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Institutionen för Neurovetenskap

Modulation by Substance P in the Lamprey Spinal Cord

AKADEMISK AVHANDLING

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ABSTRACT

Neuromodulation is a key element for animal adaptation to environmental circumstances. Neuromodulators can alter the output of a physiological system by acting on the motor circuit by transforming intrinsic firing properties and altering synaptic strength. Substance P belongs to the family of tachykinin, which are peptidergic neuromodulators. The main focus of this thesis has been to characterize the effects of substance P in neurons and networks in the lamprey spinal cord.

The spinal network underlying locomotion in lamprey is composed of excitatory and inhibitory interneurons mediating fast ionotropic actions. In addition, the tachykinin system as well as other modulator systems, is activated as locomotion is initiated. By using electrophysiological methods in the isolated spinal cord and specific agonists and antagonists, it was shown that substance P is endogenously released within the locomotor network of the adult lamprey (Paper I). Substance P is known to accelerate the burst rate by NMDA current potentiation. In paper II, it was demonstrated that substance P also utilizes the endocannabinoid system to reduce the crossed inhibition in the spinal cord. Paper III examined the effect of substance P on calcium channels in motoneurons and commissural interneurons and we further look into the subtypes of calcium channels modulated by substance P. The last study (paper IV) focuses on the inhibition of background K^+ channels as the main source of the depolarization caused by substance P.

In conclusion, substance P activates neurokinin receptor type 1 (NK_1) receptors which in turn activate several intracellular pathways; all these effects modulate the excitability response with implications at the locomotor network level.