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From two-photon microscopy to fMRI: BOLD transients as a function of single-vessel dilation and constriction

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Abstract:

The primary source of the BOLD fMRI contrast is the change in the oxygenation of blood due to mismatched changes in cerebral blood flow (CBF) and oxygen metabolism following neuronal activation. The CBF is regulated by dilation (and/or constriction) of cerebral vasculature in response to vasoactive mediators released from activated neurons and astrocytes. While a number of recent studies have focused on neurovascular signaling mechanisms that might play a role under physiological or pathological conditions, the generation and propagation of the dilation response within a vascular network *in vivo* remains unknown. In the present study, we used *in vivo* 2-photon imaging and BOLD fMRI to investigate the transformation of single-vessel diameter and blood flow velocity changes across vascular compartments into depth-resolved BOLD signal change.

We performed 2-photon micovascular measurements in cortical layers I-III (down to ~600 μm) and cortical layer-resolved BOLD fMRI under identical conditions in α-chloralose-anesthetized rats responding to forepaw stimulation (~1mA, 300 μsec, 3 Hz, 2 or 20 sec). BOLD-fMRI experiments were done at 7T on a horizontal bore animal scanner using an EPI technique and a 10-mm diameter transmit/receive surface RF coil positioned over the primary somatosensory cortex (SI). Two-photon measurements were collected following iv injection of fluorescein dextran.

Our BOLD results indicate that (1) the earliest rise of the positive BOLD response is observed in middle cortical layers, (2) the initial dip is confined to the top layers, (3) BOLD amplitude decreases with increasing cortical depth, (4) in agreement with our previous optical studies, there is a negative surround response in the contralateral SI accompanied by a negative response in

ipsilateral SI, and (5) there is a post-stimulus undershoot in response to both 2- and 20-sec stimulus. These results are in register with 2-photon measurements of the layers I-III showing that (1) the deepest measured arterioles and capillaries have the fastest dilation onset and time-to-peak, (2) dilation response of the capillary bed in top layers is delayed by ~1 sec relative to the deeper layers, (3) the largest dilation is observed at the surface arterioles, (4) there is more constriction in the surround region of contralateral SI and virtually only constriction in the ipsilateral SI, and (5) there is a post-stimulus constriction of arterioles and capillaries with the temporal profile of the diameter change closely resembling that of the BOLD post-stimulus undershoot. In addition, our results show no evidence for swelling of the venous vessels down to 600 µm.
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