A semi-automated fMRI method to determine language lateralisation in neurosurgical candidates

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Introduction Neurosurgical candidates with intractable epilepsy or brain tumours require the determination of their language-dominant hemisphere in order to minimise the risk of post-operative language deficits or surgical morbidity. The WADA test, which utilises sodium amytal injected into the carotid artery, is the gold standard test for determination of hemispheric language dominance.[1] However, this is an invasive and uncomfortable procedure that involves an inherent risk of thrombo-embolism or complications from the intra-operative catheterisation.[2] Alternatives to the WADA test include positron emission tomography (PET), magnetoencephalography (MEG), transcranial magnetic stimulation (TMS), and functional MRI (fMRI),[3] but of these methods only fMRI offers information about the location of language regions (localisation) in addition to their laterality. FMRI is a non-invasive neuroimaging technique which relies on the signal change associated with blood oxygenation changes during a task. Language fMRI has been applied in a large number of studies in combination with WADA testing[4] and, more recently, as a standalone clinical procedure for the pre-operative assessment of neurosurgical patients.[5] However, one possible confound to the interpretation of language fMRI is that the apparent (bi)laterality of language regions depends heavily on the selected statistical threshold chosen by the clinical/surgical decision-maker. The purpose of the present study was to develop a simple, semi-automated post-processing method to determine language lateralisation for presurgical fMRI patients without the requirement for user defined thresholds.

Methods Functional MRI studies were performed with a 1.5T GE HDx MRI scanner, equipped with TwinSpeed gradients (GE Healthcare, Waukesha, WI, USA). The patient group consisted of 8 participants (5 male, age range 15-62 years) referred for pre-surgical fMRI for tumour resection or epilepsy surgery. 3 healthy adult control participants (2 male) were also examined with the same protocol. Language fMRI was assessed with both verb generation (VG)[6] and verbal fluency (VF)[7] tasks, using a block-design paradigm with block lengths of 30 s (VG) or 28 s (VF). Subjects were instructed to respond subvocally. Images were acquired with a gradient echo EPI sequence with TR= 3000 ms (VG) or TR= 4000 ms (VF), TE=40 ms, FOV= 24 cm, matrix= 64x64, slice thickness = 3.0 mm, slice gap = 0.3 mm. FMRI processing was performed in Brainwave, an automated fMRI post-processing software tool (GE Healthcare) incorporating motion correction, smoothing, co-registration to a high resolution anatomical MR image, and statistical testing. Activation maps were saved with a statistical threshold of $p<0.05$, and then processed offline using a locally written linux script incorporating tools from the FSL software library (fmrib.ox.ac.uk). The MNI structural atlas was normalised to the skull-stripped anatomical images for each patient, and regional masks for Broca's area (BA) and Wernicke's area (WA) and the combination (BW) from the Harvard-Oxford cortical structural atlas were used to select the language regions for each patient. The activation within the masked regions was then calculated for each patient for both the left and right language regions (BA, WA, and BW), and a laterality index was defined from for a graded set of thresholds ranging from 10% to 100% of the maximum Z-score, according to the formula $(R-L)/(R+L)$ where R and L are the number of voxels in the right and left regions with activation above the applied threshold, respectively. The laterality was then plotted against the applied threshold in order to display the language laterality graphically in a clear and unambiguous format.

Results Laterality index plots are shown for 3 patients and one healthy participant in figure 1 (top: verbal fluency, bottom: verb generation), respectively. For the patient and 2 healthy participants with bilateral language dominance (fig 1: columns 2 and 4), the verb generation task showed stronger language laterality than the verbal fluency task. Laterality index plots were successfully generated for all patients, and were in agreement with neuroradiological assessment from the initial brainwave fMRI processing.

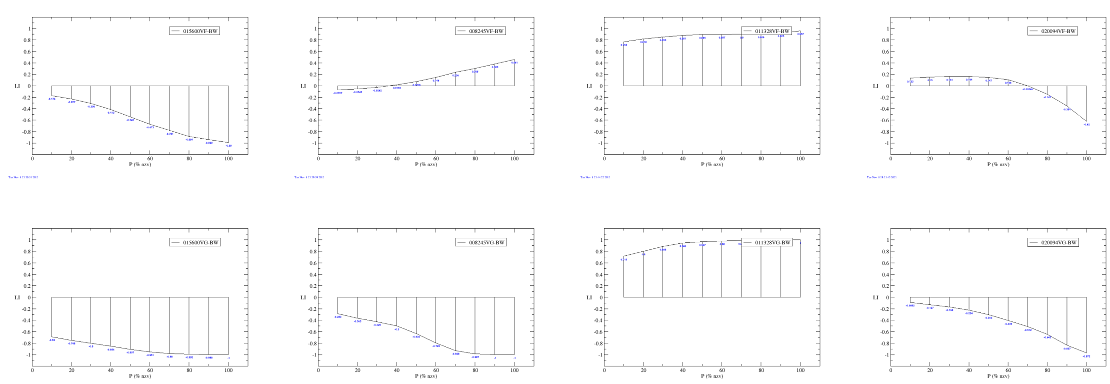

Figure 1 Laterality index plots for patients with left (col. 1), bilateral (col. 2), and right (col. 3) language lateralisation (as determined by expert neuroradiological assessment). Laterality index plots for a healthy participant with bilateral language dominance are shown for comparison in column 4.

Discussion Despite the heterogeneity of the patient population, laterality index plots were successfully generated for all participants, and were in agreement with expert neuroradiological assessment, suggesting that this method provides a simple but robust quantitative assessment of language laterality, independent from the selected statistical threshold.

References: 1. Wada J & Rasmussen T. J Neurosurg 17:266-82 (1960) 2. Dion JE, et al. Stroke 18:997-1004 (1987) 3. Pelletier I, et al. Epileptic Disorders 9(2):111-126 (2007) 4. Woermann FG, et al. Neurology 61:699-701 (2003) 5. Chlebus P, et al. Exp Brain Research 179:365-374 (2007) 6. Leslie KR et al NeuroImage 21:601–607 (2004) 7. Fu C, et al NeuroImage 17, 871–879 (2002)