On-line brain mapping using fMRI and a Magnetic Resonance Compatible Hand-Induced Robotic Device (MR_CHIROD)

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Introduction

Functional MRI (fMRI) methods combined with MR-compatible robotic devices are promising for monitoring and validating the effectiveness of stroke rehabilitation therapy (1). Previously, we reported the design, fabrication and preliminary testing of a novel, one degree of freedom, MR compatible hand induced robotic device (MR_CHIROD) that may be used in brain MR imaging during hand grip rehabilitation (2, 3). Here we propose, on-line brain fMRI using state-of-the-art fMRI methods in combination with an improved MR_CHIROD. This procedure promises to provide accurate, sensitive and specific information into the effectiveness of rehabilitation therapy beyond traditional paradigms.

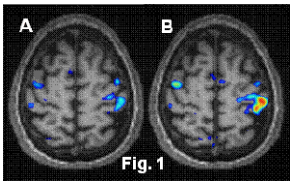

Figure 1: *Motor fMRI activation images. A = 15%, B = 60% of maximum force. Both activation area and %BOLD amplitude increased (B>A) with force.*

Materials and Methods

(A) fMRI mapping of brain activation using a motor paradigm: We monitor the changing levels of force during compression (squeezing), and compare precise measures of compression force with features of brain activation. Our experimental paradigm consists of three alternate action (A) and resting (R) epochs, 30 sec each. During the action epoch the subject compresses and releases continuously at 1Hz rate exercise gel balls at 15%, 45% and 60% of own maximum force. Maximum force is measured using a dynamometer, and the subjects are instructed to squeeze the dynamometer and the gel balls at each level until they consistently perform to the required squeeze level without having to look at the gauge. The percent levels compensate for performance confounds by constraining between-subjects performance to be approximately the same, and the 60% top level allows all to perform the task even if exerting only a limited force. Subject training typically necessitates 10-15min before scanning. BOLD FMRI was performed using an "optimized" gradient-echo EPI protocol using parallel-imaging (GRAPPA) acquisition/reconstruction on healthy volunteers (23-36 years of age, N=12) on a Siemens Trio 3T equipped with 12-channel Siemens TIM head coil. Acquisition parameters were: TR/TE=3000/31.1 ms, GRAPPA factor=3, voxel size (1.6mm)^2×3.0 mm, 128×128 acquisition matrix/200mm×200mm FOV, 48 slices (5% skip) covering the entire brain with a tilted axial orientation, 85 PE reference lines for GRAPPA calibration. Sixty volumes are collected in 180s; actual per-paradigm scan time is 207s including GRAPPA calibration scan and four volumes acquired to ensure steady state of magnetization. All volumes were registered to a standard template and processed with SPM2 (activation threshold $p<0.05$ corrected for multiple comparisons). Volunteers were able to complete each level without fatigue. Arms are kept extended at the sides of the subject and extra foam padding is used at the elbow to minimize elbow flexion and further reflexive motion, and to minimize head translational and rotational motion. Typically, translational (head) motion is well lesser than 1mm as measured by SPM2 image co-registration algorithm.

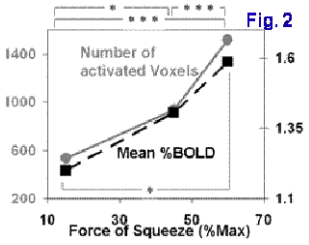

Figure 2: *Mean significantly activated pixels and mean weighted %BOLD signal in left SMC versus % maximum exerted force*

(B) A second-generation MR_CHIROD was built, exhibiting linear motion and significantly improved simplicity of fabrication and reduced cost. The second-generation MR_CHIROD consists of three major subsystems: a) a linear ERF damper; b) handles and c) two sensors, one optical encoder and one force sensor, to measure the motion and force induced by the patient. The device is configured to rest next to the person, who thus feels no weight. All components were designed so that the device is capable of withstanding 200N of exerted force by the human operator's hand holding the device handles.

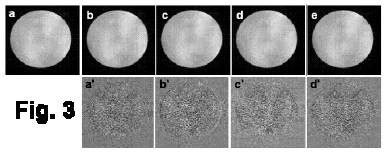

Figure 3: *Effect of MR_CHIROD on phantom images. (a-e) (a) control; (b) MR_CHIROD with ERF not activated; (c) MR_CHIROD with ERF activated at 1.5kV; (d) MR_CHIROD with ERF not activated and squeezing the device; (e) MR_CHIROD with ERF activated at 1.5kV and squeezing the device; (a'-d') subtraction of the control (a) from (b-e).*

Results

(A) With increased force of squeezing by the right hand, % BOLD signal intensity and volume of activated pixels in left somatosensory cortex (LSMC) and supplemental motor area (SMA) increased (Fig. 1, 2). ROI analysis results, averaged for all healthy volunteers, are shown in Figure 2. In the left SMC, at 15%, number of activated voxels (532±116) differed than at 45% (935±116), $p=0.046$ and both differed from 60% (1517±116), $p<0.00005$; %BOLD at 15% differed from %BOLD at 60% ($p=0.020$). In SMA, the 15% and 60% levels differed significantly both by number of activated voxels ($p=0.038$) and by %BOLD ($p=0.003$). P-values were calculated using repeated-measures ANOVA. Threshold was set to P = 0.05 and a Bonferroni correction was applied to protect against Type-I errors from multiple comparisons. **(B)** The second-generation, improved prototype of MR_CHIROD has been tested in a 3T TimTrio Siemens scanner. Phantom and human tests were conducted on the assembled MR_CHIROD using the GRAPPA EPI sequence used for human imaging. Phantom and human control images were acquired in the absence of MR_CHIROD. For the phantom tests, MR_CHIROD was attached to the scanner table in the approximate position that a volunteer in the scanner would reach and squeeze the handles. Phantom EPI images were acquired first simply in the presence of MR_CHIROD and second with a person near the magnet squeezing the handles. Image noise profiles were calculated from ROIs drawn at image edges, signal values from ROIs at the image center. Signal mean was remarkable stable across runs, deviating less than 0.2% from the central mean of all five acquisitions (Figure 3). Human images were acquired with a volunteer lying in the normal supine position squeezing the device handles. All images were acquired using a Tim 12ch head coil (Siemens), and extra care was taken to pad and immobilize the volunteer's head and elbow in order to minimize reflexive and other hand movement and to provide arm support. The introduction of MR_CHIROD in the MR environment did not affect image quality (Figure 4).

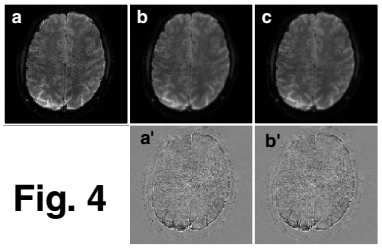

Figure 4: *Effect of MR_CHIROD on EPI human images.(a – c) (a) control; (b and c) MR_CHIROD connected, (b) ERF not activated, subject rests; (c) ERF not activated, subject squeezes; (a', b') subtraction of the control from b, c, All volumes were coregistered to the control volume prior to subtraction in order to minimize the effects of motion between scans*

Discussion

By demonstrating the utility of fMRI to monitor the effectiveness of rehabilitation in stroke patients, these studies can ultimately provide an additional method for the future evaluation of stroke rehabilitation therapies. To this end, we anticipate that our results may lead to the development of a novel optimized method for stroke patient rehabilitation; and upon further development this method could become a valuable tool to illuminate stroke-induced pathological and traumatic changes, and to provide unique prospective information for stroke patient management.

References

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