

## The role of meningeal mast cells in ATP-induced nociceptive firing in trigeminal afferents. Anti-nociceptive effects of hydrogen sulfide

Guzel Sitdikova<sup>1</sup>, Ksenia Koroleva<sup>1</sup>, Elizaveta Ermakova<sup>1</sup>, Alsu Mustafina<sup>1</sup>, Rashid Giniatullin<sup>1,2</sup>

<sup>1</sup>*Dept of Human and Anim Physiol, Inst of Fundamental Med and Biol, Kazan Federal Univ, Kazan, Russia, <sup>2</sup>A. I. Virtanen Inst for Mol Sci, Univ of Eastern Finland, Kuopio, Finland*

ATP is one of the most prominent algogens, increasing the firing of trigeminal nerve, underlying the migraine pain. Extracellular ATP released during migraine attacks activates meningeal afferents via neuronal P2X3 receptors. In addition ATP induces meningeal mast cell degranulation releasing serotonin which further induces nerve terminal excitation via 5-HT3 receptors. Thus, serotonin can be considered as the endogenous amplifier of purinergic nociception in meninges. Hydrogen sulfide (H<sub>2</sub>S) is a member of gasotransmitters family, induces both pro- and anti-nociceptive action in different tissues. It was shown that H<sub>2</sub>S donor -sodium hydrosulfide (NaHS) transiently increased firing in trigeminal nerve by activation of TRPV1 receptors however prevented pro-nociceptive effects of ATP. Moreover, H<sub>2</sub>S decreased currents and Ca<sup>2+</sup> responses mediated by activation of P2X3 receptors in trigeminal neurons. Moreover, incubation of meninges in NaHS decreased ATP release and prevented mast cells degranulation. It was suggested that H<sub>2</sub>S may prevent pro-nociceptive effects of ATP in trigeminal system by inhibition of P2X3 receptors and stabilizing of meningeal mast cells. The work is supported by Russian Fund of Basic Research 18-315-00256