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NEUROSCIENCE 2009

Presentation Abstract

Program#/Poster#:	672.18/EE135
Title:	Testing the hemoneural hypothesis: Specific control of blood flow and functional two photon imaging
Location:	South Hall A
Presentation Time:	Tuesday, Oct 20, 2009, 2:00 PM - 3:00 PM
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Abstract:	Changes in cerebral blood flow are finely controlled on a spatial and temporal scale. Changes in blood flow can affect biophysical variables such as temperature, as well as delivery of neuroactive factors such as nitric oxide, while also mechanically stimulating astrocytic endfeet. We hypothesize that changes in blood flow may be involved in functional modulation of astrocytic and neural activity, in addition to providing metabolic support. Effective investigation of this hypothesis requires means for local control of cerebral blood flow and recording any resultant changes in evoked and spontaneous activity. Topical application of pinacidil to the cortical surface selectively relaxes smooth muscle, causing vessel dilation. Optogenetic techniques which we are in the process of developing also show promise for localized constriction and dilation of vascular smooth muscle. From preliminary tetrode and whole cell in vivo recordings in rat, it appears that pyramidal cells show depolarization in response to an increase in blood flow, while activity of fast-spiking inhibitory interneurons is suppressed. To increase our sampling range, we are now using in vivo two photon microscopy to directly image vessels and nearby cells during application and washout of pinacidil, using functional calcium indicators (OGB and Fluo-4) to probe activation changes, while monitoring blood flow changes with SR101 labeling of astrocytes lining vessel walls. Preliminary data suggest that pinacidil application and removal, which drives vasodilation and re-normalization of vessel diameter, respectively,

correlates with increased calcium oscillations in the range of .1 -.5 Hz in labeled cells. Shifts in these low-frequency oscillatory dynamics have also been observed using intracellular in vivo recording during pinacidil application, and may reflect a shift in neural state driven by local hemodynamic events.

Disclosures: **R. Cao**, None; **J. Cardin**, None; **B. Higashikubo**, None; **U. Knoblich**, None; **J.C. Brumberg**, None; **E. Boyden**, None; **C.I. Moore**, None.

Keyword(s): hemodynamic

astrocyte

barrels

Support: NSF Grant 8023785

Tom F. Peterson

[Authors]. [Abstract Title]. Program No. XXX.XX. 2009 Neuroscience Meeting Planner. Chicago, IL: Society for Neuroscience, 2009. Online.