New Methods for Determining the Dominant Hemisphere in Language fMRI: A Reproducibility Study

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Introduction

Determination of hemispheric language dominance is critical in patients with epilepsy being considered for surgical resection. The current method of choice for determining language dominance is the intracarotid amobarbital test, known as the Wada test (1). However, there have been a number of attempts to replace the Wada test with fMRI language and memory paradigms to determine hemispheric dominance (2,3). There is still difficulty in reliably determining dominance using individual fMRI paradigms and it has been suggested that multiple language paradigms should be used (4).

The aim of this study was to determine if the hemispheric dominance of language could be reproducibly determined by combining the results from two different language paradigms and comparing the results from two separate imaging sessions. The laterality index (LI)is normally measured using:

$$LI=(V_L - V_R)/(V_L + V_R)$$

where V_L is the number of voxels activated within a specified region of the left hemisphere and V_R is the number of voxels activated within a specified region of the right hemisphere. In this study the mean of the two LI from two paradigms were used to provide an mean LI for each session with the analysis confined to the inferior and middle frontal lobes. The mean LI calculated was compared for the two scanning sessions in a number of normal volunteers.

A second measure of laterality was also investigated. The ratio of the average z-statistic within the inferior and medial frontal lobes was calculated. This was averaged over the two paradigms to produce an mean z-statistic laterality ratio (mean ZR). Mean ZR was compared for the two scanning sessions in the same volunteers.

Methods

One left and seven right handed volunteers were imaging with fMRI using two separate block design paradigms. The first a word generation paradigm required the subject to think of as many words starting with a particular letter in the activation state, whilst observing a crosshair in the baseline state. The second was a noun/verb association paradigm. In the activation state the subject was shown a different noun every two seconds and subject was required to think of a verb relating to the noun. Once again the baseline condition was observation of a crosshair. Each subject returned two weeks later and the fMRI paradigms were repeated.

The data were collected on a GE 1.5T NV/I, with a single-shot gradient-echo EPI sequence. All scans had a matrix size of 64x64, a TR of 3 seconds, and a TE of 40 msec. The slice thickness was 5mm, with 20 slices collected in total aligned with the subjects AC-PC. Each fMRI scan was 5 minutes long, with 5 active blocks of 30 seconds duration. 3D T1-weighted data was also collected (IR-FSPRG, 256x256x124).

The fMRI data was analysed using the FEAT tool in FSL. The z-statistic images were thresholded using a cluster threshold of $z>3.5$ and a corrected cluster significance threshold of $p=0.01$. All data sets were normalised to the standard template. Masks were applied to the normalised, thresholded z-statistic data, allowing the number of active voxels with the left and right inferior and middle frontal lobes to be measured and the LI calculated. The mean LI from each paradigm was calculated and compared for the two scanning sessions. Using the same masks ZR for the left and right hemispheres were calculated providing a ratio. This ratio was averaged for the two paradigms and compared for the two scanning sessions.

Results

The mean LI index over the two paradigms at the two scanning sessions had a strong correlation of 0.87 and was statistically significant ($p=0.005$). For mean ZR the equivalent correlation over the two sessions was 0.67 but was not significant with $p=0.072$. However, when the calculated values were used to determine laterality by setting thresholds for left, right and mixed dominance mean ZR had better reproducibility that the mean LI. Only for subject 8 does one of the measures (LI) not agree for the two scanning sessions.

Subject	Mean LI (1)	Mean LI (2)	Dominance (1 2)	Mean ZR (1)	Mean ZR (2)	Dominance (1 2)
1	0.92508	0.96689	Left Left	1.2680	1.6914	Left Left
2	0.84926	0.48264	Left Left	1.2256	1.1837	Left Left
3	0.70106	0.47708	Left Left	1.1195	1.1678	Left Left
4	0.49254	0.35756	Left Left	1.3482	1.2346	Left Left
5	0.86463	0.51424	Left Left	1.2525	1.1951	Left Left
6	0.19736	-0.21326	Mixed Mixed	1.0110	0.9010	Mixed Mixed
7	0.46553	0.39388	Left Left	1.3649	1.3670	Left Left
8	0.45432	-0.06890	Left Mixed	1.0800	1.0937	Mixed Mixed

Table 1: Comparing results from the mean LI and ZR for scanning session 1 and 2. The thresholds for dominance were LI: Left >0.25, Mixed 0.25 to –0.25, Right <-0.25. ZR: Left >1.1, Mixed 0.9 to 1.1, Right <0.9

Conclusions

The laterality index (LI) has been modified to account for two language paradigms and a new mean z-statistic ratio (mean ZR) has been developed for the assessment of language hemisphere dominance. Both the mean LI and mean ZR measures appear to be reproducible when assessed at imaging sessions two weeks apart. By setting arbitrary thresholds it was possible to determine an index of laterality which was reproducible in all but one instance (subject 8, mean LI measure). Further studies should investigate the reproducibility of these parameters with larger numbers of subjects and in the patient population. More importantly, however, the laterality results produced from these measures will need to be assessed in patients who have also had Wada testing. This will allow the laterality results produced using these measures to be directly compared to the Wada test results. A Wada comparison study would provide information on the accuracy of the mean LI and mean ZR results in defining dominance. The thresholds used to determine dominance could also be refined using the Wada information.

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