Measuring language laterality using functional connectivity

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Introduction

The determination of language lateralisation prior to neurosurgery aids in surgical planning, and can improve the preservation of language function in epilepsy patients. Language fMRI can be used to measure language laterality index (LI), and gives results that correlate well with the Wada test (1). The problem with language fMRI is that activation can be variable, with some subjects showing little activation. Further, the task can be difficult to reliably perform for children, and for patients with cognitive impairment. The purpose of the present study was to test the utility of using functional connectivity to measure language laterality, without the need for active performance of a language task. Connectivity uses low frequency fluctuations in resting brain activity to detect functionally related areas. It can detect language networks largely similar to those seen in an activation study (2) and detect subtle changes in these networks in patients with epilepsy (3).

Methods

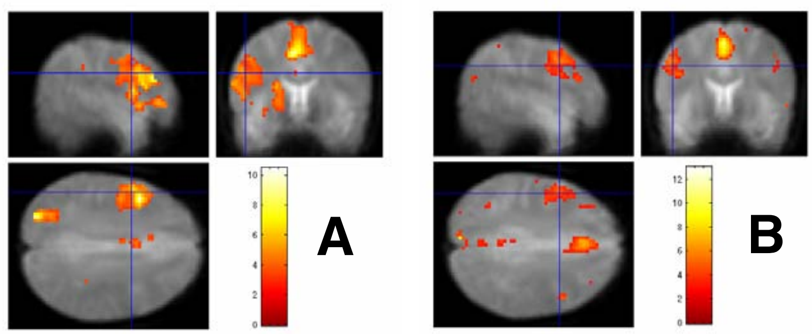
Twelve healthy volunteers were used in this study. The fMRI studies were performed with a 3 tesla GE Signa LX scanner (GE, Milwaukee, WI). Functional images were acquired as a series of gradient-recalled echo planar imaging (GR-EPI) volumes (TR/TE=3600/40ms, flip angle=60 degrees, 25 oblique slices 4mm thick+1mm gap, 24cm FOV, 128x128 matrix).

Between 90 – 300 volumes of resting state data were acquired for each subject, together with a block-design language paradigm. During the language paradigm, a visual fixation block was interleaved with a block of orthographic lexical retrieval (OLR), where the subject generated words beginning with a displayed letter. Standard block-design fMRI analysis of the OLR task was performed using SPM2 (www.fil.ion.ucl.ac.uk/spm). The time series for each subject was motion corrected, transformed to standard space and smoothed (8mm isotropic Gaussian kernel). In the statistical analysis of the language activation data, motion correction parameters were included as covariates of no interest.

The seed for the connectivity analysis was a sphere of 5mm radius centred on the anterior cingulate cortex (ACC) (approximate MNI coordinates, -2 14 52). This seed was chosen as it activated strongly for this task in an independent cohort of 30 healthy controls, but didn't introduce a laterality bias, as would have happened by choosing a lateral language area, such as Broca's area. Connectivity analysis was performed using SPM2 and custom scripts written in MATLAB. Each dataset was low pass filtered (f<0.08Hz). The seed timecourse for each subject was then regressed against all brain voxel timecourses to obtain a connectivity map for each subject. A second level (random effects) analysis was used to generate group activation and connectivity maps.

LI was calculated for each subject and dataset by counting the number of voxels above threshold in a left and right region of interest (ROI). The threshold was chosen on a subject by subject basis, by taking half of the mean t score of the top 5% of voxels in either ROI (4). This was done in order to optimise detection of truly activated voxels relative to a subject specific noise level. ROIs were drawn to represent left and right cerebral cortex, excluding midline cortex.

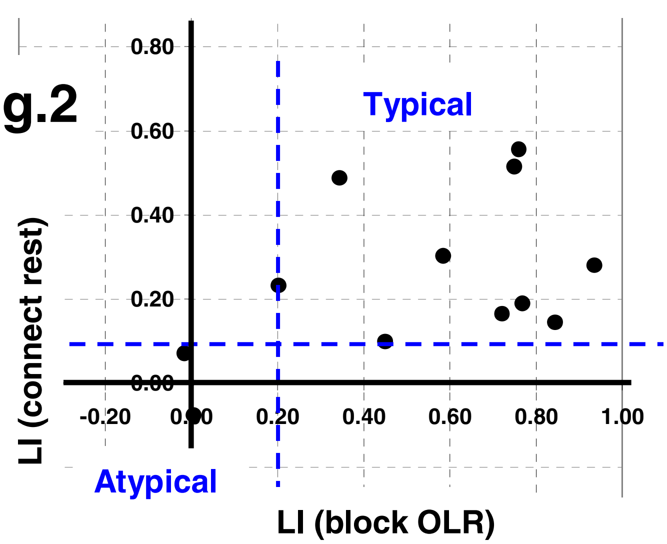
Fig.1



Results

Fig 1 shows the group block-OLR activation of the 12 controls (A), and group connectivity maps for the resting state dataset (B) Fig 2 shows the relation between each subject's LI calculated using block OLR and rest connectivity maps.

Fig.2



Discussion

Resting connectivity maps evaluated on individuals can be used to measure language LI. As demonstrated in Fig.1, group connectivity maps are qualitatively similar to those obtained using traditional block activation maps. Further, the individual LI obtained using the block OLR and connectivity maps showed a strong relationship, albeit with significant scatter. Most importantly for clinical decision-making, it was possible to choose a threshold connectivity LI to distinguish between typical (left) language laterality and atypical (right or bilateral) laterality using only resting connectivity maps that was 100% concordant with the activation-based LI with a "standard" threshold of LI=0.2. Further subjects are being recruited to substantiate these findings.

This study represents the first attempt to measure language laterality in a task independent, non-invasive manner. This approach promises to permit measurement of language laterality in subjects of any age, and with any degree of cognitive ability.

References

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