# Dissociation of BOLD and local field potentials

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**Introduction:** The blood oxygenation level dependent (BOLD) MRI signal is tied to local neural activity via neurovascular coupling [1, 2]; however, the relationship is likely to be nonlinear. We have developed a combined measurement technique to examine the relationship between BOLD and neural activity in the rodent, using simultaneous recording of intracortical electrophysiological signals and fMRI BOLD signals. By comparing local field potentials (LFPs) and BOLD measured simultaneously in rat somatosensory cortex under different anesthesia states, our studies demonstrate a dissociation between BOLD and LFPs during low-level neural activity.

**Materials and methods:** 5 male SD rats, 200~250 g, were used in our studies. All imaging was performed on a 9.4T animal MRI system (Bruker, Germany). Two glass microelectrodes were implanted separately in the forepaw region of primary somatosensory cortex in both hemispheres and fixed in place, with a reference electrode in the posterior subcutaneous area. The rat was transferred to the MRI cradle and a 2 cm transmit/receive surface coil was fastened above the brain, with the electrodes protruding from the center. The electrophysiological signals were bandpass filtered between 0.1 Hz and 5000 Hz, amplified (x 1000) by an AC amplifier located just outside the scanner room, and digitized at 12 KHz. To avoid potential artifacts in the fMRI, the electrodes were obliquely inserted so that only the tiny electrode tips were included in imaging slice, and the removed skin/muscle over the skull were replaced with toothpaste to avoid Gibbs ringing artifacts near the brain surface. A coronal slice over the somatosensory cortex was imaged with GE-EPI (TR/TE=500 ms/15 ms, slice thickness 2 mm). The studies involved two anesthesia types (isoflurane/medetomidine) and states (deep/light). Both spontaneous activity (all five rats) and activity induced by electrical stimulation of the forepaw were examined (two of five rats). The artifact structure induced in the electrical recordings by the rapidly-switching magnetic fields during image acquisition was characterized by averaging all cycle scans of spontaneous activities for each sequence run. The noise structure during imaging was then subtracted from original recordings.

**Results:** Several findings demonstrate the inconsistency of the relationship between neural and BOLD signals. First, the forepaw stimulation causes an electrophysiological response in the contralateral cortex even when the current is very low (0.1 mA). However, the BOLD responses can only be observed when higher currents are used (1~4 mA, Fig.1 and 2). Next, in lightly anesthetized states (either isoflurane or medetomidine), we observed a high peak in the spontaneous low frequency BOLD fluctuations (0.01~0.25 Hz) that are usually linked to spontaneous activity, whereas for the deeply anesthetized state, no significant low frequency peak or only an ultra low frequency peak (<0.02 Hz) was detected, though spontaneous LFP oscillations can be clearly observed in the simultaneous recordings. However, forepaw stimulation under the same conditions can still cause a significant BOLD response (Fig.1), indicating the neurovascular coupling is preserved for evoked activity.

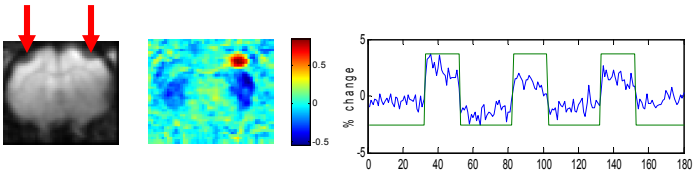


Fig. 1 (left) Microelectrodes implanted in forepaw primary somatosensory cortex of both hemispheres (red arrows). Forepaw electrical stimulates caused observed BOLD response in contralateral cortex in case of stimulation current > 1mA. (center) Activation map based on BOLD changes during forepaw stimulation. (Right) time course of activation region (blue) and predicted box-car curve (green).

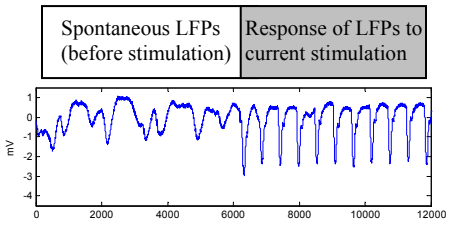


Fig. 2 When the stimulation current is less than 1mA (0.1~1mA, 9Hz), simultaneous recordings indicate a clear electrical response in contralateral cortex, but no BOLD response (not shown).

**Discussions:** The combined measurements of LFPs and BOLD allow us to examine the limitations of using the BOLD signal as a proxy for neural activity. The preliminary findings suggest BOLD fMRI may not be as sensitive as electrophysiological recordings to measure neural activity, which might mirror the limitation of neurovascular coupling, the bridge between BOLD and neural activity. Particular care must be taken in the interpretation of spontaneous BOLD fluctuations, as it appears that their link to ongoing neural activity is weaker than the coupling between BOLD and LFPs during stimulation.

**References:** [1] Logothetis N. K., et al., Nature, 2001, 412(6843):150-157 [2] Shmuel, A. and D. A. Leopold, HBM 2008, 29(7): 751-761