Imaging of extracellular Ca^{2+} in the hippocampus by a novel CMOS ion image sensor

Bijay Parajuli[1], Hideo Doi[2], Eiji Shigetomi[1], Youichi Shinozaki[1], Youna Lee[2], Toshihiko Noda[2], Kazuhiro Takahashi[2], Kazuaki Sawada[2], Schuichi Koizumi[1]

[1]Dept. Neuropharmacol., Interdisciplinary Grad. Sch. Med., Univ. Yamanashi, [2]Dept. Electrical and Electronic Information Tech., TUT

Intracellular calcium ion (Ca^{2+}i) is one of the most important cation that controls several cellular functions, and thus there were already huge number of literature about Ca^{2+}i imaging in various cells. Although it is believed that Ca^{2+}i increase is accompanied by extracellular Ca^{2+}(Ca^{2+}o) decrease, the kinetics of Ca^{2+}o decrease remain unknown because of the limited imaging options. To overcome this limitation, we developed a Ca^{2+} image sensor (CIS) that is highly selective to Ca^{2+} but not to other cations within wide dynamic range (from 100 mM to 100 mM). We used CIS for the imaging of Ca^{2+}o in acute hippocampal slices. Stimulation with glutamate (Glu) decreased Ca^{2+}o to around 200 nM within 3 s, which returned to the baseline level (2 mM) with slow kinetics (5 min). Glu stimulates both neurons and glial cells to evoke Ca^{2+}i elevation, thereby reducing Ca^{2+}o. Thus, we tested NMDA to selectively stimulate NMDA receptor in neurons. NMDA mimicked Glu-evoked Ca^{2+}o decrease. Interestingly, Ca^{2+}o decrease was initiated at hippocampal CA1-2, before spreading along the pyramidal layers. Glutamate- and NMDA-evoked Ca^{2+}o decreases were inhibited by a NMDA receptor antagonist D-APV, suggesting involvement of neuronal NMDA receptors in decrease in Ca^{2+}o. So far, many scientists neglected Ca^{2+}o, but the CIS would tell us its importance for understanding brain functions.