BMC Pharmacology

Meeting abstract

Nucleotides excite sensory neurons via two P2Y receptors and a dual signaling cascade

Arsalan Yousuf and Stefan Boehm*

Address: Institute of Pharmacology, Centre for Biomolecular Medicine and Pharmacology, Medical University of Vienna, 1090 Vienna, Austria

Email: Stefan Boehm* - stefan.boehm@meduniwien.ac.at

* Corresponding author

from 15th Scientific Symposium of the Austrian Pharmacological Society (APHAR) Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT) and the Slovenian Pharmacological Society (SDF)
Graz, Austria. 19-21 November 2009

Published: 12 November 2009

BMC Pharmacology 2009, **9**(Suppl 2):A17 doi:10.1186/1471-2210-9-S2-A17

This abstract is available from: http://www.biomedcentral.com/1471-2210/9/S2/A17

Background

Sensory neurons innervating the skin provide information about physical contact between organisms and the environment including stimuli that lead to pain sensation. Metabotropic P2Y receptors have been suggested to be important in the signaling of sensory neurons, but their effects and signaling mechanism remained controversial.

Methods

Patch-clamp recordings were performed in primary cultures of dorsal root ganglion (DRG) neurons from neonatal rats, P2Y receptor ligands and signaling interceptors were applied.

Results

ADP (EC_{50}: 7.5 μM), ATP (EC_{50}: 0.5 μM), UTP (EC_{50}: 0.8 μM), and thio-UTP (EC_{50}: 0.4 μM) increased the number of action potentials fired in response to current injection; UDP failed to affect action potential firing. The effect of ADP was attenuated by a $P2Y_1$ antagonist. This enhancement of excitability was abolished by flupirtine (30 μM), a K_V7 channel opener, and slightly, but insignificantly attenuated by iodoresiniferatoxin (0.3 μM). Under voltage clamp, the same nucleotides inhibited currents through K_V7 channels in a concentration-dependent manner with similar EC_{50} values. The $P2Y_1$-specific agonist MRS2365 also caused an inhibition of K_V7 channels (EC_{50} value of 8.68 nM), and the $P2Y_1$ antagonist MRS2179 attenuated the inhibition by ADP. Treatment of sensory neurons with the phospholipase C inhibitor U73122, with the Ca^{2+}-ATPase inhibitor thapsigargin, or the Ca^{2+} chelator BAPTA-AM abolished the inhibition of K_V7 channels by ADP. Moreover, ADP and ATP increased amplitudes of currents through TRPV1 receptors evoked by capsaicin.

Conclusion

Activation of $P2Y_1$ and $P2Y_2$ receptors increases the excitability of sensory neurons via a dual mechanism: an inhibition of K_V7 channels via phospholipase C and increases in intracellular Ca^{2+}, and a sensitization of TRPV1 receptors, with the former mechanism being the decisive one.

Acknowledgements

Supported by FWF.