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Role of mGluRs in slow synaptic transmission in the rat spinal dorsal horn

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It is now well established that glutamate is the major excitatory neurotransmitter in the central nervous system including the spinal cord. Glutamate acts through two broad classes of receptors, such as ion channel-linked (AMPA, kainate and NMDA receptors), and metabotropic receptors (mGluRs), which couple via G-proteins to the intracellular second messenger cascades.

Although the presence of multiple mGluRs in the spinal dorsal horn has been shown, their roles in physiology and pathophysiology of synaptic transmission are still not clear and are complicated by the diversity of pre- and postsynaptic receptors. We have examined the possibility that mGluRs are activated by the primary afferent input by using conventional intracellular recording from dorsal horn neurons (laminae II-V) within a transverse slice preparation of the young rat lumbar spinal cord.

Experiments were carried on in 300-450 μm thick spinal cord slices with dorsal roots attached from Sprague-Dawley rats of either sex aged between 17 and 24 days. Single slices transferred to the recording chamber were perfused with oxygenated Krebs-bicarbonate solution. Conventional intracellular recordings were made from dorsal horn neurons with single fiber-glass microelectrodes filled with 4M potassium acetate (pH 7.2; DC resistance 110-220MΩ). Mono- and polysynaptic excitatory postsynaptic potentials were evoked by orthodromic electrical stimulation of ipsilateral dorsal roots with a suction-electrode. The data acquisition and analysis software package pCLAMP (version 9.0, Axon Instruments) was used. Identification of the evoked EPSPs as monosynaptic was based on their constant latencies and absence of failures with a repetitive stimulation at frequency of 10Hz. The effect of different chemicals added to the perfusing solution on recorded traces was examined.

High intensity repetitive stimulation of primary afferents evoked a slow EPSP consisting of a short-lasting slow EPSP (seconds) and a long-lasting slow EPSP (minute) in the dorsal horn neurons.

Kynurenate, an ionotropic excitatory amino acid receptor antagonist blocked the short-lasting slow EPSP evoked by primary afferent stimulation, while the long-lasting slow EPSP was enhanced.

The group I mGluR agonist, S-DHPG induced a depolarization and increase in the baseline-noise in both superficial and deep dorsal horn. In the presence of TTX, and ionotropic glutamate receptor antagonists D-AP5 and NBQX, the depolarization was not modified. This finding suggests a postsynaptic site of action.

AIDA, a group I mGluR (mGluRI) antagonist reduced the long-lasting slow EPSP evoked by high intensity repetitive stimulation of primary afferents, in a deep dorsal horn neuron. The short-lasting slow EPSP was only slightly reduced.

These data suggest that in addition to excitatory amino acids and neuropeptides (tachykinins), the group I mGluRs, in particular mGluRI, may be implicated in the slow synaptic transmission in the spinal dorsal horn. These potentials are likely to be important both for short-term change in excitability of dorsal horn neurons and also for the induction of long-term synaptic plasticity and nociception.

Abbreviations: **D-AP5:** D(-)-2-amino-5-phosphonopentanoic acid; **CNQX:** 6-cyano-7-nitroquinoxaline-2.3-dione disodium; **NBQX:** 6-nitro-7-sulphanoylbenzol[f]quinoxaline-2.3-dione; **DHPG**: (S)-3,5-dihydroxyphenylglycine; **AIDA:** (RS)-l-aminoindan-l,5-dicarboxylic acid; **TTX:** tetrodotoxin