Sensitization of capsaicin-sensitive lung vagal afferents by anandamide in rats: the role of transient receptor potential vanilloid 1 receptors (in press)

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摘要

Abstract

Anandamide (AEA), an arachidonic acid derivative produced during inflammatory conditions, is an endogenous agonist of both transient receptor potential vanilloid 1 (TRPV1) receptors and cannabinoid CB1 receptors. Sensitization of capsaicin-sensitive lung vagal afferent (CSLVA) fibers by chemical mediators is important in the pathogenesis of hyperreactive airway diseases. We investigated the effect of the intravenous infusion of AEA (2 mg/kg/ml, 0.5 ml/min for 2 min) on the sensitivity of CSLVA fibers to chemical and mechanical stimulation in anesthetized rats. In artificially ventilated rats, AEA infusion only mildly elevated the baseline activity of CSLVA fibers. However, CSLVA fiber responses to a right atrial injection of capsaicin, AEA or adenosine, and to lung inflation (tracheal pressure = 30 cmH2O) were all markedly potentiated during AEA infusion, which reverted 20 min after termination of the infusion. The potentiating effect on the sensitivity of CSLVA fibers to adenosine injection or lung inflation was completely blocked by pretreatment with capsazepine (a TRPV1 receptor antagonist), but was unaffected by pretreatment with AM281 (a CB1 receptor antagonist). In spontaneously breathing rats, the right atrial injection of adenosine evoked an apneic response that is presumably mediated through CSLVA fibers. Similarly, the adenosine-evoked apneic response was potentiated during AEA infusion and this potentiating effect was also completely prevented by pretreatment with capsazepine. These results suggest that AEA infusion at the dose tested produces a mild activation of 3 TRPV1 receptors and this nonspecifically increases CSLVA fiber sensitivity to chemical and mechanical stimulation