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NEUROSCIENCE 2014

Presentation Abstract

Program#/Poster#:	738.07/PP13
Presentation Title:	Oxygen distribution in cortical microvasculature reveals a novel mechanism for maintaining a safe tissue oxygenation
Location:	WCC Hall A-C
Presentation time:	Wednesday, Nov 19, 2014, 10:00 AM -11:00 AM
Presenter at Poster:	Wed, Nov. 19, 2014, 10:00 AM - 11:00 AM
Topic:	++E.09.a. Energy metabolism
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Abstract:	What is the microscopic level of cerebrovascular organization that allows sufficient oxygen delivery to all cells irrespective of their position within the microvascular network across a wide range of activity levels? The detailed cortical microvascular oxygen distribution is currently largely unknown, primarily due to a lack of imaging technologies for high-resolution deep imaging of cortical oxygenation and vascular morphology. In this work we developed and applied a multi-modal microscopy imaging setup based on “Two-Photon PO2 Microscopy” - a novel technology that can provide comprehensive maps of oxygen partial pressure (PO2) with sub-capillary resolution in both cortical vasculature and tissue. We used Two-Photon PO2 Microscopy to measure PO2 in a large subset of arterioles, venules, and capillaries in the mouse (C57BL/6J) cerebral cortex at different levels of cerebral blood flow (CBF), and to obtain microvascular morphology. In the multimodal microscopy setup we also applied Doppler Optical Coherence Tomography (Doppler OCT) imaging of CBF to acquire blood flow in arterioles and venules. The measurements were combined with a detailed analysis of the microvascular morphology and computation

of oxygen delivery based on realistic vascular anatomical modeling under different levels of oxygen metabolism. Surprisingly, our measurements show that during the baseline level of neuronal activity parenchymal arterioles are responsible for a 50% of the extracted O2. Most of the remaining O2 exchange is taking place at the level of the first few capillary branches after precapillary arterioles, while majority of the capillaries (those of higher branching orders) on average release little O2 at rest. Cerebral microvascular oxygenation measurements during CBF changes and modeling during cerebral metabolic rate of O2 (CMRO2) changes support this finding showing that high branching order capillaries may act as a dynamic O2 reserve that is recruited on demand to ensure adequate tissue oxygenation during increased neuronal activity or decrease in the blood flow. Our results may overturn the textbook view that O2 is almost exclusively released from the capillaries and provide a novel understanding of the distribution and dynamics of O2 extraction along the capillary paths in the cortex. The baseline O2 distribution and dynamic shift in O2 supply along the arterio-capillary path during an increase in neuronal activity may have profound implications for the interpretation of BOLD fMRI signal changes and for evaluating the capacity of microvascular networks to support a sufficient level of cerebral tissue oxygenation in disease.

Disclosures: **S. Sakadzic:** None. **E.T. Mandeville:** None. **L. Gagnon:** None. **J.J. Musacchia:** None. **M.A. Yaseen:** None. **M.A. Yucel:** None. **J. Lefebvre:** None. **F. Lesage:** None. **A.M. Dale:** None. **K. Eikermann-Haerter:** None. **C. Ayata:** None. **V.J. Srinivasan:** None. **E.H. Lo:** None. **A. Devor:** None. **D.A. Boas:** None.

Keyword (s): MICROVESSEL

OXYGENATION

TWO PHOTON MICROSCOPY

Support: AHA SDG7600037

NIH EB000790

NIH NS055104

NIH NS057476