A new hardware-software coil positioning system for interleaved TMS/fMRI: A motor cortex stimulation study

M. Moisa[1], K. Uludag[1], K. Ugurbil[1], and A. Thielscher[1]

[1]High Field MR Center, Max Planck Institute for Biological Cybernetics, Tübingen, Germany

Interleaved TMS/fMRI is a promising technique to study connectivity between brain areas. Functional connectivity can be assessed by targeting a cortical area-of-interest using TMS (Transcranial Magnetic Stimulation) and directly monitoring the effects on local and remote BOLD activity by means of fMRI. An important practical challenge is the accurate positioning of the coil inside the MRI scanner. Here, we describe a novel positioning method and report pilot results on its usage studying the motor system.

TMS Coil Positioning: Neuronavigation systems used in many TMS studies for the precise targeting of cortical areas (Schönfeldt-Lecuona et al., Brain Topogr., 2005) cannot be utilized inside the MR cabin. To circumvent this limitation, Bohning et al. developed a mechanical holding device in combination with a simple software program which enables positioning of the TMS coil over a desired target area (Bohning et al, Clin Neurophysiol., 2003) within the MRI scanner. Critically, the target has to be manually located in a structural scan acquired directly before the start of the interleaved TMS/fMRI experiment based on the individual brain anatomy. Here, we describe an improved positioning method which allows accurate TMS coil placement (Medtronic Magpro X100 with figure-8 coil MRi-B88; see Fig. 1) inside the MR scanner using pre-planned coil positions previously determined using a neuronavigation system, thereby eliminating the need for the manual and time-consuming identification of individual brain structures. Initially, a T_1-weigthed high-resolution (1mm iso-voxel) structural image is acquired once for each subject for usage in our neuronavigation system (BrainView, Fraunhofer IPA, Stuttgart, Germany). In BrainView, coil positions-of-interest are saved with respect to the coordinate system defined by the high resolution image. Inside the scanner, the position of the subject's head is determined using a fast structural image (FLASH) lasting ~1 min, which is automatically coregistered to the high resolution image using custom-written software (MATLAB, Natick, USA) and SPM5 (Wellcome Department, UCL, Great Britain) functions. The software automatically determines the parameters of the coil holding device corresponding to the pre-planned coil position, thereby preventing the need to manually identify brain structures. Accuracy of the method was assessed using agar phantoms, demonstrating that pre-planned coil positions can be reached within 3.9 ± 1.0 (SD) mm (5.5 mm maximum offset) which is in comparable range of spatial accuracy reported for neuronavigation systems used outside of the MRI scanner.

Motor cortex stimulation: BOLD activity induced by paired TMS pulses on the motor cortex was investigated in 5 subjects. The TMS "Hot Spot" of a particular finger muscle in the motor cortex (M1) was determined offline and its position was saved using the neuronavigation system. Inside the MR scanner, the parameters for the coil holding device corresponding to the "Hot Spot" were determined at the beginning of the study using the procedure described above. Subsequently, the lowest TMS intensity resulting in activation of the finger muscle (the "Motor Threshold", MT) was determined using electromyographical recordings. Interleaved TMS/fMRI was performed in two sessions with 8 experimental runs in total, corresponding to three different conditions: four runs with supra-threshold stimulation (120% MT), three runs with sub-threshold stimulation (80% MT) and one run with volitional movement (acoustically triggered by 50% MT stimuli). A run consisted of 255 EPI volumes (27 slices oriented parallel to the TMS coil plane, matrix 64*64, voxel size 3.4x3.4x4 mm^3, 1 mm gap, TR 2000 ms, TE 30 ms, 1562 Hz/Px bandwidth, 1ch head coil) acquired at a 3T scanner (Siemens Tim Trio). During one run, 27 pairs of TMS pulses were applied (first pulse applied 80 ms after end of volume acquisition; 20 ms pause between pulses; 100 ms gap to start of next volume; mean intertrial interval 8 volumes; jitter: +/-2 volumes). The EPI data was analyzed using FSL 3.3 (FMRIB, Oxford University, UK). The results of the supra-threshold stimulation are in concordance with previous findings (Bohning et al., Invest Radiol., 2000; Bestmann et al., Eur J Neurosci., 2004). Significant BOLD responses were observed in brain areas mainly related to the motor system and in auditory areas activated by the acoustical noise of the TMS pulses (Fig. 2). Sub-threshold stimulation activated mostly auditory areas (data not shown). By contrasting runs with supra- versus sub-threshold stimulation, more localized activations in M1/S1, left putamen, left thalamus, cingulate gyrus, parietal cortex and insula (Fig. 3) were observed. To conclude, the results of the pilot study demonstrate the viability of our positioning method as well as of the overall interleaved TMS/fMRI setup.

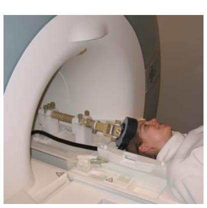

Fig 1: Coil-holding device and MR-compatible TMS coil (Medtronic)

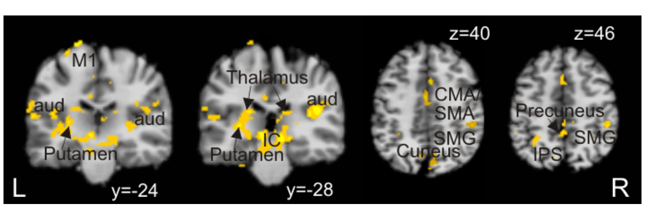

Fig 2: Group analysis for supra-threshold stimulation (N=5, p=0.005 uncorrected, FSL FLAME mixed effects analysis, MNI space) shown on an individual structural image

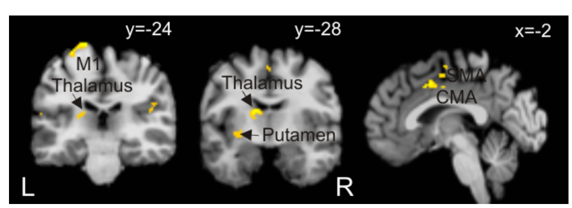

Fig 3: Group analysis for supra > sub-threshold stimulation (p=0.005 uncorrected)