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NEUROSCIENCE 2014

Presentation Abstract

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Presentation Title:	The role of nNOS for hyperemia induced by sensory and optogenetic stimulation *in vivo*
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Presentation time:	Monday, Nov 17, 2014, 10:00 AM -11:00 AM
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Topic:	++E.09.b. Blood flow
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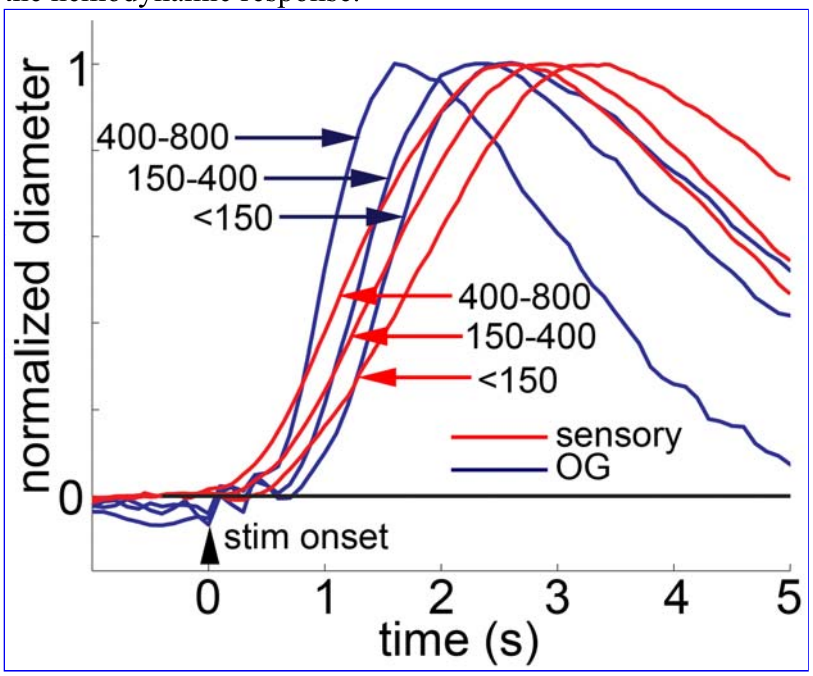
Abstract:	Multiple vasoactive molecular messengers of different cellular origins have been identified. Not all of these messengers, however, are expected to act at once. Rather, specific pathways are likely to be differentially involved across spatiotemporal scales and physiological conditions providing a means to studying their unique role in neurovascular regulation. Previously, using 2-photon measurements of dilation in the rodent primary somatosensory cortex (SI) during stimulus-induced functional hyperemia we parameterized normal dilation timecourse and its dependence on the cortical depth. In the present study, we coupled microscopic measurements of vascular diameters, pharmacological interventions, and optogenetics to address the question of whether vasodilation kinetics could be affected through manipulation of specific vasoactive signaling pathways. We used 2-photon microscopy to image diving arterioles and their branches down to ~900 μm in response to a 2-s electrical forepaw stimulus at 3 Hz. Blocking of neuronal nitric oxide (NO) synthase (nNOS) - expressed in cortical inhibitory interneurons (IN) - slowed dilation kinetics while reducing the amplitude. The presence of NO could promote faster dilation through suppression of a vasoconstrictor 20-HETE produced downstream astrocytic activation of mGluRs. To avoid activation of glutamatergic pathways inherent in the natural

neuronal circuit response to a sensory stimulus, we employed optogenetic (OG) stimulation (200-ms flash of blue light) in VGAT-ChR2(H134R)-EYFP mice expressing ChR2 in all GABAregic cortical neurons. OG-induced dilation in these mice had fast kinetics comparable to that evoked by the sensory stimulus (Figure 1; the shorter duration of OG stimulus may underlie faster time-to-peak in blue curves). In both cases, the fastest dilation occurred in deep cortical layers. OG-induced dilation was abolished by blocking nNOS. These results suggest that nNOS-positive IN in deep cortical layers may play an important role ensuring prompt dilation during the hemodynamic response.



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