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Feature Article Commentary

Highlights: Transcranial imaging of functional cerebral hemodynamic changes in single blood vessels

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Speeding up the functional brain imaging is the holy grail, or appropriately the ‘holy technology’, of cognitive neurosciences because of its compelling potential to localize and investigate functional or cognitive brain responses to realistic, rapidly presented stimuli. Advances in functional magnetic resonance imaging continue to result in improved spatial resolution, but temporal resolution—imaging the early response to any stimulus—remains a challenge. This is where a novel optical technique that improves temporal resolution would come in handy. Optical methods may offer added benefits of lower costs and potential to carrying out continuous, long-term functional imaging.

The manuscript by Liao *et al* (2012) describes a novel functional photoacoustic microscopy technique for detecting multiparameter functional responses evoked by peripheral stimuli. Functional photoacoustic microscopy is able to measure the total hemoglobin concentration (HbT), cerebral blood volume, hemoglobin oxygen saturation (SO_2), and the transient hemodynamic response in single cortical vessels of mice with intact skulls. This transcranial imaging technique complements other existing neuroimaging approaches for longitudinal investigation of the hemodynamic response with high temporal resolution. It uses the optimal balance between spatial resolution, temporal resolution, and depth of imaging that is possible with ultrasonic imaging to achieve high intrinsic optical contrast while imaging through an intact skull. Thus, the method shows tremendous potential for small animal imaging for basic science research.

Optical intrinsic signal imaging studies have consistently encountered a brief stimulus-evoked darkening, dubbed the *initial dip*, followed by a strong brightening when imaged under illumination that is preferentially absorbed by deoxyhemoglobin (HbR) (Grinvald *et al*, 1986; Malonek and Grinvald, 1996). In parallel, some functional magnetic resonance imaging studies have reported an initial dip in the blood oxygen level-dependent signal before its eventual rise (Menon *et al*, 1995; Kim *et al*, 2000). The initial dip in the blood oxygen level-dependent signal affords the promise of speeding up the imaging responses to rapidly delivered stimuli by shortening the image acquisition time. However, there are still a number of unclear issues some questions about the interpretation of the initial dip which has been robustly and reliably distinguished in optical intrinsic signal imaging, but proven to be elusive in functional magnetic resonance imaging (Ances, 2004; Buxton, 2001). This paper shows for the first time the consistent occurrence of the initial dip phenomenon using the new functional photoacoustic microscopy system. The results also display more localized blood flow changes in the cerebral arterioles, but no significant initial dip was observed in the superior sagittal sinus. Thus, further experimentation and validation are needed before functional photoacoustic microscopy becomes a universal method of imaging vascular responses to evoked neuronal activity.

Overall, this innovative work serves two purposes. First, it establishes the capabilities and utilities of the noninvasive photoacoustic microscopy system for brain function studies. Second, it contributes to the understanding of vascular response to functional stimuli. It is important that this work be replicated by other investigators; this highlight is an encouragement to just do that. In addition, the investigators and the scientific community are encouraged to show compelling applications of this technology that evidently complements the other methodologies ranging from optical intrinsic signal imaging to blood oxygen level-dependent functional magnetic resonance imaging.

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References

Ances BM (2004) Coupling of changes in cerebral blood flow with neural activity: what must initially dip must come back up. *J Cereb Blood Flow Metab* 24:1–6

Buxton RB (2001) The elusive initial dip. *Neuroimage* 13:953–8

Grinvald A, Lieke E, Frostig RD, Gilbert CD, Wiesel TN (1986) Functional architecture of cortex revealed by optical imaging of intrinsic signals. *Nature* 324:361–4

Kim DS, Duong TQ, Kim SG (2000) High-resolution mapping of iso-orientation columns by fMRI. *Nat Neurosci* 3:164–9

Liao L-D, Lin C-T, Shih Y-Y, Duong T, Lai H-Y, Wang P-H, Ponticorvo A, Wu R, Tsang S, Chang J-Y, Li M-L, Chen Y-Y (2012) Transcranial imaging of functional cerebral hemodynamic changes in single blood vessels using *in vivo* photoacoustic microscopy. *J Cereb Blood Flow Metab* (this issue)

Malonek D, Grinvald A (1996) Interactions between electrical activity and cortical microcirculation revealed by imaging spectroscopy: Implications for functional brain mapping. *Science* 272:551–4

Menon RS, Menon RS, Ogawa S, Hu X, Strupp JP, Anderson P, Uğurbil K (1995) BOLD-based functional MRI at 4 Tesla includes a capillary bed contribution: echo-planar imaging correlates with previous optical imaging using intrinsic signals. *Magn Reson Med* 33:453–9