Effect of Nicotine on Peptidergic Vasodilator Nerve Function in Mesenteric Resistance Blood Vessels of the Rat

We have reported that, in the rat mesenteric artery, nicotine caused a concentration-dependent and endothelium-independent vasodilator response, which is mediated by capsaicin-sensitive nerves and is associated with the intact adrenergic nerves. In the present study, mechanisms underlying the nicotine-induced vasodilation were further investigated in the rat mesenteric resistance blood vessels. Isolated mesenteric vascular beds without endothelium were perfused with Krebs solution and contracted by 2.5 μM methoxamine and perfusion pressure was measured with a pressure transducer. Vasodilation induced by nicotine (100 μM) was inhibited only by the nicotinic receptor α3β4 subtype antagonist mecamylamine (1 and 10 μM). Bolus injections of HCl (0.1 N) induced long-lasting vasodilation, which was inhibited by capsaicin, capsazepine, ruthenium red, CGRP (8-37) and denervation. Immunohistochemical staining of the mesenteric artery showed dense innervation of CGRP- and vanilloid receptor-1-positive nerves, with both immunostainings appearing in the same neuron. Double immunostainings showed that both NPY- and CGRP-immunoreactivities appeared in the same neuron. These results suggest that vanilloid receptors on CGRP ergic nerves are activated by proton released by nicotine to cause vasodilation in the mesenteric resistance artery of the rat.