Neurovascular Coupling is Mediated by Different Signalling Pathways at the Capillary and Arteriole Level

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The Center for Magnetic Resonance Research (CMRR) and the Institute for Engineering in Medicine (IEM) are pleased to co-sponsor and announce a seminar by Dr. Anusha Mishra, “Neurovascular Coupling is Mediated by Different Signalling Pathways at the Capillary and Arteriole Level.”

Neuronal activity results in a spatially and temporally localized increase in blood flow to meet the increased demand for energy, a phenomenon that underlies BOLD fMRI signals. Neurovascular coupling can occur at both the arteriole and capillary level, but there is considerable debate over the relative contribution of the two vascular compartments and whether or not astrocytes participate in increasing blood flow. I will show that activity-evoked capillary and arteriole dilation in the cortex are controlled by two separate signalling pathways. Electrically stimulated neuronal activity in cortical slices resulted in a capillary dilation of 14.7±0.5% and an arteriole dilation of 7.1±0.7%. When Ca2+ was buffered in nearby astrocytes to reduce the neuronal activity-evoked increase in [Ca2+]i in astrocytic endfeet along the vessels, stimulation-evoked dilation in capillaries was reduced by 64%, but arteriole dilations were unchanged. Furthermore, capillary dilation was dependent on a rise in astrocytic [Ca2+] via the ATP-gated ion channel P2X1, and subsequent synthesis and release of vasoactive prostaglandin E2 via a phospholipase D2, diacylglycerol lipase and cyclooxygenase1 dependent pathway. Arteriole dilation, on the other hand, depended upon NMDA receptor driven production of nitric oxide. These results reveal a novel dichotomy in the molecular and cellular signalling cascades that regulate cerebral blood flow in different vascular compartments and provide significant insight into the mechanisms underlying the BOLD signal. This work was funded by the Fondation Leducq, the Wellcome Trust and the ERC.