Ghrelin reduces A-type potassium channels in nigral dopaminergic neurons via PKC but not PKA pathway

J. Xie, L. Shi, B. Xue
Department of Physiology, Shandong Provincial Key Laboratory of Pathogenesis and Prevention of Neurological Disorders, Shandong Provincial Collaborative Innovation Center for Neurodegenerative Disorders and State Key Disciplines: Physiology, Qingdao University, China

Background: The excitability of dopaminergic neurons in the substantia nigra pars compacta (SNc) that supply the striatum with dopamine determines the function of nigrostriatal system for motor coordination. Our previous studies showed that the brain-gut peptide ghrelin could enhance pacemaker firing of nigral dopaminergic neurons by inhibiting voltage-gated potassium Kv7/KCNQ/M-channels. However, whether the other potassium channels are also involved in the ghrelin-induced excitability of dopaminergic neurons still remain unclear. In this study, we focus on A-type potassium channels (I_A), which has a wide expression on dopaminergic neurons and play a key role in pacemaker control. Methods: Brain slices of the SNc were prepared from C57BL/6 mice of postnatal 15-20 days. The effects of ghrelin on discharge frequency and I_A current of dopaminergic neurons were observed by whole cell patch clamp technique. Results: Ghrelin (100 nM) can significantly increase the discharge frequency of dopaminergic neurons and inhibit the amplitude of I_A current. Application of either PKA selective inhibitor H89 or PKC inhibitor GF109203X alone had no effect on I_A; However, GF109203X abolished ghrelin-induced inhibition of I_A. In addition, GF109203X and the I_A specific blocker 4-AP could occlude the excitatory effects of ghrelin. Conclusion: These results demonstrated that inhibition of I_A may contribute to the ghrelin-induced excitation of dopaminergic neurons. Ghrelin reduces I_A by activation of PKC but not PKA pathway.