

Receptor mechanisms mediating the pro-nociceptive action of hydrogen sulfide in rat trigeminal neurons and meningeal afferents

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Abstract

© 2017 Koroleva, Mustafina, Yakovlev, Hermann, Giniatullin and Sitdikova. Hydrogen sulfide (H_2S), a well-established member of the gasotransmitter family, is involved in a variety of physiological functions, including pro-nociceptive action in the sensory system. Although several reports have shown that H_2S activates sensory neurons, the molecular targets of H_2S action in trigeminal (TG) nociception, implicated in migraine, remains controversial. In this study, using suction electrode recordings, we investigate the effect of the H_2S donor, sodium hydrosulfide (NaHS), on nociceptive firing in rat meningeal TG nerve fibers. The effect of NaHS was also explored with patch-clamp and calcium imaging techniques on isolated TG neurons. NaHS dramatically increased the nociceptive firing in TG nerve fibers. This effect was abolished by the TRPV1 inhibitor capsazepine but was partially prevented by the TRPA1 blocker HC 030031. In a fraction of isolated TG neurons, NaHS transiently increased amplitude of capsaicin-induced currents. Moreover, NaHS by itself induced inward currents in sensory neurons, which were abolished by the TRPV1 inhibitor capsazepine suggesting involvement of TRPV1 receptors. In contrast, the inhibitor of TRPA1 receptors HC 030031 did not prevent the NaHS-induced currents. Imaging of a large population of TG neurons revealed that NaHS induced calcium transients in 41% of tested neurons. Interestingly, this effect of NaHS in some neurons was inhibited by the TRPV1 antagonist capsazepine whereas in others it was sensitive to the TRPA1 blocker HC 030031. Our data suggest that both TRPV1 and TRPA1 receptors play a role in the pro-nociceptive action of NaHS in peripheral TG nerve endings in meninges and in somas of TG neurons. We propose that activation of TRPV1 and TRPA1 receptors by H_2S during neuro-inflammation conditions contributes to the nociceptive firing in primary afferents underlying migraine pain.

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Keywords

Ca²⁺-imaging, Hydrogen sulfide, Pain, Trigeminal nerve firing, Trigeminal neurons, TRPV1-and TRPA1 receptors

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