A FEASIBILITY STUDY OF FMRI AND EEG ACTIVATION WITH CHEPS (CONTACT HEAT EVOKED POTENTIAL STIMULATOR)

K. Roberts[1,2], A. Papadaki[1,2], C. Gonçalves[2,3], M. Tighe[4], D. Atherton[1,2], R. Shenoy[1,2], D. McRobbie[1,2], and P. Anand[1,2]

[1]Imperial College, London, United Kingdom, [2]Hammersmith Hospitals NHS Trust, London, United Kingdom, [3]East Kent Hospitals NHS Trust, Canterbury, United Kingdom, [4]Brainvision UK, London, United Kingdom

A feasibility study of fMRI and EEG activation with CHEPS (Contact Heat Evoked Potential Stimulator).

Introduction Contact heat evoked potentials have been shown to be useful in studying pain activation related to thermal and nociceptive pathways [1,2,3]. In this study we used contact heat to study nociceptive pathways in healthy volunteers and to evaluate whether it is feasible to record contact heat evoked Aδ electroencephalographic (EEG) potentials in the MRI scanner environment. The combined use of EEG and fMRI exploits the advantages of both techniques – the high temporal resolution of EEG, and the high spatial resolution of fMRI. Co-registration of contact heat evoked Aδ potentials using EEG, fMRI and the contact heat evoked potential stimulator (CHEPS) (MEDOC, Israel) has not previously been attempted, and poses a number of technical challenges.

Methods Baseline contact heat evoked responses from five healthy volunteers were monitored by EEG outside of the MRI scanner using a protocol involving a series of ten 51°C stimuli (7s apart and 250ms in duration), applied to the skin of the left arm of the subject. To avoid habituation, the thermode was moved around the arm for each stimulus. After the protocol was completed the volunteer was asked to rate the pain of thermal stimulation using a visual analogue scale (VAS), 0 being not painful at all and 10 being the worst pain imaginable. The volunteers were then scanned using an event-related protocol consisting of a sequence of 32 stimuli. The thermode was again applied to the left arm of the subject, and the position of the thermode changed for each stimulus. The inter-stimulus interval varied randomly between 8-30 sec. VAS scores were obtained again after the MRI scan was completed. A total of 265 fMRI scans per session were acquired using gradient echo EPI sequences (time of repetition [TR], 2.3 s; echo time [TE], 53ms; flip angle [FA] 90; field of view [FOV] 230 mm; matrix 64 x 64, in-plane resolution, 3.5 x 3.5 mm; 19 slices of 5-mm thickness, 1mm gap covering the whole brain) on a 1.5T magnetic resonance scanner with a standard head coil matrix (Avanto; Siemens, Erlangen, Germany). A high-resolution T1-weighted anatomical brain image of the subject was obtained using a magnetization-prepared rapid gradient-echo sequence with the following parameters: TR = 11 s, TE = 5.2 ms, FA = 15, FOV = 230 mm, resolution = 1 x 1 x 1. Processing of fMRI images was performed using SPM5 (http://www.fil.ion.ucl.ac.uk/spm). Data was analysed individually and then group analysis was performed using a random effects model. EEG was recorded using a dedicated fMRI compatible EEG recorder. The characteristic fMRI induced technical and physiological artefacts were removed using specialised signal analysis software (BrainAmp MR Plus EEG system and Analyzer analysis software by Brain Products GmbH). Latency was measured from the first definite negative peak (N1) and the amplitude measured peak to peak (N1 to P1).

Results Contact heat evoked responses were obtained by EEG from four of the five volunteers, both outside and inside the MRI scanner. The average (mean ± SD) amplitude of evoked potentials monitored outside the scanner was 31.41 ± 14.4μV, and the average latency was 245 ± 18ms. The average amplitude inside the scanner was 21.02 ± 7.7μV, and the latency 231 ± 22.9ms. The average VAS score for thermal stimulation by CHEPS was 4, both pre and post scan. There was no significant difference between the amplitude of responses outside and inside the scanner ($p = 0.058$) or between the latency of the responses ($p = 0.197$). There was no correlation between evoked response amplitude and VAS score. Group analysis of the five subjects scanned (uncorrected $p<0.005$) showed blood oxygen level dependent (BOLD) activation in the cingulate gyrus, postcentral gyrus (SI), superior temporal gyrus, and the superior, inferior and medial frontal gyrus contralateral to the site of stimulation and in the left precentral gyrus (MI). This is consistent with previous pain related studies [4,5].

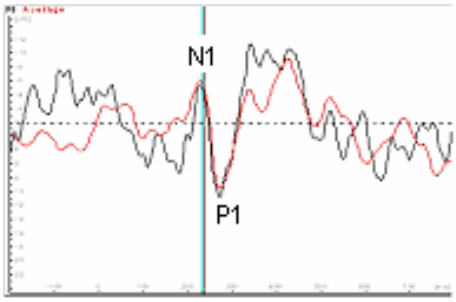

Figure 1. Evoked potentials recorded before and during fMRI

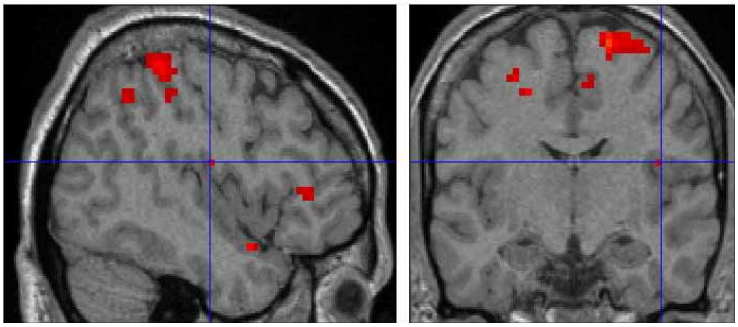

Figure 2. fMRI maps showing activation in cingulate gyrus, insula and S1

Discussion This study demonstrates the feasibility of recording CHEPS evoked potentials with fMRI. The combined use of the two methods can lead to identification of distinct patterns of brain activity indicative of pain and pro-nociceptive sensitisation in healthy subjects and chronic pain patients. Further studies are required to determine the usefulness of this technique to progress clinical trials of novel analgesics.

References

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