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Ghrelin enhances the excitability of nigral dopaminergic neurons by inhibition of A-type potassium channels

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Ghrelin, an endogenous ligand for growth hormone secretagogue receptor (GHS-R, a G-protein-coupled receptor), is a 28-amino-acid peptide that regulates growth hormone secretion, food intake, reward-seeking behavior and memory performance. In the substantia nigra pars compacta (SNc), ghrelin electrically activates dopaminergic neurons, and increases dopamine concentration in the striatum. However, how ghrelin enhances neuronal excitability remains largely unknown. In the present study, we focus on A-type potassium channels (IA), which has a wide expression on dopaminergic neurons and plays a key role in pacemaker control. Brain slices of the SNc were prepared from C57BL/6 mice of postnatal 15–20 days. The effects of ghrelin on spontaneous firing and IA current of dopaminergic neurons were observed by whole cell patch clamp technique. IA specific blocker 4-AP (1 mM) significantly enhanced the spontaneous firing of dopaminergic neurons, whereas further application of ghrelin (100 nM) had no additional effect on neuronal firing. The application of ghrelin reversibly and significantly decreased the amplitude of IA to 54% of control. Application of H89 (1 μ M, PKA selective blocker) did not alter the IA current or the response to ghrelin. However, GF109203X (5 μ M, PKC inhibitor) abolished ghrelin-induced inhibition of IA. To assess the involvement of the possible PKC specific subspecies, we then used Gö6976 (20 nM, conventional PKCs selective inhibitor) and rottlerin (10 μ M, PKC δ selective inhibitor). Our results showed that bath application of Gö6976 or rottlerin alone had no effect on the IA currents, whereas rottlerin totally abolished the IA current response to ghrelin. Therefore, our findings indicate that inhibition of IA may contribute to the ghrelin-induced excitation of dopaminergic neurons. Ghrelin reduces IA by activation of PKC δ pathway.

Biography

Limin Shi completed her PhD from Qingdao University. She is an Associate Professor of the Department of Physiology and Pathophysiology in Qingdao University. She has published more than 10 papers in reputed journals.

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