Visualization of Ca^{2+} release and filling mechanisms in the endoplasmic reticulum of astrocytes

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Accumulating evidence indicates that astrocytes are actively involved in the physiological and pathophysiological functions of the brain. Intracellular Ca^{2+} signaling, especially Ca^{2+} release from the endoplasmic reticulum (ER) via inositol 1,4,5-trisphosphate receptor (IP_3R), is considered to be crucial for the regulation of astrocytic functions. Although intraluminal Ca^{2+} dynamics within the ER should be a key determinant of astrocytic Ca^{2+} signaling, technical difficulties have impeded direct analysis. In this study, we developed and used a genetically encoded ER Ca^{2+} indicator, G-CEPIA1*er* to visualize Ca^{2+} dynamics within the ER in astrocytes in acute brain slices. G-CEPIA1*er* enabled highly sensitive and selective detection of ER Ca^{2+} release as a decrease in ER Ca^{2+} concentration. This allowed us to reveal a novel mechanism of Ca^{2+} release in astrocytes. Furthermore, we confirmed the crucial role of store-operated Ca^{2+} entry for refilling and maintaining ER Ca^{2+} content after spontaneous and stimulus-induced ER Ca^{2+} release in astrocytes. Collectively, these ER Ca^{2+} visualization studies provide important new insights to Ca^{2+} handling in astrocytes.