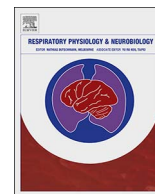




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## Muscle activation and sound during voluntary single coughs and cough peals in healthy volunteers: Insights into cough intensity

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## ABSTRACT

Very few studies have addressed how coughing varies in intensity. We assessed the influence of cough effort and operating volume on the mechanics of coughing using respiratory muscle surface electromyography (EMG), oesophageal/gastric pressures and cough sounds recorded from 15 healthy subjects [8 female, median age 30 (IQR 30–50)years] performing 120 voluntary coughs from controlled operating volume/effort and three cough peals. For single coughs, low operating volumes and high efforts were associated with the highest EMG activity ( $p < 0.001$ ); the resultant pressures increased with effort but volume had little influence. In contrast, cough sounds increased with both volume and effort. During cough peals, EMG fell initially, increasing towards the end of peals, pressures remained stable and sound parameters fell steadily to the end of the peal.

In conclusion, effort and operating volume have important influences on cough mechanics but modulate muscle activation, pressure and cough sound amplitude and energy differently. Consequently, these cough sound parameters poorly represent voluntary cough mechanics and have limited potential as a surrogate intensity measure.

## 1. Introduction

The study of cough has, until recently, been hampered by the lack of validated measures reflecting cough severity (Decalmer et al., 2007; Marsden et al., 2008; Smith et al., 2006). Many factors impact how patients perceive the severity of coughing including how frequently they cough, disruption to normal activities, and the cough intensity, described by patients as the harshness or physical discomfort of coughing (Vernon et al., 2009). Although recently developed quality of life scores reflect disruption to normal activities (Irwin, 2006; Birring et al., 2003) and objective monitoring of cough frequency is in use in clinical trials (Kelsall et al., 2009; Key et al., 2010; Smith and Woodcock, 2006), very few studies have addressed how coughing may vary in its intensity and how this might best be quantified. Indeed there is no agreed definition of cough intensity. High intensity coughing is important as it is likely to be associated with physical complications which may include dizziness, chest pain, vomiting, syncope and incontinence. Equally low intensity coughing may be less distressing but could suggest impaired cough effectiveness.

Cough is initiated by contraction and shortening of the expiratory muscles against a closed glottis, developing high intra-thoracic and

intra-abdominal pressures prior to a sudden glottal opening resulting in rapid air flow from the lungs. The flow generated during coughing depends on a number of factors including the volume of air in the lungs prior to the cough (operating volume) (Quaranta et al., 2007), the muscular effort applied to this volume and its translation into the driving force necessary for effective cough. Cough sounds arise as a result of this flow and vibration of the tissues of the respiratory tract.

The intensity of a cough perceived by a patient is likely to be related to a number of attributes; intuitively the magnitude of the muscle activation might be expected to be most important, but the resulting pressure and flow might play a role. Investigating the relationships between these measures and how they are modulated by cough effort and operating volume, may enable a better understanding of how cough intensity may vary. It is clearly impractical to directly determine most of these parameters during spontaneous coughing, so we have also studied the cough sound, which is easily recorded and its nature determined by the flow generated as a consequence of the muscle activation and pressures developed.

Previous studies have investigated muscle activation during coughing using surface abdominal electromyography (Cox et al., 1984; Fontana et al., 1997), whilst others have studied flow and pressure only

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(Lee et al., 2015), but none have explored or controlled for the effects of cough operating volume or the effort applied when coughing. In one study, subjects were trained to produce voluntary coughs at specific flow rates irrespective of operating volume or effort (Lasserson et al., 2006). Chest and abdominal EMG signals were recorded and increased with the targeted cough flow but as all coughs followed a deep inspiration, low operating volume coughs were not studied which may not well represent all spontaneous coughing. Moreover previous studies have focussed on single coughs, an uncommon pattern in spontaneous coughing in our experience of recording cough sounds in ambulatory patients. Even in studies that have evoked peals of coughing, the analysis has been limited to the first cough of the peal, disregarding the subsequent coughs (Lee et al., 2015). During a cough peal, consecutive coughs occur from reducing operating volumes which could conceivably range from total lung capacity TLC down to below FRC, supporting the approach of studying single coughs from different operating volumes and including cough peals.

A few authors have also investigated cough sound intensity which, as expected, is correlated with the flow responsible for generating the sound (Lee et al., 2015; Lee et al., 2017). Cough effort has also been shown to influence cough sounds (Pavesi et al., 2001; Subburaj et al., 1996) but again the impact of cough operating volume was not taken into account in these studies and low operating volume coughs, where flow is severely restricted, were not included. Studies exploring the relationships between cough sounds and measures of EMG are lacking.

We hypothesised that the key factors capable of modulating cough intensity were the volume inspired prior to coughing (operating volume) and the level of effort applied. Therefore we explored how respiratory muscle EMG during coughing was modulated by the effort applied during each cough and the cough operating volume. We then related these signals to the pressures and cough sounds produced. We predicted that both cough effort and operating volume would significantly influence muscle activation, pressure flow and therefore the cough sounds. We also compared single coughs and cough peals.

## 2. Methods

### 2.1. Subjects

Fifteen healthy participants were studied. All were non-smokers, had normal spirometry and no history of respiratory infection during the previous 4 weeks. Ethical approval was granted by the local research ethics committee (Kings College Hospital, no: LREC 02-120) and written informed consent obtained from all subjects.

### 2.2. Protocol

All procedures were performed in a quiet room with the subject seated. A total of 120 single voluntary coughs were completed by each subject. Coughs were performed from four different operating volumes (10%, 30%, 60% or 90% of forced vital capacity (FVC)) and with three different levels of effort (low, medium and high); ten coughs were performed for each condition. Single coughs were followed by three cough peals. During coughs, audio, electromyography and pressure were simultaneously recorded (online Supplement Figure E1). Surface EMG electrodes were placed over the abdomen and chest, and catheters were inserted per nasally to measure oesophageal pressure (Poes) and gastric pressure (Pgas) Audio recordings were made using a piezoelectric contact microphone placed below the suprasternal notch (online Supplement Figure E2).

#### 2.2.1. Single voluntary coughs with controlled operating volume and effort

Cough operating volume was controlled using a custom-designed system consisting of a spirometer (Vitalograph Ltd, Buckingham, England) interfaced to a laptop computer via an analogue to digital converter (USB1608 FS, Measurement Computing Corporation, Norton,

MA). Interface control and data management were accomplished using custom-written software (Visual basic 6, Microsoft Corporation, Redmond, WA). Firstly the subjects' FVC was determined from the best of three measures in accordance with ATS/ERS criteria (Miller et al., 2005) (online Supplement Figure E3 A). The required cough operating volume was then entered into the software as a percentage of FVC. Subjects, wearing a nose clip, were instructed to take a full breath in (to TLC), and then to breathe out into the spirometer mouthpiece until the target operating volume was reached. The volume expired into the spirometer and target operating volumes were displayed on a screen from the onset of the manoeuvre (online Supplement Figure E3 B), and when target volume was reached a loud beep and a visible message 'cough' appeared. At this point the subject stopped breathing out and the mouthpiece and nose clip were removed by a researcher prior to the cough, ensuring the cough sound was not distorted by the mouthpiece/nose clip and that non-cough EMG artefact was minimized. Subjects then coughed with the prescribed level of effort, without taking any further breath in or out. For high effort coughs, subjects were asked to cough as strongly as possible, for low effort to perform gentle coughs and medium coughs intermediate between high and low. Each subject practiced the procedure several times prior to data collection. Careful observation ensured that subjects followed operator instructions.

#### 2.2.2. Voluntary cough peals

The subjects were allowed to rest briefly before performing 3 voluntary cough peals. Subjects were then instructed to take a full breath in and produce a series of coughs for as long as they were able to do so, without breathing in or out between coughs. The subjects remained seated throughout and did not wear a nose clip. This process was repeated three times for each subject. Careful observation of the subjects ensured that breaths were not taken between coughs.

## 3. Data acquisition

All data was acquired using an analogue-to-digital converter (Powerlab, AD Instruments, Inc. Colorado Springs, CO) and a computer running Chart 5 software (AD instruments). The software controlled the synchronisation, acquisition and display of EMG, pressure and sound data.

### 3.1. EMG measurement

The EMG signals were amplified and bandpass filtered between 10 Hz and 3 kHz (RA-8 biomedical amplifier, Yinghui Medical Tech Ltd, Guangzhou, China) and acquired and displayed on a laptop computer (MacBook, Apple Computer Corp, Cupertino, CA, USA) running Chart software (Chart Version 5.4 ADInstruments, Colorado Springs/CO, USA) with analog to digital sampling of 10 kHz (Powerlab, ADInstruments, Colorado Springs/CO, USA).

The skin surface was prepared using alcohol rub and Neuroline gel (Ambu, MD, USA). Ag-AgCl surface EMG electrodes were positioned on the right side of the body over the parasternal intercostal muscles (second intercostal space, 3 cm from centre of sternum, reference anterior shoulder), lateral chest muscles (8th intercostal space in the mid-axillary line, reference 5 cm lateral on the 10th rib), lateral abdominals (5 cm directly below the costal margin on a line drawn down to the anterior superior iliac spine, reference placed 5 cm medially) and medial abdominals (5 cm lateral to the umbilicus with the reference a further 5 cm laterally) see online Supplement Figure E4 .

Muscle groups rather than single muscles are named as with surface electrode recordings as it is likely the EMG signal acquired arises from several overlying muscles in a group rather than a single muscle.

### 3.2. Measurement of gastric and oesophageal pressure

Gastric (Pga) and oesophageal pressure (Poes) were measured using

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