Domínguez Rodríguez *et al.: Intrinsic Activity*, 2016; **4**(Suppl.3):A4.18
http://www.intrinsicactivity.org/2016/4/S3/A4.18
published online: 5 September 2016

INTRINSIC ACTIVITY

22nd Scientific Symposium of the Austrian Pharmacological Society: Joint Meeting with the Hungarian Society for Experimental and Clinical Pharmacology

Vienna, 8–10 September 2016

MEETING ABSTRACT

A4.18

The role of hydrogen sulfide in autonomic nervous system

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Background: Hydrogen sulfide (H_2S) is a toxic gas also produced in mammalian tissues where it can exert various functions as gasotransmitter, such as opening of smooth muscle K_{ATP} channels resulting in vasorelaxation. Recently, H_2S was found to be synthesized and released in sympathetic ganglia and to potentiate ganglionic transmission [1], but the underlying mechanisms remained unclear.

Methods: Primary cultures of rat superior cervical ganglion (SCG) were used to determine release of previously incorporated [^{3}H]noradrenaline and to measure membrane potential and ion currents via the perforated patch clamp technique.

Results: In radiotracer release experiments, basal tritium overflow as well as outflow triggered by either electrical fields or depolarizing K^+ concentrations were enhanced by 0.1 to 1 mM of the H_2S donor NaHS in a concentration-dependent manner. In electrophysiological experiments, NaHS hyperpolarized the SCG membrane potential and reduced action potential firing, probably by direct activation of K_{ATP} channels. Supporting this hypothesis, we found that pre-inhibition of K_{ATP} channels attenuated the NaHS effect on action potential firing and membrane potential. In SCG neurons, hyperpolarization of membrane potential can be caused as well by an enhancement of currents through K_V7 channels [2]. Unexpectedly, NaHS inhibited currents through K_V7 channels in a concentration-dependent manner, whether endogenously expressed in SCG neurons or heterologously expressed in tsA cells. In addition, since H_2S potentiates ganglionic transmission [1] we studied the possible effect of NaHS on cholinergic miniature excitatory postsynaptic currents (mEPSC) in long-time cultured SCG neurons and found that NaHS increased their frequency, thus indicating an increase in the probability of acetylcholine release.

Discussion: These results show that H_2S hyperpolarizes SCG neurons and reduces membrane excitability. Since diazoxide, a K_{ATP} channel opener, shared this action and K_{ATP} blockers prevented the effects of H_2S, we conclude that the effect on membrane excitability was caused by an opening of K_{ATP} channels. In addition, H_2S inhibited K_V7 channels and increased the frequency of cholinergic mEPSCs. These excitatory actions most likely underlie the previously observed increase in ganglionic transmission.

Acknowledgements: M.D.R. and I.S. are members of the doctoral programme “Cell Communication in Health and Disease” (CCHD), co-financed by the Medical University of Vienna and the Austrian Science Fund FWF (W1205).

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