Simultaneous intracranial EEG-fMRI in humans suggests that high gamma frequencies are the closest neurophysiological correlate of BOLD fMRI

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Introduction: Experimental studies have investigated the neurophysiologic correlates of fMRI relying on BOLD contrast which are both important for interpreting BOLD changes and appropriate data modeling in the increasing number of studies using combined electrophysiology and fMRI. While a general consensus has formed that BOLD better reflects post synaptic potentials and synaptic input to a region (than spiking output) [1] there are some discrepancies in studies [1-4] with regard the spectral range of local field potentials (LFPs) that are most closely related to BOLD. We aimed to investigate if the EEG-frequency dependence of the EEG-fMRI coupling was altered by brain state (rest v task) and location of the electrophysiology measurements. Human brain activity recorded in epilepsy patients undergoing presurgical evaluation using intracranial electroencephalography (icEEG), allows for exquisite temporal resolution of rich dynamic activity from small regions of cortex over a wide frequency range, while fMRI maps whole brain hemodynamic changes. We investigated EEG-fMRI coupling in a simple motor task and at rest by simultaneously recording icEEG and fMRI in human sensorimotor cortex giving us a unique opportunity to examine the local frequency-specific neurophysiological correlate of BOLD fMRI.

Methods: One patient undergoing presurgical evaluation with icEEG (76 subdural electrode contacts with frontal coverage) was scanned with approval from the ethics committee of UCL/NHNN, and informed consent from the participants. We used the following: 1.5T scanner; head transmit-receive RF-coil; low-SAR sequences (≤0.1W/Kg head-average); exact external electrode cable configuration using a foam insert for reproducibility; 64-channels invasive EEG) recorded with MR compatible equipment. N.B. this constitutes 'off-label' use of the EEG, MRI and electrodes. We acquired a localizer, T1 volume and 2x10min EPI acquisitions (TE/TR40/3000ms 38x2.5mm slices, 0.5mm gap, 3x3mm in-plane resolution) during rest. In this patient, the subdural grid covered senorimotor cortex and so a 5min EPI acquisition was performed during 30s blocks of left v right finger tap. Standard artifact correction methods were applied to the EEG. FMRI activations were obtained using standard preprocessing and a general linear model of the finger tap task with spm5 (www.fil.ion.ucl.ac.uk/spm) significance p<0.05 Family-wise error corrected. Electrophysiology from each electrode was transformed into time-frequency space [5] at frequencies of 1,3,5.. 99Hz and convolved with a standard canonical HRF. These frequency regressors were then correlated to the linearly detrended fMRI signal time course averaged over the task activated region (see Fig. 1a) firstly at the nearest electrode contact to the task activated volume. This analysis was extended over each electrode to determine if the peak correlation frequency was dependent on the electrode contact location.

Results: Activations were found within 2mm of electrode contact locations during the finger tap task. The sensitivity and spatial specificity of the icEEG allowed for a detailed spectral-spatial comparison of the relationship between EEG and fMRI signals (Fig. 1). First, we determined the local coupling by choosing the electrode closest to the task-activated region (contact #22, 2mm distance from the closest task-activated voxel). The maximum positive correlation was at 91Hz (high gamma-band) and the most negative was at 17 Hz (beta-band) during the motor task (see fig. 1b). The corresponding coupling in the resting state was weaker (see fig. 1b), with significant negative correlations only in the low beta range (13-15Hz). Secondly, we looked at the spatial extent of this coupling, by repeating this analysis at each frequency across the entire grid. There was a strong spatial component to the relationship (fig. 1 c-d) with the peak correlation frequency being spatially dependent. During the task at 91Hz (high gamma frequency), a highly focal region of very strong positive correlation was revealed, mainly involving three post-central contacts within 5mm of the task-activated region (black and bold typeface contact numbers in fig. 1c, *p<0.001). While in the beta range a strong negative correlation was seen over a wider area within 10mm of the task-activated region in the pre- and post-central cortex (black typeface contact numbers in fig. 1c for maps at 15 and 91Hz; 15Hz was used in fig. 1c to allow comparison of significant correlations between states). At rest (fig 1d, *p<0.001), weaker correlations were found with the strongest at 15Hz over a spatially similar region to that observed during the task.

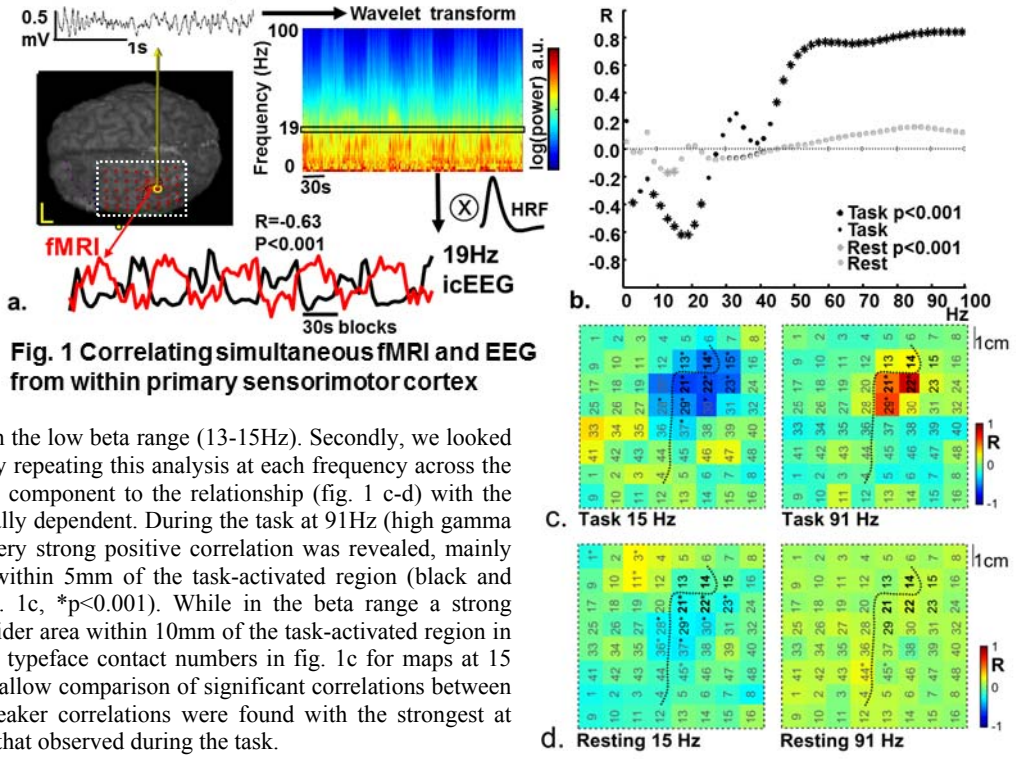

Fig. 1 Correlating simultaneous fMRI and EEG from within primary sensorimotor cortex

Conclusions: We showed coupling between icEEG and fMRI to be broadly consistent with previous theoretical and experimental studies [1-4]. However, our results suggest that high gamma frequencies are the most closely correlated to BOLD [2], rather than lower frequencies during the task [3] and that the peak correlation frequency measured is highly location dependant. On the basis of the first results presented here, the simultaneous recording of icEEG and fMRI in humans will allow a new avenue for the comparison and integration of regionally specific and high sensitivity electrophysiology with whole brain heamodynamic changes to investigate a range of pathological and physiological phenomena across brain states such as rest and epilepsy that benefit form simultaneous acquisition.

References 1. Logothetis, N. K., Pauls, J., Augath, M., Trinath, T. & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature.* **2.** Niessing, J. et al. (2005) Hemodynamic signals correlate tightly with synchronized gamma oscillations Science 309, 948-951. **3.** Goense,J.B. & Logothetis,N.K. Neurophysiology of the BOLD fMRI signal in awake monkeys. *Curr. Biol.* 18, 631-640 (2008). **4.** Rosa, M. J., Kilner, J., Blankenburg, F., Josephs, O. & Penny, W. (2010) Estimating the transfer function from neuronal activity to BOLD using simultaneous EEG-fMRI Neuroimage. 49, 1496-1509. **5.** Tallon-Baudry,C. *et al.* (1998) Bertrand,O., Peronnet,F. & Pernier,J. Induced gamma-band activity during the delay of a visual short-term memory task in humans. *J. Neurosci.*

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