Involvement of Redox Modification of Ca^{2+}-Release Channels in Cerebellar Learning and Aging

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Ca^{2+} release from intracellular store, as well as Ca^{2+} influx from extracellular fluid, contributes elevation of cytosolic Ca^{2+} revels. However, regulatory mechanisms of Ca^{2+}-release channels and their functional roles in relation to learning and memory have not been fully understood. Recently, accumulating data suggest that redox molecules such as reactive oxygen species (ROS) and nitric oxide (NO) act as signaling molecules through redox modification of proteins, although these molecules have been considered as damaging oxidizers of the macromolecules, for a long time. In this symposium, I will introduce our current studies indicating involvement of redox modulation of type 1 ryanodine receptor (RyR1) in regulation of brain functions.

Novel Ca^{2+} release mechanism, NO-induced Ca^{2+} release (NICR), was recently demonstrated in cerebellar Purkinje cells. S-nitrosylation of thiol group in RyR1 was revealed to be essential for NICR. Furthermore, using knock-in mice defect in NICR, involvements of NICR in cerebellar long-term potentiation (LTP) and motor learning were indicated. On the other hand, because thiol group is also the target of ROS, effects of ROS on cerebellar synaptic plasticity through redox modification of RyR1 are also expected. Involvements of ROS in inhibition of cerebellar LTP and induction of cerebellar long-term depression will be also discussed.