On the regulation of local cerebral blood flow by neurons and astrocytes

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Neurovascular coupling requires intricate communication among neurons, astrocytes and vascular contractile cells that make fine adjustments to microvascular diameter. To meet the energy requirements of the resting and active brain, astrocytes and neurons must regulate microvascular diameter tonically, in a manner that is independent of neural activity, as well as dynamically in response to rapid changes in neural activity. Surprisingly, little is known about how the brain coordinates these distinct modes of blood flow control. We have discovered a key role for resting astrocyte Ca2+ in the steady-state dilation of micro-vessels. Specifically, we show that reducing basal Ca2+ in astrocyte 'endfeet', which are the specialized astrocytic compartments that directly appose microvascular elements, causes a vasoconstriction, in the absence of neural influences. Furthermore, we find that astrocytes are not necessary for vasodilations in response to brief, physiologically relevant increases in neural activity. We provide evidence that preventing Ca2+ transients specifically in the astrocytes that surround a micro-vessel, has no impact on activity-dependent vasodilations. These evoked increases in microvascular diameter are, however, largely eliminated by synaptic AMPA receptor and cyclooxygenase-2 blockade. Furthermore, this type of synaptically driven vasodilation occurs independent of vascular conduction, suggesting a local synaptic effect on nearby microvasculature. Our data suggests that astrocytes and neurons act in parallel to regulate blood flow on distinct timescales.

Biography

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