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Respiratory motor training and neuromuscular plasticity in patients with chronic obstructive pulmonary disease: A pilot study

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ABSTRACT

The objective of this study was to examine the feasibility of a full-scale investigation of the neurophysiological mechanisms of COPD-induced respiratory neuromuscular control deficits. Characterization of respiratory single- and multi-muscle activation patterns using surface electromyography (sEMG) were assessed along with functional measures at baseline and following 21 ± 2 (mean ± SD) sessions of respiratory motor training (RMT) performed during a one-month period in four patients with GOLD stage II or III COPD.

Pre-training, the individuals with COPD showed significantly increased ($p < 0.05$) overall respiratory muscle activity and disorganized multi-muscle activation patterns in association with lowered spirometrical measures and decreased fast- and slow-twitch fiber activity as compared to healthy controls (N = 4). Following RMT, functional and respiratory sEMG activation outcomes during quite breathing and forced expiratory efforts were improved suggesting that functional improvements, induced by task-specific RMT, are evidence respiratory neuromuscular networks re-organization.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is currently the third leading cause of death and disability in the US (Heron, 2012) and, is projected to be ranked fifth worldwide in burden of disease by 2020 (Vestbo et al., 2013). While airflow limitations and parenchymal pulmonary destruction are the hallmarks of the disease, COPD is also associated with reduced respiratory muscle force and endurance leading to ventilatory insufficiency (Gea et al., 2012). In fact, respiratory failure remains a major cause of morbidity and mortality in COPD (Mannino and Martinez, 2011), which is in part attributed to respiratory muscle dysfunction (Gosselink et al., 2000). Consequences of decreased respiratory muscle performance include ineffective breathing and coughing, and changes in coordination of breathing and swallow (Clayton et al., 2014; Singh, 2011). In turn, these deficits may further contribute to dynamic hyperinflation and increased risk of COPD exacerbation (Vilaro et al., 2010). This explains why maintaining adequate respiratory motor function is critical for patients with COPD (McKenzie et al., 2009). Currently, there are no effective therapeutic strategies to improve respiratory motor function in those affected by COPD (Keating et al., 2011; Vestbo et al., 2013). A fundamental reason for this is that the pathophysiological mechanisms of respiratory motor dysfunction in COPD remain unclear (Gea et al., 2013). Although, these abnormalities can be linked to a variety of factors related to local and systemic insults affecting respiratory muscles (Vestbo et al., 2013). There is mounting evidence suggesting that the neural control of respiratory muscles is negatively affected in COPD resulting in an altered neural drive (Duiverman et al., 2004; Jolley et al., 2009) and abnormal motor unit activation (Mantilla and Sieck, 2013). This suggests that respiratory motor dysfunction induced by COPD involves functional disorganization of the respiratory neuromuscular network (Duiverman et al., 2004).

As it now stands, pulmonary rehabilitation is an essential non-pharmacological therapeutic option for patients with COPD (Nici et al., 2006). This therapy is meant to accompany patients throughout the course of their disease with the primary goal of reducing disability (Ries et al., 2007). However, patients with COPD complain of dyspnea following physical exertion, often due

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to significantly reduced exercise capacities (Troosters, 2013) and progressive decline in lung function associated with a poor quality of life (Kim et al., 2008). Therefore, there is a great need for the development of effective physiologically-based rehabilitative techniques to restore the dysfunctional respiratory motor system induced by COPD (de Blasio and Polverino, 2012). There is growing evidence supporting the value of task-specific training based on evidence of significant use-dependent neural plasticity (Hubbard et al., 2009). However, this concept has never been tested in respiratory rehabilitation for patients with COPD. This pilot study was undertaken to determine the capacity of the respiratory neuromuscular networks for plasticity in order to develop effective rehabilitative strategies for patients with COPD.

2. Methods

2.1. Demographic and clinical characteristics

This study was conducted in the Neuroscience Collaborative Center at the Frazier Rehab Institute after informed consent was obtained as approved by the Institutional Review Board for Human Research at the University of Louisville. Four individuals, two female and two males, with GOLD stage II or III COPD participated in this study. Data from four physically (age, sex, height, and weight) matched healthy controls with no history of respiratory dysfunction or smoking were used to calculate normative sEMG-based values (Bartuzi et al., 2007; Ovechkin et al., 2010).

2.2. Pulmonary function test

Standard spirometry testing was performed in the seated position before and after respiratory motor training (RMT) program obtaining Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), and Maximum Forced Expiratory Flow (FEF_{max}) as measures of respiratory motor function (American Thoracic Society/European Respiratory Society, 2002; Hart et al., 2005). A Differential Pressure Transducer (MP45-36-871-350) with UPC 2100 PC card and software (Validyne Engineering, Northridge, CA) was used to measure Maximum Inspiratory Pressure (PI_{max}) and Maximum Expiratory Pressure (PE_{max}) (American Thoracic Society/European Respiratory Society, 2002) while subjects were blowing into the three-way valve system through a rubber tube used as a mouthpiece (Airlife 001504, Allegiance Healthcare Corp., McGaw Park, IL) from total lung capacity. The pressure meter incorporated a 1.5 mm diameter leak to prevent glottic closure and to reduce buccal muscle contribution during measurements (Griffiths and McConnell, 2007; Smyth et al., 1984).

2.3. Respiratory motor control assessment

Respiratory muscle activation patterns were evaluated using surface electromyography (sEMG) of left and right sternocleidomastoid, scalene, upper trapezius (on midclavicular line), clavicular portion of pectoralis (on midclavicular line), diaphragm (on parasternal line), intercostal (at 6th intercostal space on anterior axillary line), rectus abdominus (at umbilical level), obliquus abdominis (on midaxillary line), lower trapezius (paraspinally at midscapular level), and paraspinal (paraspinally on iliac intercrestal line) muscles using MA300 System (Motion Lab Systems, Baton Rouge, LA) (American Thoracic Society/European Respiratory Society, 2002; Ovechkin et al., 2010). sEMG input was amplified with a gain of 2000, filtered at 4–1000 Hz and sampled at 2000 Hz. The overall amount of sEMG Magnitude (μV, Mag) and the Similarity Index (SI), that quantitate the multi-muscle distribution of activation during Maximum Expiratory Pressure Task (MEPT) in COPD subject compared to that of healthy subjects were calculated using vector-based analysis as previously described (Aslan et al., 2013; Ovechkin et al., 2010). In brief: multi-muscle activity parameters were calculated using averaged sEMG amplitudes using root mean squared (RMS) algorithm from each SCI subject for comparison to group values from NI subjects. The resulting Mag parameter was the amount of combined sEMG activity during MEPT calculated as a length of the resultant vector. The SI provides a value between 0 and 1.0 (most similar) equal to the cosine of the angle between the resultant multi-muscle distribution vectors in SCI subject to that of NI subjects. To perform MEPT, all subjects produced maximum expiratory efforts from total lung capacity for 5 s blowing into the Airlife 001504 circuit (Allegiance Healthcare Corp., McGaw Park, IL). Airway pressure; sEMG; breathing rate and chest wall kinematics monitored by using respiratory belt were recorded simultaneously using Powerlab acquisition system (ADInstruments, Colorado Springs, CO). The amount of fast-twitching and slow-twitching muscle fiber activity of intercostal, rectus abdominis, and obliquus abdominis muscles were assessed using power spectrum analysis of sEMG frequency composition (Kamen and Gabriel, 2010) assessed during three trials of MEPT when respiratory muscles were either not-fatigued or fatigued. The fatigued condition was obtained using respiratory muscle endurance protocol with incremental resistant airway loading using MicroRMA100 respiratory muscle analyzer (MicroDirect, Lewiston, ME) by increasing the airflow resistance every 3 breathing cycles with an incremental step of 0.4 KPa/L/s until the subject could not continue (American Thoracic Society/European Respiratory Society, 2002; Keenan et al., 1995). The frequency outcomes have been calculated on the basis of the distribution of data into 1-s intervals within a 5-s window using a Fast Fourier Transform approach (Brigham, 1988). Percentage of the accumulated power of the spectrum within 4–60 Hz range, representing slow-twitch fiber activity; and 60–300 Hz range, representing fast-twitch fiber activity, were calculated (Bartuzi et al., 2007; Solomonow et al., 1990; Tkach et al., 2010).

2.4. Respiratory motor training

Research participants were seated during each training session with an approximately 45° head-up tilt. A threshold positive expiratory pressure device and inspiratory muscle trainer (Respironics Inc., Cedar Grove, NJ) were assembled using a three-way valve system (Airlife 001504, Allegiance Healthcare Corp., McGaw Park, IL) with flanged mouthpiece. The participants performed 6 work sets, 5 min in duration, separated by rest intervals lasting 3 min. Participants were trained 5 days/week, for 45 min/day during 1 month. The training was initiated at an intensity equal to 20% of their individual PI_{max} and PE_{max} with progressive increases as tolerated up to 40% of these values at the end of the training program (Griffiths and McConnell, 2007; Larson et al., 1999; Mueller et al., 2006).

2.5. Statistical analysis

Comparisons between unidentified data sets obtained before and after the RMT program were made using a paired *t*-test to detect the difference for each independent parametric variable (FVC, FEV_1, FEF_{max}, and SI) and Wilcoxon Signed-Rank Test for each non-parametric variable (PI_{max}, PE_{max} and Mag). All hypothesis tests were conducted at the $p < 0.05$ with the level of significance (α) being set at 0.05. All analyses were conducted using the open-source R software 3.0.2 package (R Development Core Team, 2013).