Epinephrine enhances the sensitivity of rat vagal chemosensitive neurons: role of β3-adrenoceptor

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摘要

Abstract

This study was carried out to determine whether epinephrine alters the sensitivity of rat vagal sensory neurons. In anesthetized rats, inhalation of epinephrine aerosol (1 and 5 mg/ml, 3 min) induced an elevated baseline activity of pulmonary C-fibers and enhanced their responses to lung inflation (20 cmH2O, 10 s) and right atrial injection of capsaicin (0.5 μg/kg). In isolated rat nodose and jugular ganglion neurons, perfusion of epinephrine (3 μM, 5 min) alone did not produce any detectable change of the intracellular Ca2+ concentration. However, immediately after the pretreatment with epinephrine, the Ca2+ transients evoked by chemical stimulants (capsaicin, KCl and ATP) were markedly potentiated; for example, capsaicin (50 nM, 15 s) - evoked Ca2+ transient was increased by 106% after epinephrine ($P < 0.05$; $n = 11$). The effect of epinephrine was mimicked by either BRL 37344 (5 μM, 5 min) or ICI 215,001 (5 μM, 5 min), two selective β3-adrenoceptor agonists, and blocked by SR 59230A (5 μM, 10 min), a selective β3-adrenoceptor antagonist; whereas pretreatment with phenylephrine (α1-adenoceptor agonist), guanabenz (α2-adrenoceptor agonist), dobutamine (β1-adrenoceptor agonist) or salbutamol (β2-adrenoceptor agonist) had no significant effect on capsaicin-evoked Ca2+ transient. Furthermore, pretreatment with SQ 22536 (100 300 μM, 15 min), an adenylate cyclase inhibitor, and H89 (3 μM, 15 min), a PKA inhibitor, completely abolished the potentiating effect of epinephrine. Our results suggest that epinephrine enhances the excitability of rat vagal chemosensitive neurons. This sensitizing effect of epinephrine is likely mediated through the activation of β3-adrenoceptor and intracellular cAMP-PKA signaling cascade.