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Short communication

Somatic points for cough and urge to cough in chronic coughers

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ARTICLE INFO	A B S T R A C T
Keywords: Cough Chronic cough Urge-to-cough Sensitisation	In patients with chronic cough and age-matched control subjects, we attempted to evoke coughing and/or an urge to cough (UTC) by finger pressure along the sternocleidomastoid and sternum, on the lower cervical or first dorsal vertebrae, the jugular notch as well as with maximum neck extension and flexion These mechanical actions were ineffective in controls but reproducibly evoked coughing or UTC in about 50% of chronic coughers; sternal and spinal responses were abolished temporarily by local cooling. The results may disclose a novel paradigm of cough sensitisation possibly involving central convergence of somatic and visceral neural stimuli.

To the Editor

We recently documented the case of a patient with chronic cough who complained of the urge to cough (UTC) and/or coughing triggered by normally innocuous stimuli involving light pressure on tissues of the neck or chest [1]. Accordingly, in this patient UTC or coughing could be evoked by finger pressure along the sternocleidomastoid muscle and sternum, and on the lower cervical or first dorsal vertebrae; pressure on the jugular notch as well as maximum neck extension and flexion were also effective triggers [1]. Notably, circumstantial evidence of "paroxysmal dry cough" provoked by finger pressure on the sternum has been reported previously [2].

We clinically investigated features of this cough paradigm in chronic coughers and controls.

1. Material and methods

Fifty-eight consecutive chronic cough adult outpatients (Table 1) without a history of recent (>4 weeks) respiratory infections and thirty-four healthy, age and gender-matched, non-smokers were recruited. All normal subjects were hospital staff and non-allergic. The study followed the guidelines for observational studies [3] and was approved by the local Institutional Review Board (OSS_14131).

Demographic data were obtained from all participants. Patients rated the magnitude of the disturbance caused by their cough using a 0-9 modified Borg Scale; obtained values were termed the "Cough Score". In all participants, we attempted to evoke coughing and/or the

Abbreviations: UTC, Urge to Cough; SPC, Somatic point for cough.

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sensation of UTC with finger pressure on discrete areas of the chest wall and neck, as well as by encouraging full vertical extension and flexion of the neck [1]. Any identified area on the upper trunk or neck that gave rise to a UTC sensation or overt coughing in response to mechanical actions such as pressure, flexion, or extension, was termed "somatic point for cough" (SPC). Participants with at least one SPC were classified as being SPC+, whereas those with no identifiable SPC were classified as being SPC-. In eight sternal and spinal SPC + patients, we determined the minimum pressure required to evoke UTC or coughing by means of a calibrated force sensing resistor (Ohmite FSR03, Warrenville, IL) taped to the tip of the investigator's first finger. Patients also rated the evoked UTC intensity by using a visual 0–9 analogue scale (VAS). Cough number was detected aurally and noted. All assessments were performed in control conditions and 15 s after cooling the relevant skin surface with an ice spray.

Continuous variables were means \pm standard deviation (SD) or medians and interquartile range (IQR - 25th 75th percentile) and were compared between SPC+ and SPC- with the Student's T-test or non-parametric tests. Categorical variables were counts and percentages and were compared with the Chi-squared test. A p values < 0.05 was taken as significant.

2. Results

On no occasion did control subjects (71.3% females) report a UTC or cough with any mechanical action. However, pressure on the sternal



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Table 1

Characteristics of the pooled chronic cough population and of the patients with (SPC+) and without (SPC-) somatic points for cough and/or urge to cough.

	Pooled $(n = 58)$	SPC+ (n = 30)	SPC-(n = 28)	p-value ^a
Females, n (%) Mean (±SD) age, yr	39 (67.24) 59.7 (±15.02)	24 (80.00) 58.6(±13.23)	15 (53.57) 60.8(±16.83)	0.048 0.594
Mean (\pm SD) Body Mass Index, kg/m ²	25.56 (±4.19)	25.46(±3.95)	26.96(±4.26)	0.843
Median (25,75 IQ) cough duration, yr	2.0 (1,5)	2.7 (1,5)	1.7 (1,9)	0.417

SD, standard deviation; IQ, interquartile range.

^a Between SPC+ and SPC- patients.

bone evoked light pain in 9 control females (26.7%). Patients (68.3% females, Table 1) had a median cough duration of 2 years (range 1–9) and their cough score was 5.4 (\pm 1.08). Sternal pressure evoked pain in 14 patients (24.1%). SPC+ and SPC- subgroups had similar cough scores (5.9 \pm 1.8 and 5.0 \pm 1.7, respectively, p = 0.086) and prevalence of pain sensations. The jugular notch as well as neck flexion/extension were the most frequently identified SPCs, whereas pressure on sternum and spine was seldom effective; the magnitude of responses was similar with all SPCs (Table 2). Induced coughing and UTC were reproducible (kappa test = 0.84; 95% CI, 0.78–0.96). The mean force required to evoke a response from either the sternum and/or the spine was 2.6 \pm 0.6 kg (range 2.2–2.8 kg). Cooling of the relevant areas with dry ice temporarily (60 s) abolished all responses.

3. Discussion

The results confirm our previous observation [1] of a chronic cough phenotype with UTC and/or coughing evoked by stimulation of specific somatic points. This phenomenon, absent in controls but frequent in chronic coughers, relies on signals from cutaneous mechanoreceptors, since they are abolished by cold anaesthesia. Sternal pressure evoked pain in approximately the same percentage of normal subjects and chronic coughers, and therefore it seems logical to assume that such response is unlikely to be related to chronic cough.

The skin is innervated by mechanically sensitive fibres originating from neurons in the dorsal root ganglia and eventually projecting centrally into the medulla oblongata, namely, the nucleus tractus solitarii (NTS) that receives inputs from the airways and is also implicated in the mediation of the cough reflex [4,5]. Speculatively, signals from cutaneous receptors may converge onto secondary neurons involved in cough mediation at the NTS level, leading to cough sensitisation [6]. Stimulation of cutaneous sensory fibres in susceptible patients may cause transmitter release in the brainstem and increase the excitability of second-order neurons [7]. Therefore, the present findings do not contradict the notion of cough as a vagally-mediated reflex. Rather, they suggest central convergence of stimuli originating from different somatic and/or visceral areas facilitating the cough reflex, i.e. central reflex sensitisation. Convergence has been also implicated in the genesis of referred pain, i.e. pain perceived at a location other than the site of the painful stimulus [2]. Interestingly, a hypersensitive Arnold's reflex has been demonstrated in chronic coughers of all ages and matched controls [8]. Since Arnold's nerve is a branch of the Vagus nerve, it is not surprising that normal subjects cough following nerve stimulation; on the other hand, the increased reflex excitability in chronic coughers probably reflects sensitisation of the vagal sensory network [8], i.e. peripheral sensitisation. Both central and peripheral sensitisation are

Table 2

The number and percent of patients who were responsive to the mechanical stimulation of one or more of the identified somatic points and mean $(\pm SD)$ values of the evoked responses.

Type of somatic point	Cough (n/%)	UTC only (n/%)	cough number	UTC intensity
Neck flexion and/or extension	10/30	6/20	1.67 (±0.78)	5.65 (±2.04)
Sternocleidomastoid muscle	4/13	4/13	2.25 (±1.50)	4.00 (±2.17)
Jugular notch	10/30	11/37	2.06 (±1.12)	5.61 (±2.22)
Cervico-dorsal spine	4/13	2/7	2.60 (±1.82)	4.00 (±2.45)
Sternum	7/23	3/10	2.12 (±0.64)	5.40 (±2.59)

SD, standard deviation; UTC, urge to cough.

mechanisms of the cough hypersensitivity syndrome [9].

In conclusion, the large percentage of SPC + patients points to a relevant role of this symptom in the genesis and/or persistence of chronic cough. Why UTC and/or cough can only be induced by mechanical stimulation of specific somatic areas remains unclear. The possible impact of this novel cough paradigm on the clinical history of patients with chronic cough, especially difficult-to-treat chronic cough, deserves further investigation.

CRediT authorship contribution statement

Claudia Mannini: participants' enrolment, interpretation, Writing – review & editing. **Guja Bernacchi:** participants' enrolment, interpretation, Writing – review & editing. **Viola Bonti:** participants' enrolment, interpretation, Writing – review & editing. **Elenia Cinelli:** Conceptualization, interpretation, Writing – review & editing. **Donatella Mutolo:** Conceptualization, interpretation, Writing – review & editing. **Giovanni A. Fontana:** Conceptualization, Formal analysis, interpretation, Writing – original draft. **Federico Lavorini:** Conceptualization, Formal analysis, interpretation, Writing – original draft.

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