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The effect of pain conditioning on experimentally evoked cough: evidence of impaired endogenous inhibitory control mechanisms in refractory chronic cough

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Painful cold-water hand immersion elicited a weaker inhibitory effect on cough in patients with refractory chronic cough than healthy volunteers, suggesting a relative deficiency in conditioned pain modulation <https://bit.ly/3gedtjg>

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ABSTRACT The pathophysiology of refractory chronic cough (RCC) is unclear. We hypothesised that endogenous inhibitory control mechanisms, such as those activated by noxious stimuli inducing pain (conditioned pain modulation) may be capable of inhibiting coughing and urge to cough evoked by inhaled capsaicin. Furthermore, these mechanisms may be impaired in patients with RCC.

The objective was to investigate the effects of pain on cough and urge to cough in healthy volunteers and RCC patients. Healthy volunteers and RCC patients underwent a randomised, controlled, four-way crossover study comparing the effect of four interventions on capsaicin-evoked coughing and urge to cough. The interventions comprised immersing a hand in 1) noxious cold water; 2) warm water; 3) warm water, but subjects were instructed to voluntarily suppress coughing; and 4) no intervention. The co-primary outcomes were numbers of evoked coughs and urge to cough scores.

20 healthy volunteers (mean±SD age 50.1±14.2 years, male:female 10:10) and 20 RCC patients (age 60.1±7.9 years, male:female 9:11) participated. Overall, noxious cold water reduced capsaicin-evoked urge-to-cough scores and cough numbers compared with warm water (1.6 (95% CI 1.3–2.0) *versus* 2.2 (1.8–2.6), $p<0.001$ and 4.8 (3.7–6.2) coughs *versus* 7.9 (6.7–9.5) coughs, $p<0.001$, respectively). Healthy volunteers and RCC patients demonstrated similar reductions in the urge to cough during noxious cold-water immersion, but noxious cold water and voluntary suppression interventions were less effective at reducing capsaicin-evoked cough in RCC patients than in healthy volunteers ($p=0.041$).

Endogenous inhibitory control mechanisms, specifically those activated by pain, can reduce both coughing and the urge to cough. Impairment of endogenous inhibitory control mechanisms may contribute to excessive coughing in RCC.

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