Mediator mechanisms involved in TRPV1 and P2X receptor-mediated, ROS-evoked bradypneic reflex in anesthetized rats

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摘要

Abstract

Inhalation of H2O2 is known to evoke bradypnea followed by tachypnea, which are reflexes resulting from stimulation by reactive oxygen species of vagal lung capsaicin-sensitive and myelinated afferents, respectively. This study investigated the pharmacological receptors and chemical mediators involved in triggering these responses. The ventilatory responses to 0.2% aerosolized H2O2 were studied before and after various pharmacological pretreatments in anesthetized rats. The initial bradypneic response was reduced by a transient receptor potential vanilloid 1 (TRPV1) receptor antagonist [capsazepine; change () = − 53%] or a P2X purinoceptor antagonist [iso-pyridoxalphosphate-6-azophenyl-2',5'-disulphonate (PPADS); = − 47%] and was further reduced by capsazepine and iso-PPADS in combination (= − 78%). The initial bradypneic response was reduced by a cyclooxygenase inhibitor (indomethacin; = − 48%), ATP scavengers (apyrase and adenosine deaminase in combination; = − 50%), or capsazepine and indomethacin in combination (= − 47%), was further reduced by iso-PPADS and indomethacin in combination (= − 75%) or capsazepine and ATP scavengers in combination (= − 83%), but was not affected by a lipoxygenase inhibitor (nordihydroguaiaretic acid) or by any of the various vehicles. No pretreatment influenced delayed tachypnea. We concluded that 1) the initial bradypneic response to H2O2 results from activation of both TRPV1 and P2X receptors, possibly located at terminals of vagal lung capsaicin-sensitive afferent fibers; 2) the functioning of the TRPV1 and P2X receptors in triggering the initial bradypnea is, in part, mediated through the actions of cyclooxygenase metabolites and ATP, respectively; and 3) these mechanisms do not contribute to the H2O2-evoked delayed tachypnea.