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Effect of hydrogen sulfide on sensory neurogenic relaxation in the rat mesenteric arterial bed

Introduction: Recently, *exogenous* hydrogen sulphide (H_2S) has been shown to cause vasorelaxation through activation of TRPA1 channels on sensory nerves in rat mesenteric arterial segments (White et al., 2013). H_2S has been detected within perivascular adipose tissue (PVAT) (Fang et al., 2009). However, little is known about the crosstalk between H_2S and sensory nerves.

Methodology: Mesenteric arterial beds (MABs), vascular preparations which are surrounded with substantial amounts of PVAT, were used to investigate the crosstalk. MABs (with and without PVAT, removed by careful dissection) isolated from adult male Wistar rats (220-250g, n≥4) were perfused at 5 ml min^{-1} with Krebs' solution and electrical field stimulation (EFS; 0.5-12Hz, 0.1ms, 60V, 30s) applied in the absence/presence of pharmacological agents. Vasodilator responses of the preparations were measured as decreases in perfusion pressure (mmHg). The maximum relaxation response (R_{max}) was determined using non linear regression and Student's t-test was used to compare the responses at each concentration between two groups. $P<0.05$ was considered significant.

Results: Sodium sulfide (Na_2S; 1-300μM), a H_2S donor by a chemical reaction, caused concentration-dependent vasodilation and this effect was attenuated ($P<0.001$) by 30 minutes incubation with HC030031 (100μM), a TRPA1 antagonist and 30 minutes pre-treatment with capsaicin (10μM), a TRPV1 agonist which can cause CGRP depletion. When a second response curve to Na_2S was generated in the same preparation, the vasodilator response was greatly attenuated ($P<0.001$). EFS elicited frequency-dependent vasodilatation due to stimulation of sensory nerves but these responses were attenuated ($P<0.01$) in the presence of Na_2S (10μM). The 30 minutes incubation with H_2S-synthesizing enzyme inhibitors DL-propargylglycine (10μM), aminooxyacetic-acid (100μM) and aspartate (1mM) (inhibitors of cystathionine-γ-lyase, cystathionine-β-synthase and 3-mercaptopyruvate-sulphur-transferase, respectively) had no significant effect on EFS-evoked neurogenic vasodilatation.

Conclusion: In conclusion, H_2S causes vasodilatation of MABs by activating sensory nerves through the TRPA1 signalling pathway, and subsequently impairs sensory nerve function, demonstrating a capsaicin-like action. H_2S-producing enzymes and *endogenous* H_2S are not involved in EFS-evoked neurogenic vasodilator responses under the conditions of the present study.

References:

Fang et al. (2009). Journal of Hypertension, **27**, 2174–2185

White et al. (2013) British Journal Pharmacology, **168,** 785-793