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Measuring voluntary and reflexive cough strength in healthy individuals

Claire Mills [a, b, *], Richard Jones [a, b, c, d], Maggie-Lee Huckabee [a, b]

[a] The University of Canterbury Rose Centre for Stroke Recovery & Research, St George's Medical Centre, Christchurch, New Zealand
[b] Department of Communication Disorders, University of Canterbury, Christchurch, New Zealand
[c] Department of Medical Physics & Bioengineering, Christchurch Hospital, Christchurch, New Zealand
[d] New Zealand Brain Research Institute, Christchurch, New Zealand

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ABSTRACT

Background: Cough reflex testing is a validated tool for identifying patients at risk of silent aspiration. However, inter- and intra-rater reliabilities of perceptual judgements of cough strength are sub-optimal. Although there are clinically established methods for measuring volitional cough strength, no similar methods are identified for reflexive cough strength. This study evaluated three measurement methods of voluntary and suppressed reflexive cough strength.

Methods: Fifty-three healthy subjects (≥50 years) participated in this study. Participants produced 'strong' and 'weak' voluntary coughs and suppressed reflexive coughs to incremental doses of citric acid. Peak and area under the curve (AUC) measurements were taken of pressure, airflow, and acoustics.

Results: There was no dose effect of citric acid on measures of reflexive cough strength. Strong voluntary coughs were stronger than reflexive coughs for all measures ($p < 0.001$) and weak voluntary coughs were stronger than reflexive coughs for two measures (AUC pressure: $p < 0.020$; peak flow: $p < 0.004$). AUC pressure and peak flow had the highest correlations and effect sizes. Correlations were low between voluntary and reflexive cough strength for all measures ($r \leq 0.46$).

Conclusion: Assessing strength of reflexive cough, rather than voluntary cough, is highly desirable in the dysphagic population. Pressure and flow provide the most useful objective measurements.

1. Introduction

Coughing plays a vital role in airway protection and clearance [1,2]. A voluntary cough is cortically controlled and includes an inspiratory phase, a compressive phase, and an expulsive phase; the inspiratory phase acts to provide a greater lung volume to enable more effective lung clearance [3,4]. Conversely, reflexive coughing is primarily mediated by the brainstem [5] and usually comprises a mixture of two different types of reflexive coughs: the cough reflex and the laryngeal expiratory reflex (LER) [6]. The cough reflex has an inspiratory phase, in contrast to the LER which does not have an inspiratory phase [6–10]. Reflexive coughing acts primarily to protect the airway from threat and clear the upper airway of aspirated material [2]. Reflexive coughing, therefore, is of particular importance for individuals with dysphagia, in which food, drink, and/or saliva can enter the airway, potentially resulting in aspiration pneumonia. Dysphagic patients frequently have dystussia (disordered cough response) which has been shown to be associated with increased risk of aspiration pneumonia [11–14]. Voluntary cough and reflexive cough are physiologically different [1,15,16] and, as such, are affected differently in neurological disorders [17–19].

Cough reflex testing (CRT) in neurologically-impaired patients, particularly those who have had a stroke, has been shown to be effective in identifying individuals with impaired cough sensitivity who are at risk of silent aspiration (aspiration without cough) and development of pneumonia [12]. Historically, CRT has examined natural cough, in which individuals are instructed to 'cough if they feel the need to'. However, research has shown that reflexive cough to capsaicin can be voluntarily suppressed [20]. This indicates that either cortical inhibition of reflexive cough is possible or, alternatively, that a true reflexive cough has not been initiated. Indeed,

* Corresponding author. The University of Canterbury Rose Centre for Stroke Recovery and Research, St George's Medical Centre, Private Bag 4737, 249 Papanui Road, Christchurch 8140, New Zealand.
E-mail address: clairemills3@gmail.com (C. Mills).

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Abbreviations

AUC	area-under-the-curve
C2	two consecutive coughs without intervening inspiration
C5	five consecutive coughs without intervening inspiration
CRT	cough reflex testing
LER	laryngeal expiratory reflex

coughing behaviour is highly suggestive and the potential exists for patients undergoing natural CRT to unwittingly cough voluntarily – rather than reflexively – during the assessment, because they are aware they are undergoing CRT [21]. In order to offset this 'placebo effect', CRT can incorporate the assessment of suppressed cough, in which individuals are instructed to 'try not to cough'. This methodology helps to maximize the likelihood that resultant coughing is truly reflexive [21].

Strength of coughing is an important factor in identifying risk of aspiration pneumonia [22]. However, there is no established method of objectively assessing reflexive cough strength, and clinical CRT often incorporates a binary 'weak' or 'strong' perceptual judgement of cough strength. Inter- and intra-rater reliability of perceptual judgement of cough strength has been shown to be low [23]. In the absence of CRT, clinicians often rely on volitional cough to assess ability to protect the airway in the event of aspiration. This assessment may not be directly applicable to the process of clearing aspiration. Developing a method to objectively measure the strength of reflexive cough is crucial to identify patients at risk of aspiration pneumonia with greater specificity.

This study investigated the strength of voluntary and suppressed reflexive cough, elicited by inhalation of incremental doses of nebulized citric acid, using outcome measures of pressure, airflow, and acoustics. We hypothesized that there would be a dose-response effect, with greater cough strength with higher doses of citric acid. Voluntary cough was also postulated to be stronger than suppressed reflexive cough. Finally, we hypothesized that pressure measures would be more accurate than airflow or acoustics.

2. Material and methods

2.1. Study subjects

Fifty-three healthy individuals (33 females) were recruited for this study. Exclusion criteria included: age <50 years, history of gastro-oesophageal reflux, respiratory conditions, neurological conditions, dysphagia, smoking, and taking steroids, opiates, or codeine-based analgesia in the 24 h prior to assessment. All subjects provided informed written consent. Ethical approval was granted by an appropriate regional Human Ethics Committee.

3. Materials

A within-subject design was utilized to investigate strength of reflexive and voluntary cough using measures of pressure, airflow and acoustics. For analysis of reflexive cough, CRT was carried out using citric acid solutions at concentrations of 0.4 Mol/L, 0.8 Mol/L, 1.2 Mol/L and 1.8 Mol/L, as well as 0.9% saline. A PulmoMate® Compressor Nebulizer (model 4650I, DeVilbiss Healthcare LLC, Pennsylvania, US) was used to deliver the stimulus to participants using a pre-determined free-flow output of 8 L/min and a restricted flow output of 6.6 L/min. This same flow output was also used to apply air only during voluntary cough testing to ensure identical airflow, pressure and acoustic conditions.

A physiological pressure transducer (Model MLT844) was connected to a bridge amp (Model ML110) and a respiratory flow head 1000 L (MLT1000L) was connected to a spirometer pod (Model ML311) (all ADInstruments, Dunedin, New Zealand). These were utilized to collect information on cough pressure and flow rate, respectively. A Littmann stethoscope was attached to an Optimus omnidirectional impedance microphone (1 KΩ Model 33-3003) to obtain acoustic measures of cough. All instruments were connected to an AD PowerLab 26T-3819 (model ML856, ADInstruments, Dunedin, New Zealand) and LabChart Version 7.3.7 was utilized to collect and analyse data. A disposable Hudson RCI MICRO MIST® adult, elongated aerosol nebulizer mask and 7-foot Start Lumen® Tubing (Teleflex, Morrisville, USA) were used for each participant. This face mask had detachable tubing attached to each port: one connected to the pressure transducer, and one connected to the spirometer flow head.

The sampling rate was set at 10 kHz and anti-aliasing low-pass filters were on for all measures. The spirometer was zeroed and calibrated using set parameters (0 mV = 0.0 L/s and 1.0 V = 40.1 L/s). The pressure transducer was manually calibrated using a sphygmomanometer. The recording range was set for each measure (flow: 500 mV; pressure: 2 mV, acoustic: 2 V). A low-pass filter was set for flow (30 Hz) and pressure (2 kHz) and turned off for acoustic.

3.1. Procedures

The face mask was securely placed, using elastic straps, to reduce mask movement and minimize air escape. The stethoscope was positioned centrally over the participant's central thyroid cartilage using a neck strap. This central position reduced artefact of detection of carotid pulse. The nebulizer was placed approximately 1 m from the recording equipment and the participant to prevent artefacts in sound and pressure recordings.

A counterbalanced design determined if a participant commenced with voluntary or reflexive coughs. In addition, execution of the type of voluntary cough – two strong coughs or two weak coughs – were varied randomly across participants. Participants were given instructions to 'take a breath in and produce two strong coughs on one breath', or 'take a breath in and produce two weak coughs on one breath'. Coughs were also modelled for participants.

A counterbalanced approach to the order of doses of citric acid was not possible due to the tendency for higher concentrations of citric acid to cause tachyphylaxis, thus influencing subsequently-administered lower concentrations. Therefore, the citric acid doses were administered incrementally, adhering to the European Respiratory Society guidelines [3]. Citric acid was administered for $\leq$15 s, as continual inhalation over a period of $\geq$1 min has been shown to result in tachyphylaxis [3]. Participants were instructed to 'Breathe in and out through your mouth. If you feel the need to cough, try to suppress it'. The European Respiratory Society Task Force recommend recording either a C2 or a C5 response (two or five consecutive coughs in response to application of a tussive agent) [3]. In this study participants were observed for the production of a C2 response, as this has been found to be more reproducible [24]. A C2 response was defined in this study as two consecutive coughs without intervening inspiration [21]. Each dose of citric acid was administered once only and when a C2 response was observed the nebulizer was turned off. After a C2 response was observed on three consecutive doses of citric acid, no further doses were presented. To prevent tachyphylaxis, a 60 s rest period was