Effects of catecholamine (CA) metabolites on β-adrenoceptor (β-AR)-mediated relaxation evaluated in mouse/guinea pig (GP) trachea and rat thoracic aorta (TA)

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Effects of CA metabolites on β-AR-mediated relaxation were investigated in mouse (β_1)/GP (β_2) trachea and rat TA (β_3). Among tested seven CA metabolites, metadrenaline (MA) relaxed GP trachea even in the presence of clorgiline (CLG, MAO_A inhibitor). In mouse trachea, only in the presence of CLG, normetadrenaline (NMA) and MA significantly inhibited isoprenaline (ISO)-induced relaxation, which was also inhibited by 3,4-dihydroxyphenylglycol (DHPG) in the presence of 3,5-dinitrocatechol (3,5-DNC, COMT inhibitor). In GP trachea, NMA, MA, 3,4-dihydroxymandelic acid (DOMA), and DHPG significantly augmented ISO-induced relaxation, which was inhibited by NMA, and MA in the presence of 3,5-DNC or CLG plus 3,5-DNC, and by DHPG in the presence of 3,5-DNC. In rat TA, DHPG significantly inhibited the relaxation to CGP-12177A (β_3-AR partial agonist) in the presence of 3,5-DNC. Our findings indicate that 1) MA may have β_2-AR agonistic action; 2) NMA/MA have β_1-/β_2-AR antagonistic action although they enhance β_2-AR-mediated tracheal relaxation in the absence of CA metabolic inhibitors; 3) DHPG shows β_1-/β_2-/β_3-AR antagonistic action, and this is particularly remarkable for β_3-AR. Our observations may partly explain some of the pathologies associated with pheochromocytoma, which is characterized by elevated CA metabolites levels.