Cholinergic and noradrenergic modulation of corticothalamic synaptic input from layer 6 to the posteromedial thalamic nucleus

Thalamic relay cells constitute important node of reciprocal sensory processing which is highly dependent on brainstem neuromodulatory systems due to current behavioral demands. We have investigated the cholinergic and noradrenergic modulatory influence on synaptic transmission from cortical layer 6 to the neurons located in posteromedial nucleus (PoM) - the higher-order somatosensory thalamic nucleus. Using rats' thalamic brain slices we measured neuronal membrane potentials and currents with whole-cell patch-clamp method while general cholinergic (carbachol) or noradrenergic (norepinephrine) agonists were added to the bath in order to mimic activation of the appropriate neuromodulatory system. Excitatory postsynaptic responses were evoked in PoM cells by trains of 5 electrical stimuli delivered at 20 Hz through bipolar electrode placed at the corticothalamic fibers in the internal capsule. In all investigated cells, the consecutive excitatory postsynaptic responses evoked by the train stimuli showed pronounced frequency facilitation (i.e. increase in amplitude).

Carbachol substantially decreased amplitudes of all excitatory postsynaptic responses, but at the same time it enhanced the magnitude of frequency facilitation. Application of more specific drugs revealed that this cholinergic modulation was exerted by activation of muscarinic receptors. Moreover, the amplitudes of each consecutive excitatory postsynaptic potential in the train were characterized by much higher trial-to-trial coefficient of variation (st. dev / mean). These effects suggested presynaptic action of carbachol. To prove this, we measured the failure rate of excitatory postsynaptic currents in PoM cells in response to minimal stimulation strengths of corticothalamic fibers. The substantial increase of failure rate in the presence of carbachol supports the hypothesis that observed effects of cholinergic modulation relay on decreased probability of transmitter release from presynaptic site.

In the presence of noradrenaline all excitatory postsynaptic potentials in the train, except the first one, decreased in amplitude but this reduction was much smaller than that produced by carbachol. In contrast to the effect evoked by carbachol, the detailed analysis revealed that norepinephrine decreased the frequency facilitation of synaptic transmission from layer 6 to PoM.

Conclusions:

- Cholinergic and noradrenergic systems differently modulate the synaptic transmission from cortical layer 6 to the principal neurons of higher order posteromedial thalamic nucleus .
- Carbachol-induced modulation of this corticothalamic transmission is mediated by presynaptic muscarinic receptors.