

Serotonergic regulation of the inwardly rectifying potassium (Kir) 4.1 channel expression in mice astrocytes.

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Astrocytes regulate neuronal excitability by maintaining ion homeostasis and secreting neuroactive substances. We previously showed that expressional knockdown of inwardly rectifying potassium (Kir) 4.1 channels elevates brain-derived neurotrophic factor (BDNF) expression in astrocytes (Int. J. Mol. Sci., 19, 3313, 2018). In order to explore the neural factors influencing of the Kir4.1 expression, we investigated the effects of serotonergic agents on Kir4.1 mRNA levels in primary cultured astrocytes. Treatment of astrocytes with serotonin (5-HT; 100 μ M) inhibited Kir4.1 expression. The 5-HT_{1A} agonist (\pm)-8-OH-DPAT, 5-HT₂ agonist (\pm)-DOI, 5-HT₃ agonist SR-57227 or 5-HT₆ agonist WAY-208466 showed no effect on the astrocytic Kir4.1 expression. However, the 5-HT₇ agonist LP-211 significantly inhibited the expression of Kir4.1 in a dose-dependent manner. In addition, the 5-HT₇ antagonist SB-258719 did not affect the Kir4.1 expression by itself, but antagonized the inhibition of Kir4.1 expression induced by 5-HT₇ agonist LP-211. The present results strongly suggest that 5-HT inhibits Kir4.1 expression via the activation of 5-HT₇ receptor in astrocytes.