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HYDROGEN SULFIDE (H_2S) AUGMENTS SYNAPTIC NEUROTRANSMISSION IN THE NUCLEUS OF THE SOLITARY TRACT (NTS)

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Hydrogen sulfide (H_2S) is a gasotransmitter generated through the metabolism of cysteine to serine. In the central nervous system, H_2S is produced primarily by the enzyme cystanthionine-β-synthase (CBS). The brainstem nTS serves as the principal site for sensory afferent integration for cardiorespiratory regulation. We sought to determine the role of H_2S, and its generation by CBS, in nTS excitability in normoxia and following chronic intermittent hypoxia (CIH), a rodent model of sleep apnea. Immunohistochemistry analysis examined CBS distribution and protein levels in the nTS. Patch clamp electrophysiology in brainstem slices examined excitatory postsynaptic currents (EPSCs) in nTS neurons. CBS-immunoreactivity was observed in select nTS neurons, the area postrema, and near blood vessels associated with glial cells. In normoxic cells, exogenous H_2S (10 μM) significantly increased the amplitude of spontaneous (s)EPSCs, solitary tract (TS)-EPSCs, and asynchronous (a)EPSCs. On the other hand, the CBS inhibitor aminooxyacetic (AOA, 1 mM) significantly reduced the frequency of sEPSCs and aEPSCs and the amplitude of TS-EPSCs. Following CIH, H_2S application and blockade of CBS increased and decreased, respectively, the amplitude of TS-EPSCs. However, synaptic responses to H_2S and AOA were similar between CIH and normoxic controls. In a subset of normoxic and CIH animals, an acute hypoxic challenge (10% O_2, 3 hr) activated nTS neurons as indicated by Fos-immunoreactivity, a portion which co-labeled with CBS-positive neurons as well, which suggests a functional role of H_2S. These data suggest endogenous H_2S plays a role in excitatory neurotransmission in the nTS and possibly chemoreflex function. Supported by HL085108