Hydrogen sulfide activates TRPV1 receptors in rat trigeminal neurons and increases the activity of trigeminal nerve

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Hydrogen sulfide (H_2S) a member of gasotransmitters family,is involved in regulation of great variety of physiological functions, including nociception and inflammation. H2S produced endogenously from L-cysteine by the enzymes cystathionine B;-synthase (CBS), cystathionine γ;-lyase (CSE) and 3-mercaptopyruvate sulfurtransferase (3-MST) along with additional contribution of cysteine aminotransferase (CAT) or D-amino acid oxidase (DAO). It was shown that CBS is abundantly expressed in rat TG neurons and H_2S donor - NaHS increases the excitability of trigeminal neurons by suppression of potassium conductance. In pathological inflammatory conditions, the increase of CBS expression in trigeminal neurons was demonstrated suggesting a role for H_2S in inflammation-induced hyperalgesia. Controversial data existed about the activating effects of H_2S on the family of TRP receptors, obtained in in vivo and vitro experiments.

The aim of our study was to reveal the effect of NaHS on the firing of trigeminal (TG) nerve using suction electrode recordings in peripheral branches of the TG nerve in isolated rat meninges. We also studied the effects of NaHS on TRPV1 currents by patch clamp recordings in isolated trigeminal neurons.

All animal experiments were performed in accordance with the European Community Council Directive of September 22, 2010 (2010/63/EEC) and approved by the Animal Care and Use Committee of University of Eastern Finland and the Ethics Committee of Kazan Federal University. Recordings of electrical activity of trigeminal nerve were performed using isolated rat hemiskull preparations obtained from adult (P35–36) rats at room temperature.

The TRPV1 currents were recorded in isolated trigeminal neurons from P9-P12 rats. TRPV1 currents were evoked by focal application of capsaicine in concentration 1 μM. Sodium hydrogen sulfide (NaHS) was used as donor of H_2S.

Bath application of NaHS (100 μM) increased the action potential frequency of trigeminal nerve and this effect was prevented by the inhibitor of TRPV1 receptors capsazepine (10 μM). At the same time NaHS increased the amplitude of capsaicine induced currents in isolated trigeminal neurons. Moreover the focal application of NaHS (100 μM) on trigeminal neurons induces inward currents which was inhibited by capsazepine. The obtained data suggest that NaHS directly activates TRPV1 receptors and induces the inward currents, which may increase the firing rate of trigeminal neurons.

We propose that activation of TRPV1 receptors by H_2S during chronic inflammation process is contributes to the increased excitability of the trigeminal system and may be implicated in the generation of nociceptive firing underlying migraine pain.

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