Investigation of neurovascular coupling within brain by simultaneous recordings of LFP and fiber-optic hemodynamic signals

Wen-Ju Pan[1], Jacob Billings[1], and Shella Keilholz[1]

[1]*Biomedical Engineering, Emory University/ Georgia Institute of Technology, Atlanta, Georgia, United States*

Target audience Researchers considering neurovascular coupling in functional neuroimaging.

Purpose

The widely used fMRI technique for mapping functional brain activity is based on the simplistic assumption that neurovascular coupling is more or less consistent throughout the whole brain. A considerable amount of variation in neurovascular coupling has been observed across structures within the brain (1), but this important issue has not been fully investigated due to the technical difficulty of comparing measurements of neural activity and hemodynamics in sub-cortical brain regions. Intrinsic optical spectroscopy (IOS) provides multiple hemodynamic parameters, such as cerebral blood volume (CBV) and oxygenation information, and measurements can be made with high time resolution similar to that of the electrophysiological signal, which allows fine comparisons in neurovascular coupling studies. However, the IOS method is typically applied only on the surface of the brain, as in functional near-infrared optical brain imaging for example. In order to develop an ideal neurovascular coupling probe and examine neurovascular coupling at local sites within brain, we utilized an implantable small fiber-optic probe combined with a glass microelectrode to record hemodynamic signals and local field potentials (LFP) simultaneously in the rodent brain. The LFP signal and OIS signals are sensitive to similar volumes of tissue and the probe can be used in cortical or subcortical areas.

Methods

To minimize the effect of the probe on the brain tissue, we selected a small optical fiber, 105um in outer diameter (FG105LCA, Thorlabs), as an optical probe, which is much smaller than a typical within-brain hemodynamic measurement by a needle laser Doppler flow probe (500 um). Infrared light delivery was conducted through the same fiber by single-direction light coupling from fiber side, or separately through an adjacent fiber. The fiber successfully detected total hemoglobin absorption signals (tHb, reflecting cerebral blood volume, CBV) at the frontal fiber tip, ranging roughly a few hundred microns in diameter (>25° acceptance range), The photon signals were converted to current in a photodiode (FDS100, Thorlabs). Along with the optical probe, a micro-glass electrode (2) was set at the same site. The signals, from both optical and electrical channels, were amplified (×1K, 0-3k Hz, Model 3000, A-M Systems) and recorded (PCI-6281, National Instruments) in MATLAB with sample rate of 1200 Hz. In our preliminary experiments, the simultaneous LFP/CBV recordings were performed in the middle of somatosensory cortex (1mm lower from surface) and caudate putamen in 3 SD rats (male, >300g) under 1.8% isoflurane. The animals maintained a normal physiological condition during all experiments. All data collection was conducted within a custom-made noise shield enclosure (Mu-metal) for isolation from potential noise of all frequencies from magnetic, electric and light sources in the environment. The probe assembly validation was estimated by a correlation of the hemodynamic signal to the spontaneous neural activity; the amplitudes of LFP signals (1-100 Hz) were convolved with an optimized canonical hemodynamic response function (HRF, a sum of two gamma distributions) and compared with CBV signals (0.01-0.3Hz, i.e. filtered out high-frequency physiological pulse noise).

Results

Raw data are shown in figure 1 for visual inspection of data quality. Clear spontaneous LFP bursting activity interleaved with suppression periods can be observed, as expected under 1.8% isoflurane in normal rats (2). Following each LFP burst, CBV signals show clear positive responses, along with physiological pulses (~1 Hz respiration and higher frequency cardiac responses seen by zooming in, not shown here). Assuming a linear hemodynamic response to neural signal amplitude, the LFP amplitudes were convolved with a canonical HRF to predict hemodynamic responses (3). As expected, a robust correlation between the two is demonstrated in figure 1 for somatosensory cortex, which agrees well with previous simultaneous recording/imaging reports (4). We also successfully recorded concurrent LFP/CBV in rat caudate putamen by same approach (not shown).

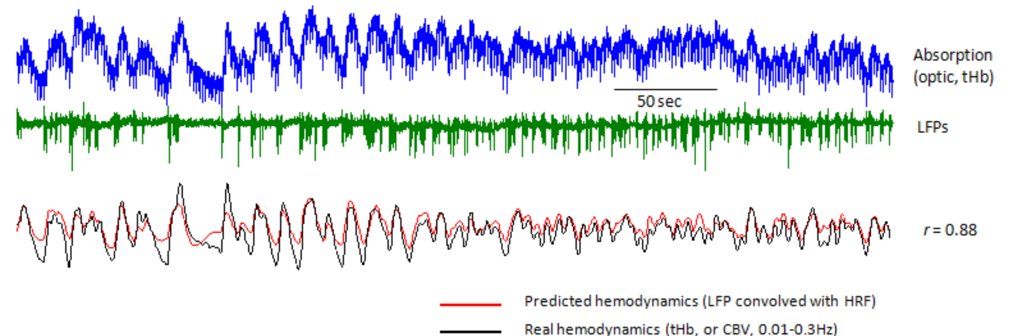

Figure 1. Validation of probes assembly by within-cortex recordings. The optic fiber-based probe designed here is expected to record hemodynamics within the tissue volume of LFP recording. At the same site, 1mm below cortical surface, both LFP and CBV were recorded simultaneously during spontaneous neural activity under anesthesia. The top and middle lines of plots show raw data from a representative rat. The bottom line shows robust correlation (*r*>0.8) between CBV and HRF-convolved LFP.

Discussion/Conclusion

fMRI relies on consistent neurovascular coupling. The latter is not well characterized throughout the brain due to limitations of current techniques for sub-surface-brain studies. We therefore developed a method to characterize neurovascular coupling for given sites in the brain. LFP is believed reflecting primarily local synaptic processes in a neural tissue volume of a few hundred microns in diameter (5). Here a fine fiber-based IOS method was introduced for simultaneous hemodynamic recordings within LFP space. Our preliminary results demonstrate the combination of fiber-electrode is a promising platform for further investigation of the neurovascular coupling mechanism within brain. Future work will include comparison between neuronal signals and hemodynamic responses, such as between LFP bands, multi-unit activities, CBV and oxygenation at cortical and subcortical sites within the brain.

References

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