

Reproducibility of fMRI localisation within the human somatosensory system.

R. Vidyasagar¹, and L. M. Parkes^{2,3}

¹MARIARC, University of Liverpool, Liverpool, Merseyside, United Kingdom, ²School of Cancer and Imaging Sciences, University of Manchester, ³Biomedical Imaging Institute, University of Manchester, Manchester, United Kingdom

Introduction: fMRI provides a powerful method of monitoring functional changes in the brain across a timescale, such as in the case of a longitudinal study incorporating multiple sessions across subjects (1). The reproducibility of the location of activation in such cases needs to be considered to ensure accurate interpretation of data. This becomes particularly relevant when issues such as physiological (e.g. vascular), and scanner noise contribute to the quality of the data. Additionally, errors introduced during the co-registration process could contribute to misinterpretation of data. Past studies have addressed the issue of reproducibility of the fMRI response based on analysis techniques requiring large numbers of data averages and an involved statistical approach (2), but do not account for issues introduced by registration errors. Another factor to consider is how significant activated clusters of fMRI data are reported. Two common methods employed for reporting key activation areas relates to the use of peak voxel or central voxel location within a cluster. It has yet to be established which of these two methods produce the most reproducible and thus reliable means of localising functional activation. This study had two aims: 1. Compare the reproducibility of using peak or central voxel values from functional data in the somatosensory system. 2. Use the relative distance between two activation sites as a means of measuring reproducibility without registration errors.

Methods: Ten right handed subjects took part in the study (mean age 23.3 ± 3 years, 5 female, 5 male). MR data was acquired on a Siemens 3 T Trio system. T2*-weighted BOLD data were acquired with prospective motion correction with a TR of 2 seconds; TE: 35 ms, 2 mm isotropic voxels in addition to high resolution T1-weighted structural images that were acquired at each scan session. The study had two phases, a 'First Day (FD) scan' performed in the morning, and a 'Return Day (RD) scan' performed at no particular time of the day. The RD scan was carried out > 3 weeks following the FD scan. The same scan protocol was carried out on both FD and RD. The protocol involved the activation of Digits 2 and 4 of the right hand using a vibrational factor placed on each digit, which vibrated at 30Hz. The task paradigm was a block design consisting of each factor vibrating in turn for an ON period of 6 seconds (with intermittent vibration to avoid adaptation) and an OFF period of 10 seconds in a randomised order.

Results: All data were temporally and spatially smoothed (4mm Gaussian kernel) and analysed on an individual basis using Brainvoyager (Brain Innovation, The Netherlands). FD structurals were normalised to Talairach space. Activation maps from both FD and RD sessions were registered to the normalised FD structural. Activated volumes relating to individual digits were thresholded to the most significant 200 voxels, central voxel and peak voxel location values from each activated cluster were acquired. The difference in distance between each digit for these two measures was calculated for individual subjects. A 95% confidence interval (3) for the x, y and z coordinate of the central voxel and peak voxel for each digit, and the distance between the two digits, was computed and used as a measure of reproducibility.

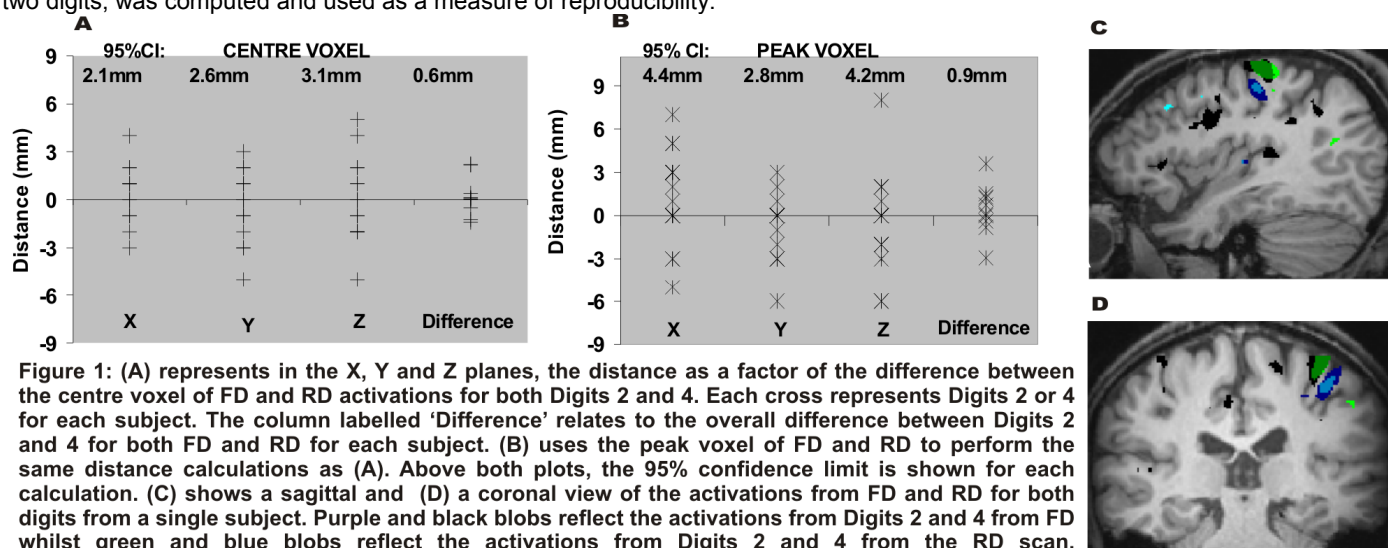


Figure 1: (A) represents in the X, Y and Z planes, the distance as a factor of the difference between the centre voxel of FD and RD activations for both Digits 2 and 4. Each cross represents Digits 2 or 4 for each subject. The column labelled 'Difference' relates to the overall difference between Digits 2 and 4 for both FD and RD for each subject. (B) uses the peak voxel of FD and RD to perform the same distance calculations as (A). Above both plots, the 95% confidence limit is shown for each calculation. (C) shows a sagittal and (D) a coronal view of the activations from FD and RD for both digits from a single subject. Purple and black blobs reflect the activations from Digits 2 and 4 from FD whilst green and blue blobs reflect the activations from Digits 2 and 4 from the RD scan.

Conclusions: This study shows that fMRI has the ability to provide robust digit localisation that is reproducible to approximately 3 mm over a period of > 3 weeks, an improvement on previous reports (4). On removal of registration errors (shown by the reproducibility of the distance between digits), this reduces to less than 1 mm. Importantly, this suggests minimal contributions from physiological and scanner errors. We have also shown that the interpretation of the localisation of functional activity using the central voxel of a cluster is more accurate than the use of the peak voxel location. However, when using the distance between digits for these techniques, the difference is negligible. The application of this finding is particularly useful in situations where the longitudinal positional precision of fMRI measurements is of importance. By incorporating a paradigm with a known activation area, it may be possible to use that activated area as a marker and measure changes that might take place in other areas in relation to this marker, thus removing registration errors. This could be an important strategy in learning and plasticity based paradigms or pharmacological studies where longitudinal changes in the location of activation are measured.

References 1. Feydy, A., et al. *Stroke* 33, 1610-1617. 2. Le, T.H., and Hu, X.P. (1997) *Nmr in Biomedicine* 10, 160-164. 3. Bland, J.M., Altman, D.G., (1996). *British Medical Journal*, 313, 744; 4. Weibull, A., et al, (2008) *Magnetic Resonance Imaging* 26, 1342 - 1351

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