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Title: Lessons learned from apnoe in cough down regulation

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Body: Afferents from the nose do not trigger cough, but the reflex is sensitized by experimental rhinitis. Most published data suggest that nasal sensory nerves are involved in up-regulation of cough, little evidence is available to support down-regulation of it from nose. Based on the data published recently about suppression of cough during water induced apnoe (Poussel et al., 2012), we decided to conduct a study on the model of irritant induced nasal apnea. Dunkin Hartley guinea pigs (n=8) were anaesthetized and tracheotomized. Trachea was lengthwise open at the proximal end and superfused with oxygenated saline. Cough was induced after nasal allylisothiocyanate AITC (TRPA1 agonist) by application of citric acid (CA) to the tracheal surface in ascending concentrations (0.001 - 2 M). Cough was also induced in conscious animals (n=22) by inhaling 0.4M CA for 10 min after nasal AITC. Cough response was estimated from the airflow traces and cough sound analysis. In anaesthesia, nasal AITC induced drop of respiratory rate (RR) $p < 0.05$ and cough induced afterwards by CA was suppressed when comparing to control data (8 vs 7 vs 4, $p<0.05$). In awake animals, nasal AITC induced reproducible, dose dependent symptoms, including drop of RR, $p = 0.05$. Cough induced by inhalation of CA was suppressed after nasal AITC ($p<0.05$), and this effect was prevented by supramaximal concentration of AP-18 TRPA1 antagonist. While suppression of cough in anaesthetized model could be attributed to apnoe/hypopnoea, explanation of the results in conscious animals needs complex approach. There are important issues of the consciousness (C-fiber signalling), mucus overproduction and central coordination of cough and sneeze.