EFFECTS OF TETRAETHYLAMMONIUM ON THE NON-ADRENERGIC NON-CHOLINERGIC RELAXATION OF THE RAT GASTRIC FUNDUS

1)Ipavec V.. 2)Currò D..

Università Cattolica del Sacro Cuore

K+ channels play important roles in setting the membrane potential and modulating overall excitability and firing rates of excitable cells. The aim of this study was to characterize the effects of the non-selective K+ channel blocker tetraethylammonium (TEA) on non-adrenergic non-cholinergic (NANC) relaxation of the proximal stomach. NANC relaxations were induced by electrical field stimulation (EFS, 2 or 13 Hz, 2 min) of U46619 (0.1 μM)-precontracted rat gastric fundus strips mounted inside 5-ml organ baths containing Krebs solution maintained at 37° C and continuously bubbled with carbogen under NANC conditions (1 M atropine + 5 M guanethidine). The relaxant responses induced by 2 Hz or 13 Hz EFS were measured as peak amplitudes or areas under the curves (AUCs), respectively, which are mainly due to nitric oxide, the first, and vasoactive intestinal polypeptide, the second. All responses were normalized by dividing them for the maximal relaxation induced by papaverine (300 M). The effects of TEA (1-10 mM), and the combination of TEA (3 mM) with the selective high-conductance Ca2+-activated K+ (KCa 1.1) channel blocker iberiotoxin (IBTX, 50 nM) or the selective KCNQ voltage-gated K+ (KV 7) channel blocker XE-991 (20 M) were studied. TEA significantly increased the amplitude of EFS (2 Hz)-induced relaxation at all concentrations tested, with the maximal increase observed at the concentration of 3 mM (by 38.76.6 %, n=7, P<0.01, of controls). Neither the addition of IBTX (50 nM) nor that of XE-991 (20 μM) to TEA (3 mM) produced significantly higher increases in the relaxation amplitude (by 42.5±3.1 %, n=7, p<0.001, and 39.4±9.4 %, n=7, p<0.01, of controls, respectively). TEA (1-10 mM) significantly increased also the AUC of EFS (13 Hz)-induced relaxant response, with the maximal increase induced at the concentration of 10 mM (by 45.55.6 %, n=8, P<0.001, of controls). The addition of IBTX (50 nM) to TEA (3 mM) did not produce AUC increases significantly higher than those induced by TEA (3 mM) (by 30.2±4.9 %, n=7, p<0.01, and 29.8±6.1 %, n=7, p<0.01, of controls, respectively). The AUC of EFS (13 Hz)-induced relaxation observed with TEA (3 mM) plus XE-991 (20 μM) in the bath was not significantly different from that of the control relaxation (95.6±5.4 %, n=8), finding probably related to the blockade of KV7.4 channels in the smooth muscle cells by XE-991. These data indicate that K+ channels blocked by TEA are involved in the modulation of neurotransmitter release from the inhibitory motor neurons of the proximal stomach. Very probably, these channels are mainly identifiable with KCa 1.1 and KV 7.2 channels, to which TEA is known to bind, among others, at the concentrations used.