



Functional and molecular identification of 5-hydroxytryptamine receptors in rabbit pulmonary artery: involvement in complex regulation of noradrenaline release

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Abstract:

The rabbit pulmonary artery was used to examine whether presynaptic serotonin (5-HT) receptors modulate noradrenaline (NA) release also in this blood vessel and to confirm their presence with molecular biology techniques. Arteries preincubated with [³H]NA were superfused in the presence of the α_2 -adrenoceptor blocker rauwolscine and the effects of 5-HT receptor ligands on the electrically evoked ³H overflow were determined. The 5-HT₄ receptor agonist cisapride inhibited ³H overflow in a manner sensitive to blockade by atropine. The 5-HT_{1B/1D} receptor agonist 5-carboxamidotryptamine inhibited ³H overflow only in the presence of atropine. The 5-HT₄ and 5-HT_{1B/1D} receptor agonists 5-HT and 5-methoxytryptamine reduced ³H overflow in the absence and presence of atropine, and this effect was blocked by methiothepin, a non-selective 5-HT receptor antagonist, in the presence of atropine. PCR with cDNAs derived from reverse transcribed blood vessel mRNA suggested the expression of the 5-HT_{1B}, 5-HT_{1D} and 5-HT₄ receptors, the latter being highly homologous to the human one. In conclusion, the cholinergic nerves are endowed with excitatory 5-HT₄ receptors mediating release of acetylcholine which, in turn, activates muscarinic receptors on the sympathetic nerves leading to inhibition of NA release. Blockade of the presynaptic muscarinic receptors involved is necessary to disclose an inhibition of NA release *via* 5-HT_{1B/1D} receptors. Taking results reported in the literature into account, the 5-HT_{1D} and 5-HT₄ receptors identified by molecular biology techniques probably are located predominantly on the noradrenergic and cholinergic neurons, respectively.

Key words:

presynaptic 5-HT receptor, pulmonary artery, neuron interaction, receptor interaction, 5-HT heteroreceptor, 5-HT₄ receptor, 5-HT_{1B/1D} receptor, mRNA expression
