Frontal Lobe Intraconnectivity

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

S.R. Cox[1,2,3*], B.S. Aribisala[1,2,4,5*], K.J. Ferguson[2,6], S.E. MacPherson[2,3], S. Muñoz Maniega[1,2,5,] M.C. Valdéz Hernández[1,2,5], N.A.Royle[1,2,5], A.M.J. MacLullich[2,7,8], J.M. Starr[2,8,9], I.J. Deary[2,3], J.M. Wardlaw[1,2,5], M.E. Bastin[1,2,5]

* First Joint Authors

[1]Brain Research Imaging Centre, University of Edinburgh, UK, [2]Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, UK, [3]Department of Psychology, University of Edinburgh, UK, [4]Department of Computer Science, Lagos State University, Lagos, Nigeria, [5]Scottish Imaging Network, A Platform for Scientific Excellence (SINAPSE), [6]School of Clinical Sciences, University of Edinburgh, UK, [7]Endocrinology Unit, University of Edinburgh, UK, [8]Geriatric Medicine Unit, University of Edinburgh, UK, [9]Alzheimer Scotland Dementia Research Centre, University of Edinburgh, UK.

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.***

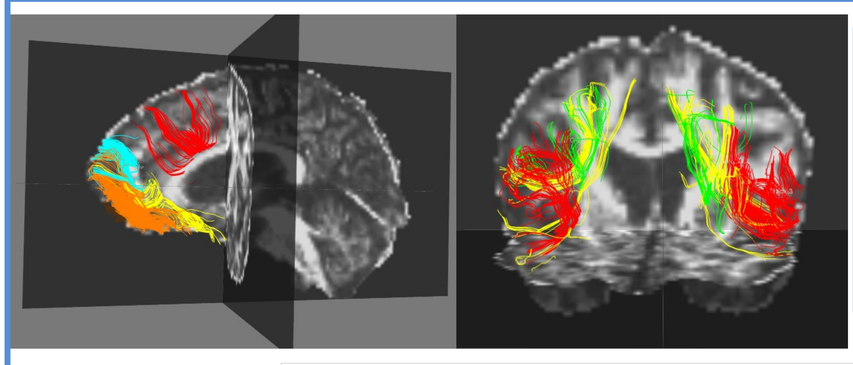

Fig. 1. Examples of intralobar frontal tracts.

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%

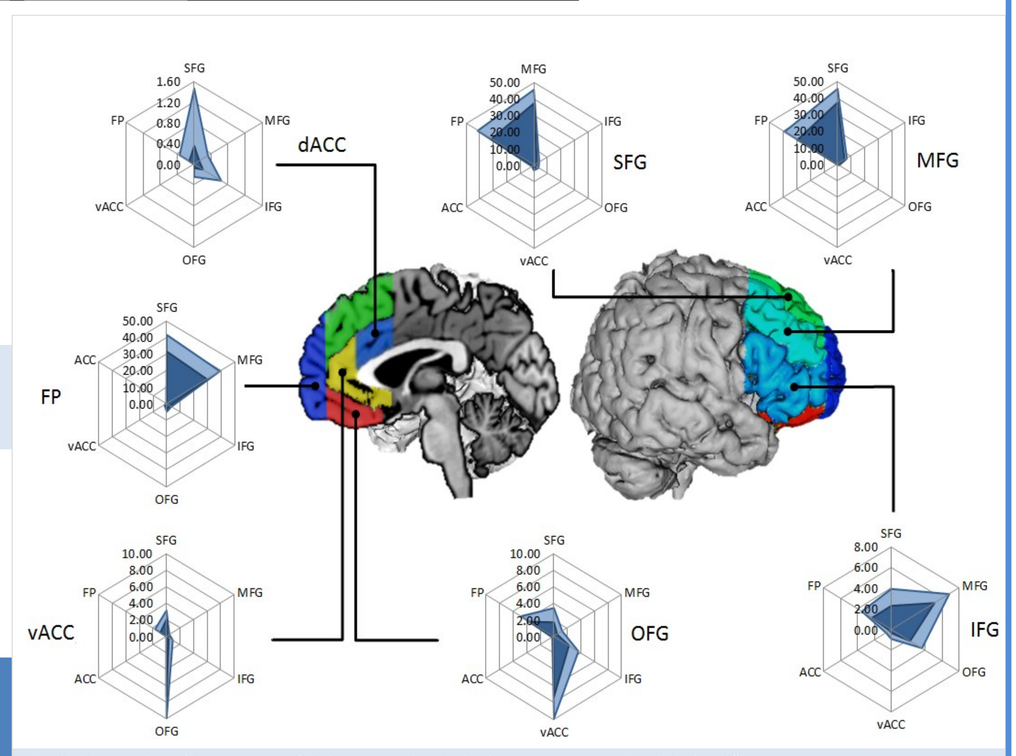

Fig. 2: Radar plot of the mean + SD (dark and light blue) connection probability (x 10^2)

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

CoV of FA values range = 0% - 30%

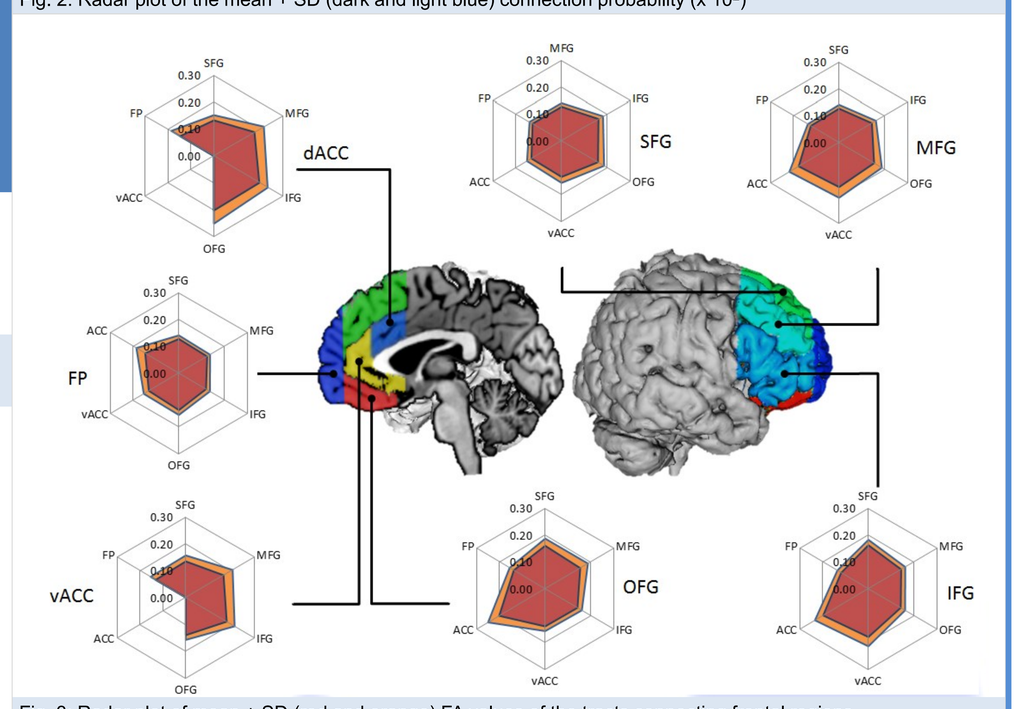

Fig. 3: Radar plot of mean + SD (red and orange) FA values of the tracts connecting frontal regions

Variation in connectivity and FA were tightly related across frontal lobe tracts (β = .89, p<.000001)

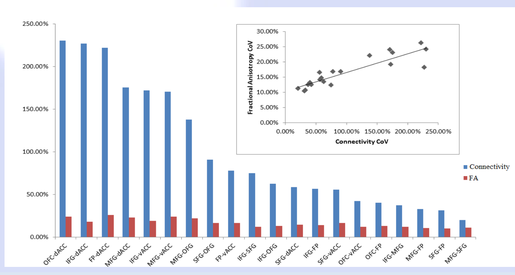

Fig. 4: Coefficient of variation (CoV) bar chart showing variability in the connection probability and FA values of the connecting tracts, and scatter plot with regression line (inset; top right) of the association between connection probability CoV and FA values CoV.

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.

References

[1] Zald, D.H. (2007). Orbital versus dorsolateral prefrontal cortex: anatomical insights into content versus differentiation models of the prefrontal cortex. *Ann. of the New York Academy of Sc.*, vol. 1121, pp. 395-406. **[2]** Fjell, A.M. et al. (2009). High consistency of regional cortical thinning in aging across multiple samples. *Cerebral Cortex*, vol. 19, pp.2001-2012. **[3]** MacPherson et al. (2002). Age, executive function and social decision making: a dorsolateral prefrontal theory of cognitive aging. *Psychology and Aging*, vol.17, no.4, pp.598-609. **[4]** Catani M. et al. (2012), Short frontal lobe connections of the human brain, *Cortex*, vol. 48, no. 2, pp. 273-291. **[5]** Deary, I. J. et al. (2007). The Lothian Birth Cohort 1936: a study to examine influences on cognitive ageing from age 11 to age 70 and beyond. *BMC Geriatrics*, vol. 7, pp. 28. **[6]** Cox S.R. et al. (2014), A systematic review of brain frontal lobe parcellation techniques in magnetic resonance imaging, *Brain Structure and Function* vol. 219, no. 1, pp. 1-22. **[7]** Jenkinson, M., & Smith, S. (2001). A global optimisation method for robust affine registration of brain images. *Medical Image Analysis*, vol. 5, no. 2, pp. 143-156. **[8]** www.trackvis.org **[9]** Beckmann M. et al. (2009), Connectivity-Based Parcellation of Human Cingulate Cortex and Its Relation to Functional Specialization, *The Journal of Neuroscience*, vol. 29, no. 4, pp. 1175–1190.

Correspondence: simon.cox@ed.ac.uk | 7 George Square, Edinburgh, EH8 9JZ, United Kingdom | www.ccace.ed.ac.uk www.bric.ed.ac.uk
benjamin.aribisala@lasu.edu.ng | Computer Science Department, Lagos State University, Lagos, Nigeria | www.lasu.edu.ng