Image-guided versus function-guided coil placement for TMS of motor cortex: relative anatomical location and intensity of BOLD-fMRI response

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Background Placement of a TMS coil for motor cortex stimulation during interleaved TMS/fMRI [1-2] can be guided by a visible behavioral response (e.g. thumb movement) or by individual anatomic images (e.g. MRI). We hypothesized that (1) reasonable resolution and reproducibility can be attained during image-guided placement of the TMS coil and (2) comparison of results from these two approaches would help elucidate relationships among anatomical cortical structure, magnitude of behavioral response and precise TMS coil placement. Using a calibrated TMS coil holder/positioner [3] with interleaved TMS/fMRI, we conducted a two-phase study of coil placement based on either thumb motion (function-guided) or structural MR images acquired immediately before functional scanning (image-guided).

Methods With local ethics approval, 9 healthy volunteers (mean age mean age 32 years, SD 11, 3 women, 1 left-handed man) participated in the function-guided phase and were scanned 3 times each with acceptable results (27 datasets total). Five subjects (mean age 42 yr, SD 17, 1 woman, 1 left-handed man) from the function-guided phase participated in the image-guided phase and were scanned up to 3 times each with acceptable results (13 datasets total). fMRI was conducted at 1.5T (Picker EDGE) using a GE, single-shot, EPI sequence (tip=90°, TE=40 ms, TR=3 s, FOV=27 cm, matrix=128xl28, 15 6 mm axial slices, 1 mm gap, frequency selective fat suppression). TMS was applied using a non-ferromagnetic figure-8 coil (B70 Dantec Medical A/S, Skovlunde, Denmark) connected to a Dantec MagPro stimulator via an 8m cable and locked into the calibrated holder/positioner. Placement of the TMS coil for function-guided experiments was based on maximizing the visible motion of the thumb in response to TMS pulsing. For the image-guided experiments, a cortical target on the lateral aspect of the left-hemisphere hand knob [4] was selected from initial transverse T1 weighted scans. Sagittal and oblique coronal scans determined the scalp location that would allow the isocenter line of the TMS coil to intersect the anatomical target. Finally the angle of coil around this isocenter line was adjusted to maximize thumb response. The TMS coil holder/positioner was then locked with the coil in position against the scalp. Scans (15.2 min) lasted for 7 cycles of 6, 21-second epochs each: Rest-TMS-Rest-Rest-VOL-Rest. "Rest"=no task, "TMS"=TMS stimulation at 110% MT, "VOL"=volitional mimic of TMS-induced movement, cued by low level (20% MT) pulses. During task epochs, TMS pulses occurred after every fifth image (1 Hz) in trains of 21. Data were processed on Sun SPARCstations (Sun Microsystems, Mountain View, CA) using SPM99 (Wellcome Dept. Cognitive Neurol., London UK). Image sets were realigned to the first volume acquired. Statistical parametric maps, SPM(t)'s, were calculated for condition specific effects within a general linear model. Modeled epochs were convolved with a canonical hemodynamic response function. Estimated movement parameters (6) were used as confounds in the linear model design matrix. Temporal high-pass filtering was carried out with cutoff frequency at twice the cycle length (252 s). T-maps were thresholded at p=0.10 corrected for multiple comparisons. All clusters examined had p values less than 0.05 when assessed by spatial extent

Results Under MRI image-guidance, thumb response was elicited in every case at thresholds similar to those found 6-9 months earlier under function-guidance. For both methods of positioning, observed BOLD locations centered on the crown of the precentral gyrus, and displayed no consistent differences in intensity, location or variability in location between-subjects or within-subjects. In contrast, TMS coil location showed significant differences both in global Talairach location and location with respect to local sulcal anatomy (Figs 1&2). Function-guided coil locations were clustered over sulci, while the image-guided locations were clustered over the targeted crown of the gyrus. Additionally, the direction of applied field displayed a difference between the different positioning protocols. As can be seen, from subject to subject, image-guided protocols produced more consistent TMS coil placement relative to anatomy with, however, no improvement of within-subject coil location variation. Unexpectedly, time courses of BOLD contrast from image-guided experiments showed significantly slower return to baseline after TMS than was observed for the function-guided results (Fig 3), suggesting location-dependent changes in mechanism of stimulation.

Discussion Our results suggest that prospective placement of a TMS coil relative to imaged individual cortical anatomy, using a calibrated holder/positioner, can produce good reproducibility and resolution for interleaved TMS/fMRI studies. This capability is especially important for investigation of cortical regions that produce no external indication of stimulation. Initial comparison of results from image-guided and function-guided experiments suggest that the locations producing maximal motor response to TMS stimulation are nearer the sulci than the crowns of the gyri although stimulation is still good over the crown. The cortical location of BOLD activations does not strictly follow TMS coil location suggesting indirect (transynaptic) links between initial depolarization sites and subsequent vascular response sites.

References [1] Bohning DE et al, Investigative Radiology 1998;33:336-340.[2] Baudewig J et al, NeuroReport 2001;12:3543-3548.[3] Bohning DE et al, Clinical Neurophysiology 2003;114:2210-2219.[4] Yousry TA et al, Brain 1997;120:141-157.

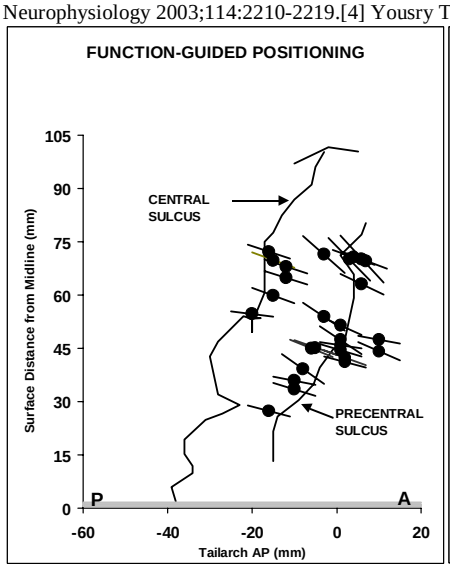

Figure 1. Normalized surface projection of sulci with coil location and induced E-field orientation. Coil positioned to the point of maximum thumb response

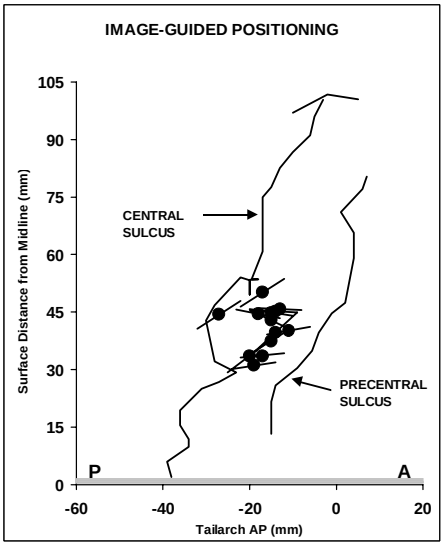

Figure 2 Normalized surface projection of sulci with coil location and induced E-field orientation. Coil positioned to target crown of precentral gyrus hand knob.

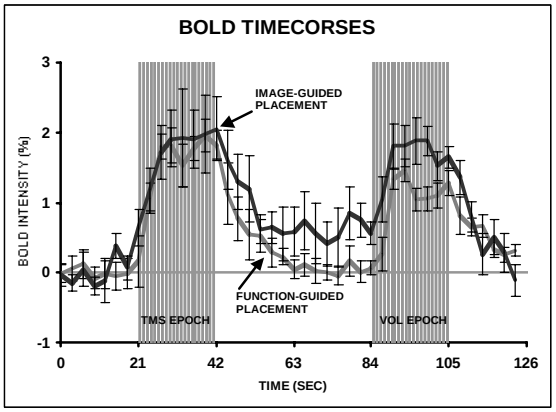

Figure 3 Cycle-averaged BOLD time courses averaged over all scans and subjects for function-guided and image-guided protocols.