

TRPA1 VERSUS TRPV1 RECEPTORS ACTIVATION IN COUGH

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TRPA1 receptor has become of interest in the cough because it is known to be activated by a number environmental pollutant and endogenous inflammatory irritants relevant for respiratory diseases. Inhalation of the TRPA1 agonists initiates cough in humans and guinea pigs, however the information on the pharmacology of the TRPA1-mediated cough is still limited. In our study we evaluated the efficacy of TRPA1-mediated cough in conscious guinea pig comparing with TRPV1-mediated cough. Inhalation of the TRPA1 agonist allyl-isothiocyanate (AITC) evoked cough with a maximally effective concentration of 10mM (n=12) that was abolished with a selective TRPA1 antagonist AP-18(1mM) (n=8, p<0.05). The maximally-effective concentration of AITC (10mM) was approximately 3-times less effective to induce cough than the sub-maximally effective concentration of the TRPV1 agonist capsaicin (50µM). Ex vivo single fiber recordings showed that AITC was 3-times also less effective that capsaicin in evoking sustained activation of the cough triggering tracheal jugular C-fibres. Another TRPA1 agonist cinnamaldehyde (CIA, 10mM) was surprisingly 2-fold more effective than AITC to induce cough. TRPA1 antagonists were less effective to inhibit the cough induced by CIA. The CIA-induced cough was only partially inhibited by AP-18 (1mM) (by ~60%, n=8), but completely abolished by combination of AP-18 and the TRPV1 antagonist I-RTX (30µM) (n=6, p<0.05) indicating contribution of TRPV1 to cough evoked by CIA in this setting. Conclusion: The TRPA1 activation initiates cough that is relatively modest compared to cough initiated by the TRPV1 activation.

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