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Inhibitory mechanism of melatonin on voltage-dependent Kv4.2 channels

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Melatonin is secreted from the pineal glands and regulates the circadian rhythms. It has been reported that melatonin modulates the activity of ion channels. In the present study, the effects of melatonin on voltage-dependent K^+ (K_v) channels, which contribute to the regulation of resting membrane potentials and action potentials, were examined in rat pinealocytes and reconstituted HEK293 cells. The expression analysis by quantitative real-time PCR revealed that $K_v4.2$ channels was abundantly expressed in rat pineal glands. In rat pinealocyte, 5 mM 4-aminopyridine-sensitive $K_v4.2$ currents were detected using whole-cell patch-clamp configuration. In HEK293 cells expressed with $K_v4.2$ channels, the application of melatonin (100 μ M, 300 μ M, and 1 mM) inhibited $K_v4.2$ currents in a concentration-dependent manner. The inhibitory effects of melatonin on $K_v4.2$ currents were observed even in the presence of 100 nM luzindole, an inhibitor of the melatonin receptors. Neither 1 mM tryptophan nor 1 mM serotonin, which are the precursors to melatonin, affected the activity of $K_v4.2$ currents. These results strongly suggest that melatonin inhibits $K_v4.2$ channels directly, which may contribute to the regulation of physiological functions in pineal glands.