The Minimum Detectable Change in fMRI Measurements of Brain Activity Across Imaging Sessions

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Introduction

There is an extensive literature demonstrating the reorganization of motor and cognitive function as a result of ischemic stroke; however, to advance the clinical use of fMRI to track the progression of post-stroke recovery and/or to assess treatment, there is a need to obtain precise and reproducible fMRI measurements of brain function from individual stroke patients. Modest reproducibility of fMRI has been demonstrated previously,[1] and the laterality index (LI, defined as contralateral minus ipsilateral divided by contralateral plus ipsilateral activation) has shown better reproducibility.[2,3] In this study we examined between-session and within-session variance to determine the *minimum detectable change* in fMRI measurements of brain activity (both LI and number of pixels) across imaging sessions. As a result, this will determine the usefulness of fMRI for clinical evaluations of the progression of functional recovery and reorganization following stroke in individual patients.

Methods

Seven healthy volunteers were scanned during three sessions on separate days. A 3 Tesla scanner (Signa Excite, GE Healthcare, Waukesha, WI) and a standard quadrature head coil were used to collect all images. Each session included a 3-plane localiser to prescribe slices, a 3D T_1-weighted high-resolution volume for anatomical registration, and eight fMRI data sets (gradient-echo EPI: TR/TE=1500/30 ms, FOV=24x24 cm, matrix=96x96, slice thickness=5 mm). Four fMRI sets were collected during the execution of a motor task (visually paced finger flexion at 3 rates - 0.75 Hz, 1.5 Hz, self paced - randomized into 9 blocks of 12 sec task and 24 sec rest) and four were collected during a 2-back task (3 seconds per digit; volunteer was required to respond on a keypad to any digit that was the same as one presented 2 digits previously; 8 alternating blocks of 30 sec task, 30 sec rest; a visual cue during rest also required a keypad press). Analysis was performed using FSL (www.fmrib.ox.ac.uk/fsl) using a Gaussian kernel of FWHM 6mm. Z-statistic images were thresholded using clusters determined by Z>2.3 and a (corrected) cluster significance threshold of p=0.01. Registration to high-resolution images was carried out using FLIRT. Primary motor cortex (M1) and pre-frontal cortex (PFC) regions of interest (ROIs) were determined with the aid of anatomical MRI. The number of activated pixels within each ROI was recorded. For each session, LI was also calculated by successively averaging LI over runs (run 1, run 1+2, run 1+2+3, run 1+2+3+4). A two-factor repeated measures analysis of variance (ANOVA) was performed on each ROI/(LI, # of pixels) combination to obtain mean squares for estimates of variance components due to N_p people being scanned (σ^2_p), due to N_d scan sessions (σ^2_d), due to the interaction between the scan session and the people being scanned (σ^2_{pd}), and due to the within-session variability (σ^2_e) of N_s scans, according to[4]:

$$\sigma_p^2 = (MS_p - MS_{pd})/(N_p N_s), \quad \sigma_d^2 = (MS_d - MS_{pd})/(N_d N_s), \quad \sigma_{pd}^2 = (MS_{pd} - MS_e)/N_d, \quad \sigma_e^2 = MS_e .$$

The within-session and between-session standard errors of measurement (SEM) were calculated as $SEM_{within} = \sigma_e$ and $SEM_{between} = \sqrt{\sigma_d^2 + \sigma_{pd}^2 + \sigma_e^2 / N_s}$, respectively. The minimum detectable change (MDC) across sessions was also calculated for increasing number of within-session averages as $MDC_{between} = Z_{\alpha=0.05}\sqrt{2}SEM_{between}$.

Results and Discussion

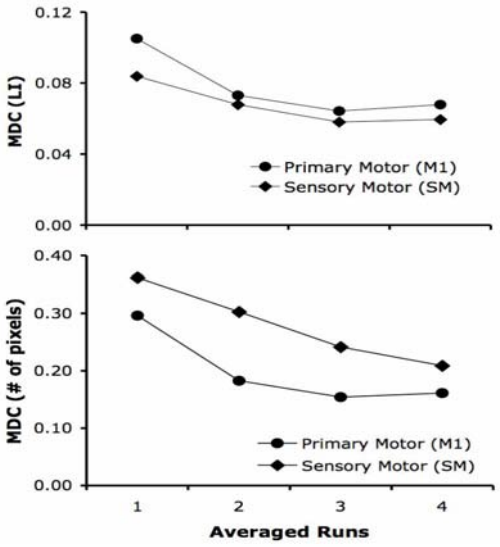

Figure: The minimum detectable change (MDC) in fMRI activity across imaging sessions expressed as a fractional change.

The MDC was below 0.1 for LI, but remained in excess of 0.15 for the number of activated pixels within the contralateral hemisphere ROI (see Figure for motor task). No significant improvement was seen beyond 3 within-session averages. Within-session variability (σ^2_e) was comparable to the between-session variability, suggesting that longitudinal studies may benefit both from reduction of within-session variability by combining multiple runs and controlling for between-session variability.

For the motor task, there was significantly more ipsilateral motor activity during run 1 compared to run 4. For both tasks, there was more activity within prefrontal cortex on day 1 compared to day 3, indicative of the subject becoming more familiar with the tasks. Additional training prior to imaging would eliminate these effects.

We now have a method to detect <10% changes in fMRI measurements of brain activity over longitudinal scans with as few as 3 scans per session. This has important implications for the design of an efficient scanning session in the study of functional recovery following stroke.

References

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