Antitussive effects of α2-adrenergic receptor agonists in the rabbit

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We investigated the effects of the α2-adrenergic receptor agonists clonidine and tizanidine microinjected (30-50 nl) into the caudal nucleus tractus solitarii (cNTS) and the caudal ventral respiratory group (cVRG) as well as administered intravenously on cough responses induced by mechanical and chemical (citric acid) stimulations of the tracheobronchial tree in pentobarbital sodium-anesthetized, spontaneously breathing rabbits. Bilateral microinjections of clonidine into the cNTS or the cVRG reduced cough responses at 0.5 mM and abolished the cough reflex at 5 mM. Bilateral microinjections of 0.5 mM tizanidine into the cNTS completely suppressed cough responses, whereas bilateral microinjections of 5 mM into the cVRG only caused mild reductions of them. Microinjections of 10 mM yohimbine completely reverted depressant effects on the cough reflex induced by clonidine and tizanidine. Downregulation of the cough reflex was also observed after intravenous administration of clonidine (80-120 μg/kg) or tizanidine (150-300 μg/kg). These effects were reverted by intravenous administration of yohimbine (300 μg/kg). Taken together, present results demonstrate that medullary α2-adrenergic receptors exert potent inhibitory effects in the central sensory pathways involved in the genesis of the cough motor pattern and confirm that both the cNTS and the cVRG are important components of the neural system involved in the central regulation of cough. Our results are at variance with previous data obtained in guinea pigs and humans (O'Connell et al. J Appl Physiol 1994;76:1082-1087). However, recently it has been shown that the intravenous administration of clonidine depresses fentanyl-induced cough in humans (Horng et al. Acta Anaesthesiol. Scand. 2007; 51:862-865). In the light of the strong α2-adrenergic receptor agonist-induced effects on cough responses in the rabbit, we suggest that this subject deserves further investigations. Finally, present data also encourage further studies to develop novel antitussive α2-adrenergic compounds.

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