] (www.trackvis.org). Tracts connecting each pair of manually-segmented frontal ROIs were isolated.

- Primary measures were:

  - Connection Probability (# tracks connecting each pair of regions / the total # frontal lobe tracks).
  - Mean FA values of the connecting tracts.
  - Coefficient of variation (CoV) was used to index tract variation across individuals.

Results

- *Tracts (Fig. 1) and connectivity profiles (Fig. 2) concurred with previous anatomical reports of healthy younger participants[4,9].*

- *Individual variation in connection probability and tract FA (Fig. 3) was high. Particularly for lateral and cingulate regions.*
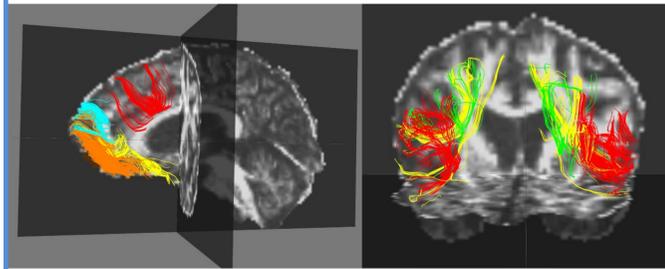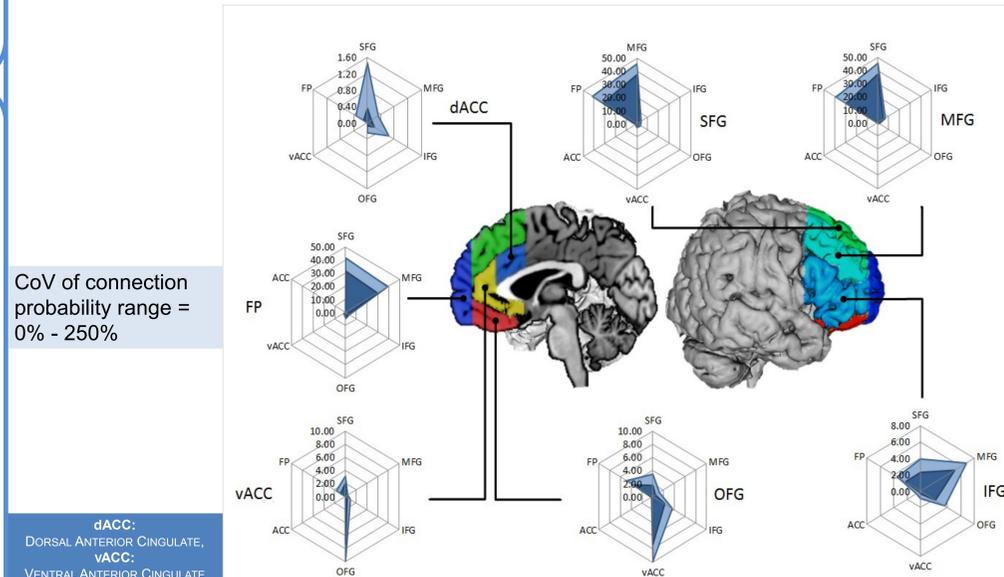

Fig. 1. Examples of intralobar frontal tracts.

Left Image
Red: dACC and SFG
Cyan: SFG and FP
Orange: OFC and FP
Yellow: vACC and OFC

Right Image
Yellow: SFG to IFG
Green: SFG to MFG
Red: MFG to IFG

CoV of connection probability range = 0% - 250%

dACC: Dorsal Anterior Cingulate, **vACC:** Ventral Anterior Cingulate, **SFG:** Superior Frontal Gyrus, **MFG:** Middle Frontal Gyrus, **IFG:** Inferior Frontal Gyrus, **OFG:** Orbitofrontal Gyrus, **FP:** Frontal Pole

Fig. 2: Radar plot of the mean + SD (dark and light blue) connection probability (x 10^2)
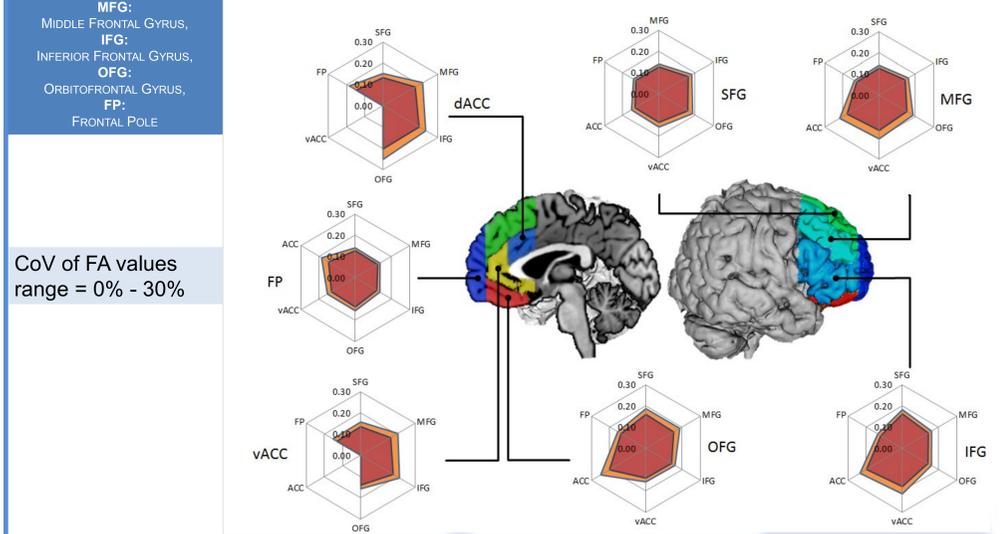
CoV of FA values range = 0% - 30%

Fig. 3: Radar plot of mean + SD (red and orange) FA values of the tracts connecting frontal regions

Variation in connectivity and FA were tightly related across frontal lobe tracts (β = .89, p<.000001)
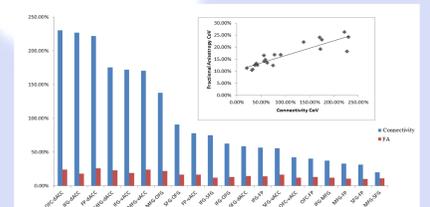
Fig. 4: Coefficient of variation (CoV) bar chart showing variability in the connection probability and FA values of the connecting tracts, and scatter plot with regression line (inset; top right) of the association between connection probability CoV and FA values CoV.

Conclusions

- The results show that the measures of connections involving cingulate and lateral frontal regions are highly variable in older age.
- This is a promising approach from which to examine the relationship between cognitive ability and the number, density and integrity of short range frontal lobe connections in old age.
- Longitudinal data or comparison with a younger group would help to determine if this variability is a feature of ageing, rather than pre-existing individual differences.
- More advanced tractography algorithms such as those based on probabilistic methods with 2 fibre populations per voxel will be investigated.

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