Krystal Nizar, Lydia Reznichenko, Qun Cheng, Sava Sakadžic, David A.Boas, Eliezer Masliah, Anders M. Dale, Gabriel A. Silva, Anna Devor

Unreliable and delayed astrocytic calcium response does not support the hypothesis of calcium-dependent astrocytic regulation of blood flow

It has been proposed that vascular dilation in response to an increase in neuronal activity is mediated by astrocytes. According to this hypothesis, astrocytes respond to neuronal activation by an increase in metabolism accompanied by a rise in intracellular calcium concentration that, in turn, triggers synthesis and release of vasoactive gliotransmitters. However, the onset of astrocytic calcium response reported by the majority of experimental studies is significantly delayed relative to the known kinetics of vasodilation. Moreover, the frequency of the occurrence of astrocytic calcium transients temporally locked to the stimulus presentation is unclear.

We used 2-photon laser scanning microscopy to measure calcium activity in neurons and astrocytes, and diameter changes of cerebral arterioles and capillaries down to 500 μm in rat and mouse primary somatosensory cortex. Calcium indicator OGB-1 was microinjected at the center of neuronal response determined by surface potential mapping immediately before the injection. Astrocyte-specific fluorescent dye SR101 was applied topically. We varied the stimulus conditions (different durations of whisker or forepaw stimulus, tactile or electrical) and anesthesia conditions (a-chloralose, urethane, isofluorane, ketamine/xylazine). Our data indicate that astrocytes do not exhibit reliable calcium transients temporally locked to the stimulus. When observed, the astrocytic calcium response was considerably delayed relative to the arteriolar/capillary dilation. These results challenge the idea that astrocytes trigger vasodilation and the associated blood flow response through calcium-dependent mechanisms.