

ME4: Astrocyte Ca^{2+} waves and subsequent non-synchronized Ca^{2+} oscillations coincide with arteriole diameter changes in response to spreading depolarization

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Introduction: Spreading depolarization (SD) arising in acute cerebrovascular diseases is a wave of mass depolarization of neurons that also has an impact on all cell types of the cortex. Furthermore, through inducing profound changes in the local circulation, SD may further compromise cerebral perfusion after injury. Even though astrocyte response appears secondary to neuronal depolarization, it is yet to be explored how the passage of SD alters glial activity and function. In the present study we describe enhanced post-SD astrocyte Ca^{2+} oscillations and investigate the concurrent vascular diameter changes in the mouse cortex.

Methods: Intracellular Ca^{2+} events indicated by Fluo-4 AM fluorescence intensity changes were visualized in astrocytes selectively labelled by SR101 by multiphoton microscopy in anesthetized mice. The SD-related arteriole diameter changes were investigated simultaneously with astrocyte Ca^{2+} transients.

Results: Astrocytes displayed a simultaneous Ca^{2+} wave with SD propagation, engaging all astrocytes in the field of view. High frequency, unsynchronized Ca^{2+} oscillations occurred minutes behind the Ca^{2+} wave of SD and engaged fewer astrocytes at a given time. Ca^{2+} oscillations were associated to smaller amplitude fluorescence intensity increases compared to Ca^{2+} waves. Finally, our data confirmed a coincidence of arteriolar constriction and Ca^{2+} waves, while post-SD Ca^{2+} oscillations coincided with the peak of the SD-related vasodilation.

Conclusion: The present study is the first to describe the high frequency post-SD astrocyte Ca^{2+} oscillations *in vivo*. Our results provide novel insight into the spatio-temporal correlation between glial reactivity and cerebral arteriole diameter changes behind the SD wavefront.