Portraying the relationship between frontal lobe volumes and complex cognition: Different parcellation protocols paint very different pictures.

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Portraying the relationship between frontal lobe volumes and complex cognition: Different parcellation protocols paint very different pictures.

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The Disconnected Mind
Unlocking secrets of healthy mental ageing

THE UNIVERSITY OF EDINBURGH

Introduction & Aims

The frontal lobe of the human brain is functionally and cytoarchitecturally diverse.
Volumetric analysis is commonly used to research frontal lobe functions and clinical significance.
How to divide this lobe into meaningful regions from MRIs is a matter of significant discord. *But how much difference does parcellation method make?*

Aims: •To illustrate the implications of protocol selection • select 2 methods of manual frontal lobe parcellation
• contrast their correlations with cognitive scores in 90 healthy community-dwelling males from the Lothian Birth Cohort 1936 (aged 73).

Methods

IMAGE ACQUISITION

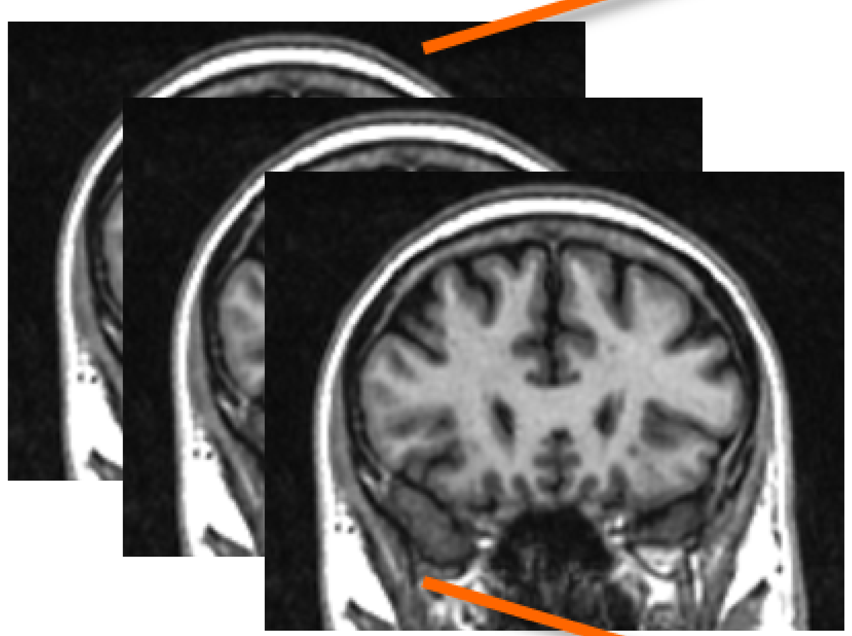
T1 weighted MR images were acquired at 1.5T in the coronal plane at 1 x 1 x 1.3mm resolution. All images were AC-PC aligned prior to image analysis. Raters were blind to participants' cognitive scores.

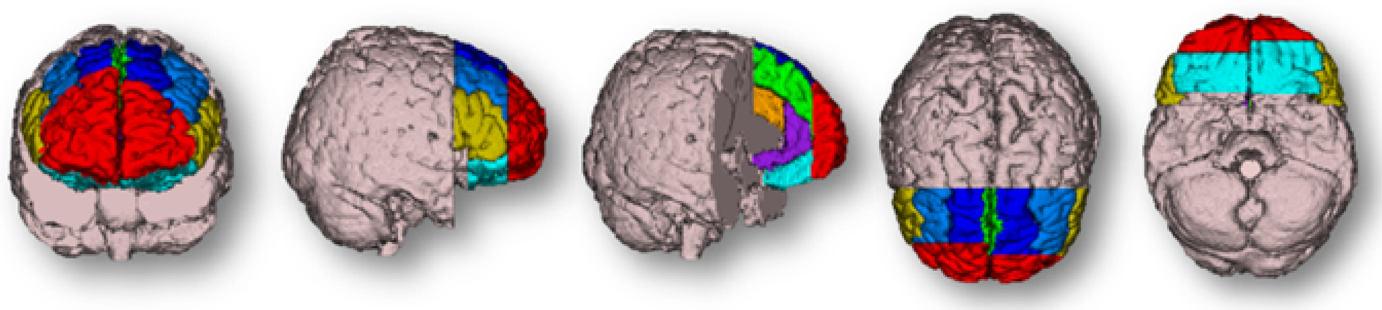
MRI ANALYSIS

We selected two highly reproducible manual methods for FL parcellation:
GYRAL - sympathetic to local gyrification & based on a systematic review of methods (Cox et al., *under review*).
GEOMETRIC - geometrically-derived frontal lobe volumes (Howard et al., 2003).

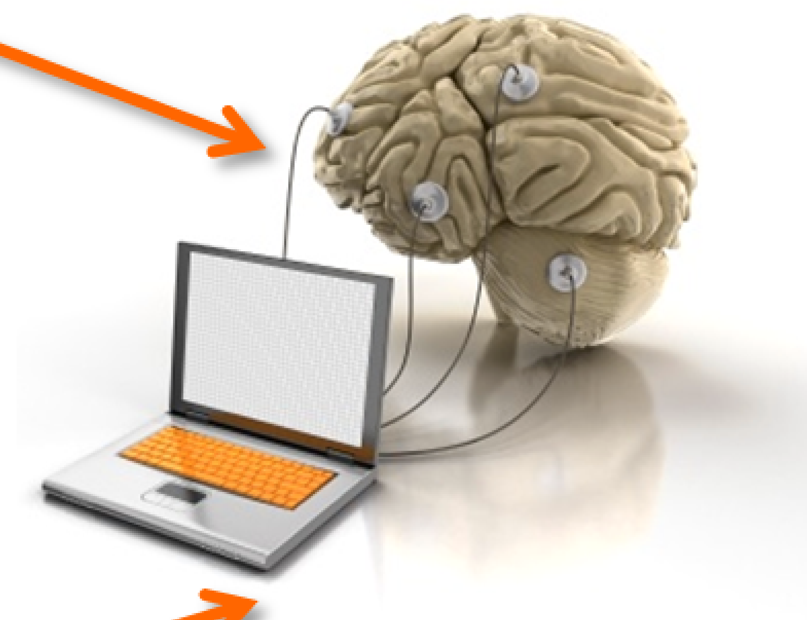
COGNITIVE TESTS

D-DKEFS Tower (Delis, Kaplan & Kramer, 2001)
Self-Ordered Pointing Task (Petrides & Milner, 1982)
Faux Pas (Stone, Baron-Cohen & Knight, 1998)
Reversal Learning (Rolls et al., 1994)
Simon Task (Simon, 1969)
Dilemmas Task (Green et al., 2001)





GYRAL: 7 ROIs per hemisphere, ICCs>.96[§]



GEOMETRIC: 4 ROIs per hemisphere, ICCs >.99 [§]

[§] *Intra-rater ICC consistency based on measurement of 10 brains (20 ROIs) measured twice, at least 2 weeks apart.*

Results

Regional volumes from the two different parcellation methods showed very different correlational patterns with the cognitive scores.

- Correlations of sub-regional volumes between methods were modest (<.44)
- ACC volumes from the GYRAL method correlated with all cognitive scores, but equivalent dorsomedial GEOMETRIC regions only correlated significantly with one task (red box). Dorsolateral correlations were also discrepant (green box).

GYRAL	FP		dACC		vACC		mSFG		DLPFC		IFG		OFG	
	L[a]	R	L[a]	R[a]	L	R[a]	L	R	L	R	L	R	L	R
Tower	-.02	.13	**.22***	-.04	.11	-.06	-.11	-.05	.10	.04	.13	.13	.02	-.03
SOPT	.17	-.13	**-.29****	-.06	**-.22***	.10	.08	.12	**-.21***	-.04	-.09	-.11	.04	.03
Faux Pas◊	.01	.02	**.26***	.08	.07	-.06	-.09	-.12	.19	.12	.13	**.22***	.08	.05
RL errors◊	-.03	-.06	**-.26***	.10	-.14	-.11	**.25***	.08	.11	.11	**-.23***	-.07	.06	.05
PES	-.09	**.24***	.02	-.19[†]	.05	**-.31****	.13	.10	.12	-.07	.09	-.05	.18	-.08
Simon Effect	-.11	**-.26***	.11	.37***	-.01	**.19[†]**	**.21***	.15	**.24***	**.44*****	.03	**.25***	.15	**.22***
Dilemmas RT[b]	-.12	.01	**-.23***	**-.26***	-.02	-.06	-.04	-.01	**-.22***	-.17	-.12	-.14	.05	-.09

GEOMETRIC	Dorsomedial		Ventromedial		Dorsolateral		Ventrolateral	
	L	R	L	R	L	R	L	R
Tower	.04	.11	-.07	.10	.08	.11	.01	-.01
SOPT	-.15	.05	-.12	-.15	.08	-.19	-.04	-.10
Faux Pas◊	.14	.17	.12	**.21***	.11	.12	.11	.11
RL errors◊	.03	-.13	-.12	-.11	-.05	-.12	-.09	-.14
PES	.11	**.36****	.17	**.25***	-.06	-.12	.14	-.01
Simon Effect	-.05	.01	.08	.05	-.01	-.06	-.01	.02
Dilemmas RT[b]	-.08	-.08	-.05	-.06	-.10	.01	-.11	.07

*Correlations between sub-regional volumes (controlled for ICV) and cognitive performance on a series of neuropsychological tests of frontal lobe function. Pearon's r unless ◊ non-parametric variable (Spearman). [a] square root transformed, [b] natural log transformed, †.08<p>.05, *p<.05, **p<.01. Colour values indicate correlations of significantly different magnitudes in comparable regions (p<.05, using DEPCOR; Crawford et al., 1996)*

Conclusions & Implications

- ➢ Both methods are highly reproducible and have well-defined rationales, but parcellation protocol selection has a clear impact on the putative neuro-structural correlates of cognition.
- ➢ Analysis of the same dataset using different methods yields strikingly different brain structure-function relationships. The significance of the ACC for all tasks in the GYRAL results is entirely absent from the equivalent dorsomedial GEOMETRIC method.
- ➢ This highlights the need for interpretative caution and methodological consensus in studies investigating structure-function correlations.
- ➢ Though this data alone is insufficient to identify a preferred method, previous work suggests that gyral rather than sub-cortical landmarks (used in the GEOMETRIC method) are more likely to be robust indicators of underlying cortical cytoarchitecture, connectivity and therefore function (e.g. Cox et al., *under review;* Fischl et al., 2008; Frost & Goebel, 2012).

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References: full references available on request. Cox et al. (under review). *Brain Struct Funct;* Howard et al. (2003). *Brain Res Protocol* 10: 125-138; Fischl et al. (2008). *Cereb Cortex* 18: 1973-1980; Frost & Goebel (2012). *Neuroimage* 59(2): 1369-1381.

Abbreviations: dACC: dorsal anterior cingulate cortex; vACC: ventral anterior cingulate cortex; DLPFC: dorsolateral prefrontal cortex; FP: frontal pole; ICC: intraclass correlation coefficient; IFG: inferior frontal gyrus; MSFG: medial superior frontal gyrus; MRI: magnetic resonance image; OFC: orbitofrontal cortex; PES: post-error slowing ROI: region of interest; RL : Reversal Learning RT: reaction time SD: standard deviation SOPT: self-ordered pointing task.

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