

Phosphorylation of BK channels modulates the sensitivity to hydrogen sulfide (H₂S)

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Abstract

© 2014 Sitdikova, Fuchs, Kainz, Weiger and Hermann. Introduction: Gases, such as nitric oxide (NO), carbon monoxide (CO) or hydrogen sulfide (H₂S), termed gasotransmitters, play an increasingly important role in understanding of how electrical signaling of cells is modulated. H₂S is well known to act on various ion channels and receptors. In a previous study we reported that H₂S increased calcium-activated potassium (BK) channel activity. Aims: The goal of the present study is to investigate the modulatory effect of BK channel phosphorylation on the action of H₂S on the channel as well as to recalculate and determine the H₂S concentrations in aqueous sodium hydrogen sulfide (NaHS) solutions. Methods: Single channel recordings of GH3, GH4 and GH4 STREX cells were used to analyze channel open probability, amplitude and open dwell times. H₂S was measured with an anion selective electrode. Results: The concentration of H₂S produced from NaHS was recalculated taking pH, temperature salinity of the perfusate and evaporation of H₂S into account. The results indicate that from a concentration of 300 μM NaHS, only 11-13%, i.e. 34-41 μM is effective as H₂S in solution. GH3, GH4 and GH4 STREX cells respond differently to phosphorylation. BK channel open probability (P_o) of all cells lines used was increased by H₂S in ATP containing solutions. PKA prevented the action of H₂S on channel P_o in GH4 and GH4 STREX, but not in GH3 cells. H₂S, high significantly increased P_o of all PKG pretreated cells. In the presence of PKC, which lowers channel activity, H₂S increased channel P_o of GH4 and GH4 STREX, but not those of GH3 cells. H₂S increased open dwell times of GH3 cells in the absence of ATP significantly. A significant increase of dwell times with H₂S was also observed in the presence of okadaic acid. Conclusions: Our results suggest that phosphorylation by PKG primes the channels for H₂S activation and indicate that channel phosphorylation plays an important role in the response to H₂S.

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Keywords

Gasotransmitters -Hydrogen sulfide (H₂S), GH cells, Maxi calcium-activated potassium (BK) channels, Patch clamp, Phosphorylation