High amplitude spontaneous Ca^{2+} events in astrocytic endfeet may underlie the inversion of neurovascular coupling after subarachnoid hemorrhage

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Dysfunction of the intra-cerebral microcirculation may contribute to the development of delayed ischemic neurological deficits following aneurysmal subarachnoid hemorrhage (SAH). Neurovascular coupling (NVC), which links focal increases in neuronal activity with local arteriolar dilation, is essential for proper brain function and metabolism. Recently, we reported an inversion of the NVC response in brain slices obtained from SAH model animals (Koide et. al. *PNAS* 2012). Rather than dilate, brain parenchymal arterioles constrict following neuronal activation. The evidence suggests that higher amplitude spontaneous Ca^{2+} events in astrocytic endfeet set the stage for the inversion of NVC by increasing the basal perivascular K^+ concentration. While this study determined a mechanistic link between altered Ca^{2+} activity of perivascular astrocytes and impaired neurovascular communication, it only examined animals 4 days after SAH induction. Using combined infrared differential interference contrast microscopy and 2-photon laser microscopy to image acute cortical brain slices, we examined the NVC response and spontaneous Ca^{2+} activity in astrocytic endfeet at six time-points after SAH. Our results show that the onset of the inversion of NVC occurs within 24 hr of SAH and coincides with an emergence of higher amplitude spontaneous Ca^{2+} events in astrocytic endfeet. Further, all time-points showing inversion of NVC also show a greater proportion of high amplitude spontaneous Ca^{2+} events. These data support a model in which altered Ca^{2+} signaling of astrocytic endfeet contributes to the NVC deficits observed after experimental SAH.

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