

Results Samples from 14 patients (11 males, mean age 56 years) with the Cough Hypersensitivity Syndrome and 10 lung resection samples (6 males, mean age 68 years) were obtained. All the tissue samples stained for TRPA1. The TRPA1 stain was avidly taken up by the bronchial epithelium, smooth muscle bundles and nerve tissue.

Conclusion We have described the distribution of the TRPA1 ion channel in lung tissue. TRPA1 is agonised by several environmental irritants and endogenous mediators of inflammation. The presence of TRPA1 ion channel in bronchial mucosal nerves and epithelium suggests an important role in the cough reflex. The identification of these ion channels on smooth muscle could suggest a role in asthmatic inflammation as well.

S142 INVESTIGATING PATTERNS IN 24 HOURS OF COUGHING

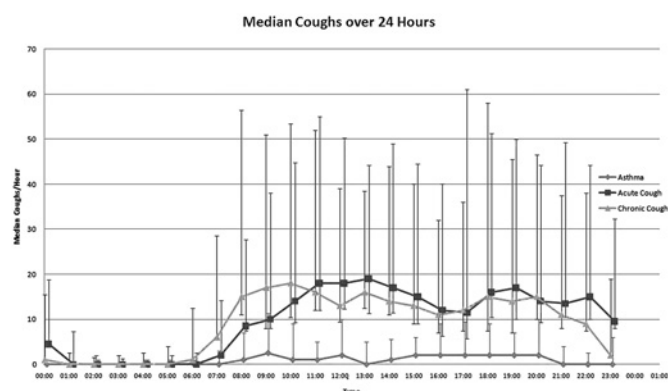
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Introduction and Objectives Ambulatory 24 h cough monitoring is a relatively new technique, and so far few studies have investigated hourly variation in cough frequency. We analysed data from previous studies in three different disease groups to compare patterns throughout the day.

Methods We studied chronic cough (duration >8 weeks) [n=70, median age 58 yrs (IQR 49–64), 67.1% female], acute cough in otherwise healthy volunteers (duration <3 weeks) [n=56, median age 22 yrs (IQR 21–25.5), 62.5% female] and physician diagnosed asthma [n=58, median age 58.5 yrs (IQR 52–67.8), 63.8% female]. Subjects wore a cough monitor (Vitalojak) for 24 h and median numbers of coughs in each hour were manually counted and plotted against the actual time of day.

Results The asthmatic group had significantly lower total cough rates compared with the other groups (geometric mean 2.3 coughs/hr (SD±3.3); chronic cough 13.1 (±2.7); acute cough 8.9 (±2.63); p<0.001). Abstract S142 figure 1 shows the median coughs in each hour of the day (interquartile ranges). The chronic and acute cough groups show a very similar cough frequency and pattern, with two peaks during the daytime, despite substantial variability. The asthma group show a similar pattern but with much lower counts. For all diagnosis coughing practically ceases overnight.



Abstract S142 Figure 1

Conclusions These data suggest that cough frequency in acute and chronic cough are remarkably similar, implying similar mechanisms may be driving coughing in these conditions, unlike in asthma

where cough frequency is much lower. However all groups show similar fluctuations in hour to hour pattern of daytime cough and effective suppression of coughing during sleep, indicating behaviour has an important influence.

S143 THE SENSATIONS PROVOKING COUGH: A QUALITATIVE INVESTIGATION

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Background Little is known about the sensations patients feel prior to or that provoke their cough.

Aims To identify, from the patient's perspective, key descriptors that relate to the sensations provoking cough in patients diagnosed with one of the following: idiopathic cough, asthma, chronic obstructive pulmonary disease (COPD), fibrotic interstitial lung disease (ILD) and cystic fibrosis.

Methods One-to-one, audio recorded, semi-structured interviews were conducted with 34 participants (7 idiopathic cough: age 40–69 years, 5 female, 6 asthma: age 42–65 years, 5 female, 7 COPD: age 52–86 years, 2 female, 7 ILD: age 58–79 years, 3 female, 7 cystic fibrosis: age 20–39 years, 2 female). Words and phrases relating to 1 of 8 top level codes, derived from the interview topic guide (triggers, sensation, sputum, emotion, location, frequency, time and relief) were extracted using simple manifest content analysis. These descriptions were then organised into similar themes. Relationships between the descriptions and themes both within and between the groups were explored.

Results All groups described the sensation of a "tickle" or an "irritation" that was felt most in the throat and upper chest. Cystic fibrosis and COPD participants most commonly described feeling a "need to clear" their airways. The ILD group mostly described a "dry", "tickly" sensation. The idiopathic cough and asthma groups used a very heterogeneous set of terms regarding the sensations provoking their cough. Common across the groups is a hyper-sensitive response to things that may trigger their urge to cough and all groups described coughing as relieving that urge. Emotionally the sensation is associated with negative emotions, however positive feelings were also described; by some who described feeling a need to clear their airways.

Conclusion The extracted list of descriptions has provided some insight into what the sensations provoking cough feel like from patient's perspective and suggest that the sensations felt relate to the pathology of the individual's diagnosis. The distinction between the need to clear and a sensation of a tickle or irritation could be important in understanding the mechanisms driving cough and may be important for the development of targeted interventions.

S144 ACUTE COUGH: A LONGITUDINAL OBSERVATIONAL STUDY

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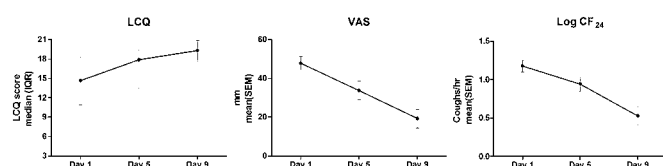
Introduction Acute cough is a common illness with more than 12 million episodes each year in the UK. More than £100 million is

spent on over-the-counter cough medicines annually, despite limited evidence to support their efficacy. The optimal cough assessment outcome parameter for clinical evaluation of anti-tussive drugs is not known. We investigated the natural course of acute cough with objective and subjective cough assessment tools.

Methods 32 healthy subjects with acute cough due to upper respiratory tract infection (median (IQR) age 30 (32–35) years, 63% female, mean (SEM) duration of cough 4.2 (0.4) days) were recruited for evaluation. Subjects taking anti-tussives were excluded. Assessments of cough severity included objective 24-h ambulatory cough frequency monitoring with the Leicester Cough Monitor, health related quality of life (HRQOL) with the Leicester Cough Questionnaire-Acute (LCQ) and cough severity visual analogue scale (VAS). Assessments were performed at baseline (day 1) and then 4 and 8 days later. Global rating of change questionnaires were completed by patients at each follow-up to assess change in cough severity and determine minimal important difference.

Results At baseline, the median (IQR) LCQ score was 14.7 (10.9–18.3) and mean (SEM) cough VAS was 48 (4) mm, consistent with a severe cough associated with significant impairment in HRQOL. Geometric mean (logSD) 24-h cough frequency (CF₂₄) at baseline was 15.0 (0.4) coughs/hr, and at days 5 and 9 were 8.7 (0.5) and 3.4 (0.7) coughs/hr respectively. At day 5, 3 subjects reported no change, 9 mild, 14 moderate and 6 large change in their cough severity. At day 9, 6 subjects reported mild, 5 moderate and 20 large change in cough severity. The minimal important difference on day 5 for the LCQ was 2.0, VAS 17 mm and CF₂₄ 54% change from baseline.

Conclusions Acute cough is associated with a significant cough frequency and impairment in HRQOL. We suggest clinical trials of anti-tussive drugs should incorporate objective and subjective cough assessment outcome measures. Anti-tussive drugs need to demonstrate a considerable reduction in cough frequency (>54% over a 4-day interval) to establish clinically important efficacy.



Abstract S144 Figure 1 Change in health related quality of life, cough severity VAS and cough frequency in acute cough.

S144a ENDOGENOUS INHIBITION OF EXPERIMENTALLY INDUCED COUGH IN HEALTHY SUBJECTS

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Background The pathophysiology of chronic cough may include peripheral/central sensitisation of afferent pathways and/or a failure of inhibitory pathways. Cough can be voluntarily suppressed in healthy subjects, but the role of endogenous inhibition is unknown. Endogenous inhibitory pain pathways can be activated by applying a painful conditioning stimulus to one body part, to inhibit pain elsewhere, described as “Diffuse Noxious Inhibitory Controls”.

Aim To investigate if a painful conditioning stimulus applied to the hand would inhibit cough in healthy subjects.

Methods This was a randomised, 4-way, cross-over study. The EC50 dose of capsaicin was pre-determined (inducing at least 50% maximal cough frequency) at screening, and subsequently administered at each of the 4 visits (>48 h apart) in 2 blocks (1 h apart) of 4 inhalations (15 s apart), simultaneous with a randomised intervention:

B: Basal-no intervention (both blocks)

W: Warm-hand placed in non-painful 32°C water (both blocks)

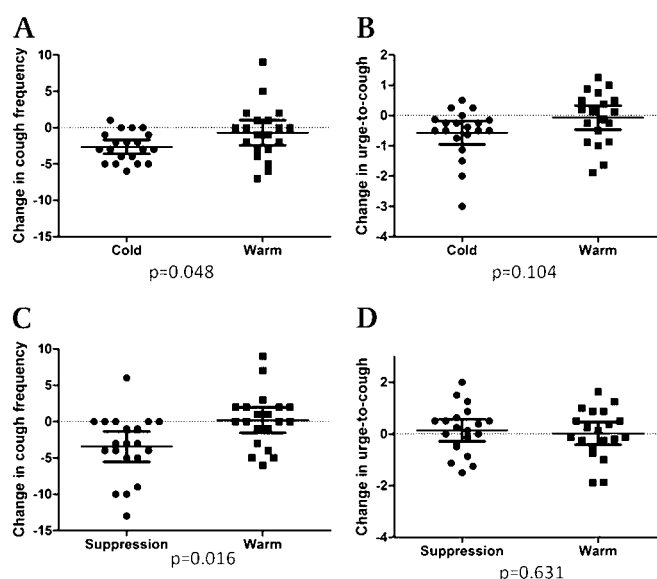
C: Cold-hand placed in painful 10°C or non-painful 32°C water (randomised order)

S: Suppression-instructed to “try not to cough” or “cough freely” (randomised order) while placing hand in 32°C warm water.

Coughs were counted and verified using sound recordings. Urge-to-cough was rated using a Modified Borg Scale (0–10).

Analysis The between-block change in cough frequency and urge-to-cough intensity was compared by intervention using paired t-tests after adjusting for an order-effect. Primary outcome was W versus C. Secondary outcomes were B versus W, and W versus S.

Results 20 non-smoking healthy subjects [10 male; mean (SD) age 55.05 (14.2) yrs] with normal lung function and median (IQR) EC50 of 15.6 (23.50) μ M capsaicin completed the study. Compared to B, W had no significant effect on cough ($p=0.623$) or urge-to-cough ($p=0.285$). Compared to W, C significantly reduced cough ($p=0.048$) (Abstract S144a figure 1A) and showed a trend towards a reduction in urge-to-cough ($p=0.104$) (Abstract S144a figure 1B). Compared to W, S significantly reduced cough ($p=0.016$) (see Abstract S144a figure 1C) but urge-to-cough did not change ($p=0.631$) (Abstract S144a figure 1D).



Abstract S144a Figure 1 Change in total cough frequency (A,C) and urge-to-cough intensity (B,D) between blocks. Horizontal lines show mean, error bars $\pm 95\%$ CI.

Conclusion Applying a painful stimulus to the hand inhibits cough in healthy subjects, and may be a useful model for measuring endogenous inhibition of coughing. Further studies to investigate whether chronic cough patients demonstrate impaired inhibition using this experimental paradigm are underway.