Semantic and Phonological Processing in the Left Inferior Frontal Gyrus: Observations from a Combined Distortion Corrected fMRI and Tractography Study

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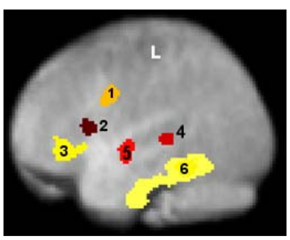
Introduction The left inferior frontal cortex (IFC) has been implicated in both language and semantic processing in many studies of functional activation (1). Although studies have indicated that both anterior and posterior regions contribute to semantic and phonological processing, work has suggested that an increase in activation for semantic relative to phonological decisions occurs in the anterior inferior frontal cortex with the opposite finding occurring in the dorsal posterior inferior frontal region (1, 2). This abstract reports on a combined semantic/language fMRI and diffusion weighted imaging (DWI) tractography study on 12 individuals. Functional activations from an object name word categorisation task were used to directly seed probabilistic tractography. The functional data revealed a left hemisphere dominance to task related activity with substantial activation in brain regions known to be associated with semantic and/or language processing, including left inferior frontal lobe and superior and inferior temporal lobe. This abstract is concerned primarily with activation in the left inferior frontal lobe.

Methods Both DWI and fMRI data were collected using distortion corrected protocols previously described (3). Parameters included fMRI: SE EPI with voxel size 1.875 x 1.875 x 4.2 mm, TR 3.2 s TE 75 ms, SENSE 2.5, 30 slices, 160 timepoints, DWI: SE-EPI sequence with TE = 54 ms, TR = 11884 ms, G = 62 mTm^{-1}, 112 × 112 matrix, reconstructed resolution 1.875 x 1.875 mm, slice thickness 2.1 mm, 60 slices, 61 diffusion sensitisation directions at b = 1200 smm^{-2} (Δ, δ = 28.5, 13.5 ms), and 1 b = 0 image. Both functional and DWI data were acquired in the same session from 12 individuals. Functional data were analysed using FSL and clusters of activation were defined for the contrast of categorisation of object names > letter strings using a fixed effects analysis of the group data with clusters significant at $p < 0.05$, Z statistic voxel level threshold $p < 0.0001$, corrected for multiple comparisons. Tractography was performed using the multi-fibre Probabilistic Index of Connectivity (4) method with probability density functions generated using a residual bootstrapping method (5). For each voxel in the functionally defined seed-point regions, 1000 Monte Carlo streamlines were generated and the results combined into a frequency of connection map. Tractography was performed at the individual level in the subject's native DWI space and results were then transformed to standard space and combined to provide maps with counts of number of individuals in which fibre tracking results were above a threshold of 1% of maximum connection frequency. Transformations between DWI, fMRI and MNI standard space were accomplished using 12 DoF registration (FLIRT, FSL) and the b=0 (DWI) and median functional images.

Results In total ten functional activation clusters were identified; the left hemisphere activations are indicated in Fig. 1. This abstract is foremostly concerned with three clusters found in the left inferior frontal lobe (1,2 & 3). The more posteriorly situated Cluster 1 in the inferior frontal opercular gyrus/post central gyrus, BA 44, produced tracking results into the arcuate fasciculus (circled magenta, Fig. 2) connecting all the way to the mid temporal lobe in 9 subjects. Substantial tracking also reached the left inferior temporal lobe, inferior and superior parietal lobules, supramarginal gyrus and functional Cluster 4 in Wernicke's area, all from tracts emanating from the superior longitudinal fasciculus, a major white matter tract system known to be heavily involved with coordination between language areas, indicating substantial involvement with phonological processing.

Fig. 1. fMRI activations in left hemisphere



cluster	cluster description	p	BA
1	Postcentral/Frontal Inf Oper	0.0075	44
2	Frontal Inf Tri/ Insula	0.047	45
3	Frontal Mid Orb/Frontal Inf Tri	0.0005	47/4

Fig. 2 Group tracking results for clusters 1-3.Plots are no. of subjects where fibre tracking reached a minimum of 1% of maximum frequency of connection

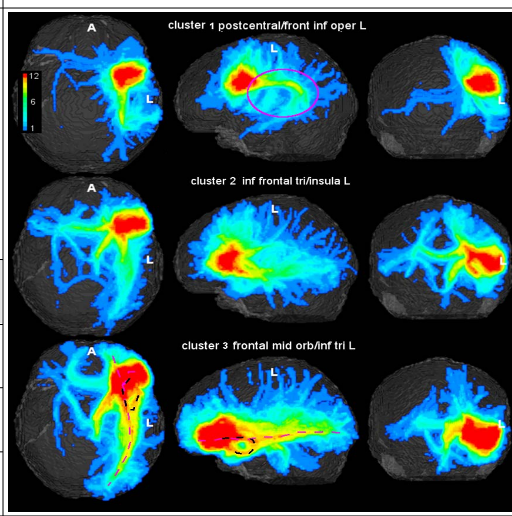
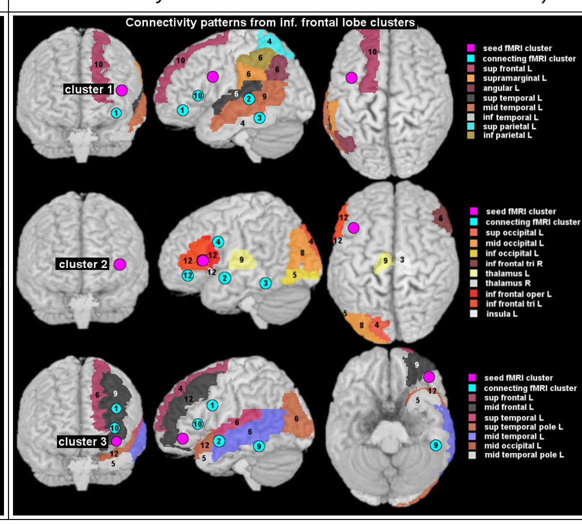


Fig. 3 Connectivity values to cortical regions and other functional activations (numbers are subjects in which connectivity reached a minimum of 1% of maximum)



Tracking from Cluster 2 showed strong connections to the left occipital gyri and the left thalamus and also to the corresponding region in the right hemisphere. Cluster 3 was situated in the orbital part of the left mid frontal gyrus continuing into the triangular part of the inferior frontal gyrus and produced extensive tracking in the frontal, occipital and temporal lobes. High connectivity within the frontal lobe included the mid frontal gyrus and the orbital part of the inferior frontal gyrus, although no subjects showed connectivity to the adjacent opercular part of the inferior frontal gyrus. High connectivity to the mid occipital gyrus was present, with tracks running from the start cluster along a path consistent with the inferior fronto-occipital fasciculus (dashed magenta line, Fig 2). Substantial connections to the middle and superior temporal lobe via the uncinate fasciculus (dashed black line) were also present. These anterior temporal lobe regions have been shown to be involved in semantic processing and indicate that the more anterior Cluster 3 is therefore likely to be a region involved with processing of semantic information.

Conclusions The functional data revealed a substantial left lateralization for the semantic/language system tested with functional activations in the inferior frontal lobe that could be differentially related to language and semantic memory by examination of patterns of connectivity to other brain regions known to have either phonological or semantic specialization. The use of tractography suggested an anterior to posterior gradient of semantic-language processing within the left inferior frontal lobe, in keeping with recent reports (1,2). The functional data alone was unable to identify this semantic/phonological specialisation as the fMRI task involved both language and semantic activity.

References (1) Price J. Anat. 197: 335-359 2000 (2) Devlin *et al*. J Cogn Neurosci 15:1 71–84 2003 (3) Embleton *et al.* ISMRM, 1070, 2006 (4) Parker & Alexander. Phil. Trans Roy Soc Series B 360: 893-902, 2005 (5) Haroon *et al.* IEEE Trans Med Imaging 2008 in press.

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