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METABOTROPIC GLUTAMATE RECEPTOR-MEDIATED LTD INVOLVES TWO INTERACTING CA^{2+} SENSORS, NCS-1 AND PICK1

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There are two major forms of long-term depression (LTD) of synaptic transmission in the central nervous system, which require activation of either N-methyl-D-aspartate receptors (NMDARs) or metabotropic glutamate receptors (mGluRs). In synapses in the perirhinal cortex we have directly compared the Ca^{2+} signalling mechanisms involved in NMDAR-LTD and mGluR-LTD. Whilst both forms of LTD involve Ca^{2+} release from intracellular stores the Ca^{2+} sensors involved are different; NMDAR-LTD involves calmodulin, whilst mGluR-LTD involves the neuronal Ca^{2+} sensor (NCS) protein NCS-1. In addition, there is a specific requirement for IP3 and PKC as well as protein interacting with C-kinase (PICK-1) in mGluR-LTD. NCS-1 binds directly to PICK1, via its BAR domain, in a Ca^{2+}-dependent manner. Furthermore, the NCS-1-PICK1 association is stimulated by activation of mGluRs, but not NMDARs, and introduction of a PICK1 BAR domain fusion protein specifically blocks mGluR-LTD. Thus, NCS-1 is a component of a novel mechanism involved in mGluR-LTD.

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