Modulation of persistent sodium current and rhythmic activity in spinal cord networks by beta-pompilidotoxin

The origin of rhythm generation in mammalian spinal cord networks is still poorly understood. In a previous study, we showed that oscillatory activity in organotypic spinal cord cultures is mainly due to depolarization block caused by a fast inactivation of the transient sodium current (INaT). Recently, toxins called alpha- and beta-pompilidotoxin (alpha- and beta-PMTX) have been extracted from solitary wasp venom. Alpha-PMTX slows the sodium channel inactivation process and beta-PMTX seems to be 6-7 times more potent than alpha-PMTX. In the present study, we therefore investigated the effect of beta-PMTX on rhythmic activity and on sodium currents in spinal networks. Using intracellular recordings and multielectrode array (MEA) recordings in dissociated spinal cord cultures, we found that beta-PMTX reduces the number of population bursts and increases the background asynchronous activity. We then uncoupled the network by blocking all synaptic transmission (APV, CNQX, bicuculline and strychnine) and observed that beta-PMTX increases both the intrinsic activity at individual channels and the number of intrinsically activated channels. This latter result suggested that previously silent cells become spontaneously active after application of beta-PMTX. To confirm this assumption, we performed intracellular recordings under uncoupled conditions. Beta-PMTX has two effects: it switches a number of silent cells into spontaneously active cells and it increases the firing rate of intrinsically spiking cells. Finally, we investigated the effect of beta-PMTX on sodium currents. We found that this toxin does not affect the inactivation of INaT but increases the peak of the persistent sodium current (INaP). Together, theses findings suggest that beta-PMTX acts on INaP thereby enhancing intrinsic activity leading to a profound modulation of spontaneous rhythmic activity. This work was supported by Swiss National Science Foundation Grants No. 3100A0_120327.