Enhancement of spontaneous glutamate release by group I mGluRs in the Medial Nucleus of the Trapezoid Body

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Neuromodulation mediated by metabotropic glutamate receptors (mGluRs) regulates many brain functions, however, the modulatory roles of mGluRs in auditory processing are not well understood. The medial nucleus of the trapezoid body (MNTB) is a critical nucleus in the auditory brainstem circuits involved in sound localization. MNTB neurons are excited by glutamatergic inputs from bushy cells in the contralateral anteroventral cochlear nucleus (AVCN) via the giant calyx of Held synapse. MNTB neurons also receive inhibitory inputs mediated by GABA and glycine. The integration of these synaptic inputs determines the MNTB's output. Our recent study shows that group I mGluRs (mGluR I) exert neurotransmitter- and release-mode-specific modulation on the inhibitory transmission in MNTB. Here, we further investigated the modulatory effects of mGluR I on the excitatory transmission, using whole-cell recordings from brainstem slices obtained from P12-P22 (postsynaptic recordings) and P8-P10 (calyx recordings) mice.

Activation of mGluR I by 3,5-DHPG (200 μM) produced an inward current, and increased glutamatergic sEPSC frequency and amplitude in MNTB neurons. Accordingly, under current-clamp configuration, 3,5- DHPG depolarized MNTB neurons, increased sEPSP frequency and amplitude, and in some cells produced action potentials, which persisted after synaptic receptors were blocked. In AVCN bushy cells, after blocking the known synaptic receptors with a cocktail of blockers (APV, 50 μM; DNQX, 50 μM; gabazine, 10 μM; strychnine,1 μM), 3,5-DHPG (200 μM) depolarized the membrane without generating action potentials. The effect on sEPSCs was blocked by a voltage-gated sodium channel (Nav) antagonist (tetrodotoxin, 1 μM). Cadmium chloride (100 μM), a non-specific voltage-gated calcium channel (Cav) blocker, partially eliminated the modulatory effects. Immunolabeling indicated a presynaptic expression of mGluR5. Presynaptic (calyx) recording showed that 3,5-DHPG shifted the persistent Na+

currents (INaP) activation to more hyperpolarized voltages and increased the INaP at the voltages around resting membrane potentials.

Our data indicated that activation of mGluR I increases spontaneous glutamate release and cellular excitability, affecting the output of MNTB neurons.

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