Visualization of Ca^{2+} dynamics within the endoplasmic reticulum for the study of astrocytic functions

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Astrocytes, a major type of glial cells in the brain, show a wide variety of intracellular Ca^{2+} dynamics spontaneously and in response to various stimuli. Accumulating evidence indicates that Ca^{2+} release from the endoplasmic reticulum (ER) in astrocytes may play a key role in physiological and pathophysiological events in the brain. Therefore, the development of techniques for sensitive detection of spatiotemporal features of ER-mediated Ca^{2+} dynamics in astrocytes is crucial to the understanding of such events. Although both synthetic and genetically encoded cytosolic Ca^{2+} indicators have been used to evaluate the Ca^{2+} release from the ER in astrocytes *in situ*, such method faces two major problems. Firstly, cytoplasmic Ca^{2+} transients are generated not only by release of Ca^{2+} from the ER but also by Ca^{2+} influx via the plasma membrane. Second, because cytoplasm has a strong Ca^{2+} buffering capacity, it is not always clear whether the sensitivity of the cytoplasmic Ca^{2+} indicators is sufficient to detect subtle Ca^{2+} release from the ER. We recently developed a genetically encoded ER Ca^{2+} indicator, G-CEPIA1*er*, to directly visualize the Ca^{2+} dynamics within the ER. Using G-CEPIA1*er* in astrocytes, we found large decreases in the ER Ca^{2+} concentration even when relatively small increases in the cytoplasmic Ca^{2+} concentration were observed. Thus, the ER Ca^{2+} visualization method allows us to detect ER-mediated Ca^{2+} signaling, which might have previously escaped detection. We also succeeded in detecting ER Ca^{2+} dynamics in astrocytes *in vivo*, which were associated with behavior of the animal. Collectively, the present ER Ca^{2+} visualization studies may provide an important new insight into ER Ca^{2+} dynamics and Ca^{2+} -mediated functions in astrocytes.