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MEETING ABSTRACT

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Signaling mechanisms of 5-HT_2 receptors in primary sensory neurons

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Background: Serotonin (5-HT) is an inflammatory mediator and involved in pain sensation. Ionotropic 5-HT_3 receptors of dorsal root ganglion (DRG) neurons are thought to mediate this effect. Here, the contribution of metabotropic 5-HT receptors and their functional interactions with K_V7 and TRPV1 channels was investigated.
Methods: Using the perforated patch clamp technique on DRG neurons of newborn rats in primary cell culture, effects of 5-HT receptor ligands on membrane potential and various currents were investigated.
Results: 5-HT increased the excitability of DRG neurons and caused depolarizations. This effect was not altered by the 5-HT_3 receptor antagonist tropisetron, but reduced by the 5-HT_2 receptor antagonist ritanserin. The 5-HT_2 receptor agonist (±)-2,5-dimethoxy-4-iodoamphetamine ((±)-DOI) also raised the excitability of DRG neurons. Currents through K_V7 channels of DRG neurons were not inhibited by 5-HT, but reduced by (±)-DOI in a concentration-dependent manner by up to 32.6 ± 6.9% (n = 20). Furthermore, K_V7 channels of DRG neurons were inhibited in the presence of ritanserin by up to 14.5 ± 3.8% (n = 9), and the effects of (±)-DOI and ritanserin were additive. Currents through channels formed by $K_V7.2/K_V7.3$ heteromers expressed in tsA201 cells (which do not express 5-HT_2 receptors) were also significantly attenuated by (±)-DOI (up to 17.1 ± 5.6%) and ritanserin (up to 24.6 ± 7.8%) (n = 13), but were not altered by another 5-HT_2 receptor antagonist (ketanserin) nor by 5-HT (n = 11). In tsA201 cells coexpressing 5-HT_2 receptors and $K_V7.2/K_V7.3$ heteromers, 5-HT also failed to suppress currents (n = 14), whereas coexpressed muscarinic M_1 and bradykinin B_2 receptors mediated an inhibition. Recombinant 5-HT_{2A} and 5-HT_{2C} receptors, nevertheless, mediated increases in intracellular Ca^{2+}. In DRG neurons, 5-HT_2 receptor activation enhanced currents through TRPV1 channels.
Discussion: These results indicate that the 5-HT_2 receptor ligands (±)-DOI and ritanserin can interact with neuronal K_V7 channels independently of 5-HT_2 receptors. In DRG neurons, activation of 5-HT_2 receptors mediates enhanced excitability, an effect that involves sensitization of TRPV1 channels.

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