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Role of Metabotropic Glutamate Receptors for Induction of Homosynaptic Long-term Depression in Rat Spinal Dorsal Horn

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We have previously reported that low-frequency stimulation of primary afferent Aδ-fibers may induce long-term depression (LTD) at synapses between Aδ-fibers and neurons in lamina II of spinal dorsal horn of young rat. Here we show for the first time that this form of LTD is homosynaptic in nature and activation of metabotropic glutamate receptors (mGluRs) is required for its induction. Synaptic transmission between dorsal root afferents and neurons in lamina II of spinal dorsal horn was examined by intracellular recording in a transverse slice-dorsal root preparation of rat spinal cord. When the dorsal root was spliced into two halfs, conditioning stimulation given at 1 Hz, 0.7 mA, 0.1 ms, 900 pulses induced an LTD of EPSP amplitudes to 60 ± 12 % of control only in the conditioned pathway, whereas the synaptic transmission in the other non-conditioned pathway was not changed. Coactivation of group I and group II, but not group III mGluRs is required for the generation of this form of LFS-induced LTD, since non-selective mGluRs antagonist (S)-MCPG, specific group I mGluRs antagonist (S)-4C-PG and group II mGluRs antagonist MSOPPE, but not group III mGluRs selective antagonist MSOP blocked the LTD induction. Moreover, the induction of LTD was severely impaired by intracellular injection of Ca^{2+} fast chelator BAPTA, indicating a rise in

postsynaptic free Ca^{2+} concentration is involved in the induction of LTD. On the other hand, activation of mGluRs by (1S, 3R)-ACPD induces an LTD only under conditions of disinhibition. The (1S, 3R)-ACPD-induced LTD is NMDA receptor independent and may be mediated by pertussis toxin (PTX)-insensitive G-proteins, since this (1S, 3R)-ACPD-induced LTD could still be induced in the presence of NMDA receptor antagonist D-AP5 and after the slices were preincubated with PTX. Both of LFS-induced LTD and (1S, 3R)-ACPD-induced LTD in spinal dorsal horn may be relevant to antinociception.