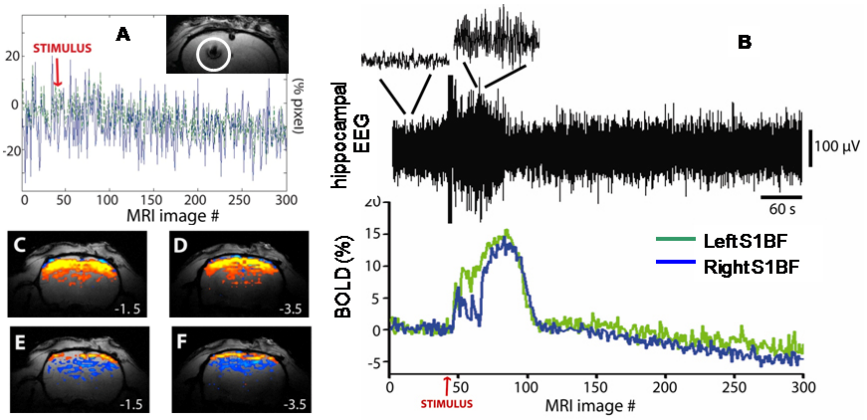
Simultaneous fMRI and electrophysiology during intracerebral stimulation of partial seizures in rats

D. J. Englot[1], A. M. Mishra[1], M. Purcaro[1], P. Herman[2], F. Hyder[2], and H. Blumenfeld[1,3]

[1]Neurology, Yale University School of Medicine, New Haven, CT, United States, [2]Diagnostic Radiology, Yale University School of Medicine, New Haven, CT, United States, [3]Neurobiology, Yale University School of Medicine, New Haven, CT, United States

INTRODUCTION: fMRI could potentially be a useful tool for studying the networks involved in partial limbic seizures, which are common in patients suffering from temporal lobe epilepsy (TLE). Although patient movement during temporal lobe seizures make human fMRI recordings in TLE technically difficult, partial seizures can be imaged in anesthetized, paralyzed animal models. Previous fMRI studies of generalized seizures in rats have produced promising results (1, 2, 3). Recently we described that electrical stimulation of the hippocampus in anesthetized rats provides a useful model of limbic seizures (4), and partial seizures induced by this method result in neurophysiological changes resembling complex-partial temporal lobe seizures in humans (5). Although fMRI acquisition during intracerebral stimulation without significant artifact is challenging, activation of local limbic circuitry using low levels of stimulation has recently been reported in animal fMRI studies (6). Here we describe simultaneous electrophysiology and fMRI during partial limbic seizures produced by intracerebral stimulation in anesthetized rats.

METHODS: At least 7 days before fMRI recordings, adult female Sprague-Dawley rats were stereotactically implanted with a bipolar tungsten stimulating/recording electrode in the right dorsal hippocampus (AP -3.8 and ML 2.5 mm from bregma, SI -3.8 mm from the cortical surface). The electrode was lowered at a 50° angle from the vertical using a posterior approach and fixed to the skull adjacent to lambda with 2 plastic screws and dental acrylic. Before fMRI scans, animals were anesthetized with ketamine (75 mg/kg) and xylazine (15 mg/kg) IP, tracheotomized, and artificially ventilated. After surgery, anesthesia was maintained at a lower dose (ketamine/xylazine 45/7 mg/kg) to prevent seizure blockade. All fMRI and electrophysiological recordings were made simultaneously. Details of animal physiology maintenance and fMRI (at 9.4T) have been described (2). Epochs of 10 images/s interleaved with 1 s of EEG recordings were obtained for 10 min continuously. After 3 minutes of baseline recordings, a seizure was induced by delivering a 2 s train of 100 µA pulses (1 ms, biphasic) at 60 Hz between the hippocampal contacts. EEG was acquired simultaneously during fMRI scans using carbon wires placed laterally between the scalp and the skull, and also from the hippocampal electrode. Data processing has been described (2).



RESULTS: A center of mass (COM) analysis of a time series of fMRI images showed no seizure induced movement artifacts (Fig. 1A). All deviations in the COM analysis were less than 25% of a pixel size in the two translational directions (Fig. 1A), suggesting that there were no movement artifacts. Placement of the intracerebral stimulating/recording electrodes in dorsal hippocampus induced a small local artifact (1-2 µL) in one posterior slice (inset of Fig. 1A, circle) out of a total of 10 slices. After stimulation of the dorsal hippocampus, the local EEG electrode in the hippocampus demonstrated significant changes in electrical activity which lasted about two minutes (Fig. 1B, upper). During this period, there were strong bilateral BOLD signal changes in the somatosensory cortex (Fig. 1B, lower) and several other areas (Figs. 1C-D). The most intensely activated areas (e.g., barrel cortex) had BOLD signal increases greater than 10% during the seizure (e.g., Fig. 1B, lower) with a delayed postictal decrease. BOLD signal increases were observed in the hippocampus, barrel cortex, and thalamus during the seizure (Figs. 1C,D), whereas widespread BOLD signal decreases were observed postictally (Figs. 1E,F).

DISCUSSION: Technical hurdles have limited the use of simultaneous fMRI and electrophysiology recordings to study temporal lobe seizures. However, our results suggest that intracerebral seizure stimulation during simultaneous EEG and fMRI recordings can produce useful information regarding these events, and may provide a practical model for studying limbic seizures and other forms of partial epilepsy.

REFERENCES: [1] Nersesyan et al., (2004) J Cereb Blood Flow Metab. 24:589-599. [2] Schridde et al, (2007) Cereb. Cortex. In press. [3] Mishra et al., (2008) Proc ISMRM abstract. [4] Englot and Blumenfeld, (2007) Soc for Neurosci abstracts. [5] Blumenfeld et al., (2004). Cereb Cortex. 14(8):892-902. [6] Angenstein et al., (2007) Neuroimage. 38(1):150-63.

ACKNOWLEDGEMENTS: Supported by R01 NS-049307 (to HB), R01 MH-067528 (FH), P30 NS-052519 (FH).