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effect on increased GMBF in response to TRH. Vagal stimulation markedly increased gastric acid secretion, GMBF and contraction, without affecting SBF. TRH significantly inhibited the gastric functional changes induced by electrical stimulation of the vagus nerve. [Conclusion] These data suggest that while gastric functional changes induced by TRH mainly occur through stimulation of the vagus nerve, these responses are extensively modified by the sympathetic nervous system.

P6.3.3

THE NEURONAL AND PHYSICAL ASPECTS OF ADAPTIVE CYTOPROTECTION AGAINST ETHANOL-INDUCED GASTRIC MUCOSAL DAMAGE.

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Most studies have emphasised the role of endogenous neuronal mediation in gastric adaptive cytoprotection; however, the contribution of the physical properties of some mild irritants to this protective action is still unclear. This study demonstrates the cytoprotective abilities of low concentrations of ethanol, NaCl or HCl, against mucosal damage by 100% ethanol. Distilled water (control), ethanol (10-30%), NaCl (2.5-12.5%) or HCl (0.15-0.45M) was given orally to male Sprague-Dawley rats (240-260g) 15 min before administration of 100% ethanol. In order to investigate the involvement of endogenous mediators in the cytoprotection of the mild irritants, indomethacin (5 mg/kg, s.c. 1 h beforehand), N^{w}-nitro-L-arginine methyl ester (L-NAME, 12.5 mg/kg, i.v. 15 min beforehand) or [D-Pro^{2}, D-$Trp^{7,9}$]-substance P (1 μmol/L per 100g, i.p. 15 min beforehand) was administered to inhibit endogenous synthesis of prostaglandins (PGs), nitric oxide (NO) or substance P (SP), respectively. The contribution of the physical factors and chemical properties of the mild irritants to cytoprotection was studied by using different concentrations of NaCl, KCl, HCl, H_2SO_4 or mannitol. Other alcohols with the same concentrations as ethanol, or other salts or acids with similar osmolarity to NaCl or HCl were also examined for cytoprotective abilities. The results show that the optimal cytoprotective concentrations of the mild irritants are: 20% ethanol, 5% NaCl and 0.3M HCl. The cytoprotective action of 20% ethanol (not of 5% NaCl or 0.3M HCl) was abolished by indomethacin or L-NAME, but not by the SP antagonist. Methanol or propan-2-ol, given in the same concentration as ethanol, also showed cytoprotective effects. Hypertonic solutions of KCl, NaCl, H_2SO_4 or HCl, of the same osmolarity, showed similar cytoprotective potentials. In addition, the osmotic agent, mannitol, also possessed a concentration- and tonicity-dependent protective action. It is concluded that adaptive cytoprotection induced by a low concentration of ethanol involves neuronal mediation through PGs and NO; the action of NaCl and HCl depends on their hypertonic property, because this is simulated by the hyperosmotic action of mannitol which protected against ethanol-induced mucosal damage.

P6.3.5

HISTAMINE H3 RECEPTORS AND GASTRIC MUCOSAL PROTECTION

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The histamine H3 receptor subtype has been involved in the inhibitory control of gastric acid secretion in different species. In the present study the effect of the selective agonist (R) α-methylhistamine (MHA) was tested for its possible gastroprotective effect against gastric lesions induced by different stimuli: absolute ethanol (1 ml i.g.), aspirin (200 mg/kg i.g. in 0.15 N HCl) and stress (restraint