Short communication

Is parasternal intercostal EMG an accurate surrogate of respiratory neural drive and biomarker of dyspnea during cycle exercise testing?

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\textbf{A B S T R A C T}

Recent evidence suggests that surface electromyography of the parasternal intercostals (EMGpara) can be a non-invasive alternative to diaphragmatic EMG (EMGdi) for estimating neural respiratory drive (NRD) during cardiopulmonary exercise testing (CPET). The purpose of this study was to determine if non-respiratory muscles influence EMGpara by having subjects place their hands on \(H_{\text{on}}\) and off \(H_{\text{off}}\) the handlebars during cycling-based CPET. Ten healthy adults performed an incremental cycling test until volitional exhaustion. Participants were instrumented with an esophageal electrode catheter to measure EMGdi, and surface electrodes on the 2nd intercostal space to measure EMGpara. Subjects alternated between 30 s of \(H_{\text{on}}\) and 30 s \(H_{\text{off}}\) during each exercise stage. There were no differences in EMGdi across all exercise intensities. However, EMGpara was significantly greater during the \(H_{\text{on}}\) vs. \(H_{\text{off}}\) condition at all exercise intensities \((p < 0.05)\). These results suggest that EMGpara may not be an appropriate surrogate of NRD during cycle exercise testing due to co-activation of adjacent skeletal muscles.

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1. Introduction

By definition, dyspnea is a subjective experience of respiratory discomfort, and as such, an objective biomarker of dyspnea could prove useful in the clinical evaluation of patients suffering from this symptom. While the mechanisms of dyspnea are complex and multifactorial, it is generally accepted that dyspnea reflects, in part, an awareness of increased neural respiratory drive (NRD) as sensed via increased central corollary discharge to sensory areas of the brain (O’Donnell et al., 2009). Historically, NRD has been estimated using minute ventilation, esophageal pressure, mouth occlusion pressure, and trans-diaphragmatic pressure. However, some of these respiratory flow and pressure-derived measurements can be affected by the presence of abnormal ventilatory mechanics that contribute to neuromechanical dissociation of the respiratory system. Diaphragm electromyography (EMGdi), measured using a multi-pair esophageal electrode catheter, represents the best available surrogate measure of NRD in humans. This is due to the fact that EMGdi-derived measures of NRD are neurophysiologically “upstream” of altered respiratory mechanics (Jolley, 2014). Indeed, several recent studies have shown a strong association between EMGdi and exertional dyspnea ratings in health and chronic respiratory diseases (Faisal et al., 2016; Jolley et al., 2015). Unfortunately, measuring EMGdi is invasive and it is a technically demanding technique that has primarily been limited to the research setting. As such, a noninvasive alternative to EMGdi could prove valuable to more objectively assess dyspnea and to evaluate responses to therapeutic interventions.

Surface electromyography of the parasternal intercostal muscles (EMGpara) has been proposed to be a non-invasive alternative to EMGdi for estimating NRD during cycle exercise testing (Reilly et al., 2011). The physiological rationale is based on the synchronic activation between the parasternal intercostals and the diaphragm (De Troyer et al., 2005). However, a well-established limitation of surface EMG is the potential contamination of the EMG signal due to co-activation of adjacent skeletal muscles. Upright cycle-exercise, commonly used in clinical and research settings, may activate the pectoralis muscles through grasping the handlebars on the ergometer. This may contaminate the EMGpara signal, thus making it an unreliable index of NRD and biomarker of exertional dyspnea. Accordingly, we sought to investigate whether
activation of non-respiratory muscles influences EMGpara measurements during upright cycling. We hypothesized that placing the hands on the handlebars would significantly increase EMGpara but would not affect EMGdi compared to cycling without use of the handlebars.

2. Methods

2.1. Subjects

This study received institutional ethical approval and all subjects provided written informed consent. Data were obtained from 10 healthy subjects (50% female) with normal spirometry and no reported history of cardiopulmonary disease.

2.2. Exercise protocol

Each subject performed an incremental exercise test on an electronically braked upright cycle ergometer (Ergoselect 200P; Ergoline, Bitz, Germany) that consisted of a 6-min rest period followed by a 1-min warm up of unloaded pedaling, and stepwise increases in work rate by 50 W every 3-min until volitional fatigue (Reilly et al., 2011). Inspiratory capacity (IC) maneuvers were performed at rest, every 3 min during exercise, and at maximal exercise. Between 90 and 150 s of each 3-min exercise stage, subjects would alternate between grasping the handlebars (“hands on”, $H_{on}$) and relaxing their hands at their side (“hands off”, $H_{off}$) for 30 s. The order was randomized between subjects. Participants maintained an upright cycling posture throughout the entirety of the exercise test. Metabolic and ventilatory responses were measured on a breath-by-breath basis using a commercially available metabolic cart (Vmax Encore 229; CareFusion).

2.3. Measurements

EMGpara, EMGdi, and EMG of the brachioradialis (EMGbr) were measured at rest and during exercise. Bipolar surface Ag/AgCl electrodes were used to collect EMGpara and EMGbr. EMGpara electrode placement was based on the work of Reilly et al. (2011). The positive electrode was placed 3 cm lateral to the sternum on the right side of the chest while the negative electrode was placed 3 cm lateral to the sternum on the left side of the chest resulting in an inter-electrode distance of ~6 cm. The reference electrode was placed on a bony surface on the lateral portion of the clavicle. EMGbr surface electrodes were placed along the belly of the brachioradialis on the right arm. EMGdi was measured using a multi-pair esophageal electrode catheter (Guangzhou Yinghui Medical Equipment Ltd., Guangzhou, China). Position of the catheter was based on previously described methods (Luo et al., 2008). All EMG signals were amplified then filtered using a bandwidth between 10 Hz and 3 kHz (Biomedical Amplifier, Guangzhou Yinghui Medical) and collected using LabChart software (version 7.3.7 Pro, ADInstruments Inc., Colorado Springs, CO) with a sample rate of 2 kHz. Peak root mean square during inspiration was determined for each breath with a time constant of 0.1 s and then averaged over each 30 s condition. Selections were carefully made during inspiration to avoid contamination from cardiac artifact in both the EMGpara and EMGdi signals. EMGpara and EMGdi data were expressed as a percentage of the maximum EMG activity obtained from either IC (at rest and during exercise), maximal voluntary ventilation, or maximal static inspiratory pressure maneuvers. EMGbr was expressed as a percentage of maximal EMG obtained during a maximal isometric handgrip contraction. The handgrip test was used to mimic the activity of gripping the handlebars of the bicycle with a pronated grip.

2.4. Dyspnea

Dyspnea intensity, defined as the “feeling of labored or difficult breathing”, was measured at rest, every 3 min during exercise, and at peak exercise using the modified 0–10 category-ratio Borg scale (Borg, 1982). The scale was anchored such that a 0 on the Borg scale represented “no breathing discomfort at all” and a 10 represented “the most intense breathing discomfort [one] has experienced or could ever imagine experiencing”.

2.5. Statistical analyses

Comparisons of EMGdi, EMGpara, and EMGbr between $H_{on}$ and $H_{off}$ conditions at standardized submaximal work rates and at maximal exercise were performed using paired t-tests. The relationship between EMG and dyspnea throughout exercise was assessed using random-coefficients regression. A p value <0.05 was considered statistically significant. All values are presented as mean ± SD.

3. Results

3.1. Subject characteristics

Table 1 outlines subject characteristics including spirometry and maximal exercise responses. All subjects were healthy, had FEV1/FVC values >0.70 and >90%predicted. Maximal aerobic capacity was, on average, 123 ± 15% predicted indicating that our subjects had high cardiorespiratory fitness.

3.2. Physiological responses

There were no statistically significant differences in minute ventilation, breathing frequency, heart rate, or oxygen consumption at any submaximal work rate between the $H_{on}$ and $H_{off}$ conditions. Minute ventilation was modestly (4.9 L/min) but significantly (p=0.03) higher in the $H_{on}$ condition at maximal exercise (Fig. 1A). There were no statistically significant differences in EMGdi between conditions at rest and throughout exercise.

Table 1

<table>
<thead>
<tr>
<th>Anthropometrics and spirometry</th>
<th>N=10 (5M:5F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>24 ± 1</td>
</tr>
<tr>
<td>Height, cm</td>
<td>171 ± 12</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>71 ± 15</td>
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<tr>
<td>BMI, kg/m²</td>
<td>24.3 ± 2.7</td>
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<tr>
<td>FEV₁, L (% predicted)</td>
<td>4.18 ± 1.19  (95 ± 18)</td>
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<tr>
<td>FVC, L (% predicted)</td>
<td>5.16 ± 1.49  (99 ± 17)</td>
</tr>
<tr>
<td>FEV₁/FVC, % (% predicted)</td>
<td>81 ± 3 (95 ± 4)</td>
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<tr>
<td>Maximal exercise data</td>
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<tr>
<td>Work rate, W</td>
<td>275 ± 63</td>
</tr>
<tr>
<td>V̇O₂, mL/kg⁻¹min⁻¹ (% predicted)</td>
<td>52 ± 8 (123 ± 15)</td>
</tr>
<tr>
<td>VCO₂, L/min</td>
<td>3.74 ± 1.08</td>
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<tr>
<td>V̇CO₂, L/min</td>
<td>4.35 ± 1.24</td>
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<tr>
<td>RER</td>
<td>1.17 ± 0.03</td>
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<tr>
<td>V̇E, L/min</td>
<td>130 ± 37</td>
</tr>
<tr>
<td>V̇E, L</td>
<td>2.72 ± 0.80</td>
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<tr>
<td>Fb, breaths/min</td>
<td>49 ± 9</td>
</tr>
<tr>
<td>V̇E/V̇MVVpred, %</td>
<td>78 ± 6</td>
</tr>
<tr>
<td>HR, bpm (% predicted)</td>
<td>182 ± 12 (93 ± 6)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; FEV₁, forced expiratory volume in one-second; FVC, forced vital capacity; V̇O₂, oxygen consumption; VCO₂, carbon dioxide production; RER, respiratory exchange ratio; V̇E, minute ventilation; V̇tid, tidal volume; Fb, breathing frequency; MVVpred, predicted maximum voluntary ventilation (calculated as FEV₁ × 40); HR, heart rate. Maximal exercise data are from the hands on condition.
(Fig. 1B). However, EMGpara was significantly greater during the H_on condition throughout all exercise intensities with the greatest absolute difference occurring at maximal exercise (Fig. 1C). A similar observation was made for EMGbr (Fig. 1D). The relationship between all EMG measures and exertional dyspnea intensity are shown in Fig. 2. EMGdi was strongly associated with dyspnea intensity ratings in both conditions (H_on: $R^2 = 0.828$; H_off: $R^2 = 0.850$, both $p < 0.01$). A significant relationship between dyspnea and EMGpara was also observed in both conditions although the relationship was stronger in the H_on condition (H_on: $R^2 = 0.332$; H_off: $R^2 = 0.642$, both $p < 0.01$).

4. Discussion

The results of this study suggest that EMGpara may not be an appropriate noninvasive surrogate of NRD, and by extension, exertional dyspnea, at least not during upright cycle exercise as used commonly during cardiopulmonary exercise testing. The increased EMGpara activity in the H_on condition suggests that activation of the pectoralis major muscle, which is superficial to the parasternal intercostals, contaminates the EMGpara signal. Thus, one must exercise caution when using surface electrodes on the chest to quantify inspiratory muscle activity during exercise. It is important to recognize that the results of this study are only applicable to upright cycle exercise and we cannot extrapolate our findings to cycle exercise performed on a recumbent ergometer or during treadmill exercise. However, we speculate that EMGpara may also be contaminated during these other forms of exercise, particularly during higher exercise intensities where upper body movement is seemingly unavoidable. In contrast, EMGpara during inspiratory threshold loading (Ramsook et al., 2016; Reilly et al., 2013), or other conditions where the upper body remains inactive is likely to minimize potential signal contamination from adjacent skeletal muscles. Under these circumstances, EMGpara likely represents a reasonable alternative to EMGdi.

The random coefficients regression analysis demonstrated that dyspnea intensity ratings were most strongly correlated with EMGdi (Fig. 2A and B). Interestingly, despite the signal contamination observed in the parasternal intercostal muscles, EMGpara was still significantly correlated with dyspnea ratings in the H_on condition (Fig. 2C). However, one must be cautious when interpreting this finding given that the brachioradialis, a muscle unrelated to the

Fig. 1. Ventilatory and EMG responses during cycle exercise. Abbreviations: $\dot{V}_E$, minute ventilation; EMGdi, diaphragmatic electromyography; EMGpara, parasternal intercostal electromyography; EMGbr, brachioradialis electromyography. *$p < 0.05$; †$p < 0.01$. 
Fig. 2. Relationship between dyspnea and EMG in the hands on and hands off conditions. Grey lines represent individual data. Thick black lines represent the fitted average curve. $R^2$ values are from the random coefficients regression analysis. Abbreviations: EMGdi, diaphragmatic electromyography; EMGpara, parasternal intercostal electromyography; EMGbr, brachioradialis electromyography.
respiratory system, had an even stronger correlation with dyspnea in the $H_{\text{max}}$ condition [Fig. 2E].

The present study only included young healthy men and women with relatively high cardiopulmonary fitness levels. Thus, we are not able to extrapolate our findings to the elderly or patients with chronic respiratory diseases that are likely to have different dyspnea and ventilatory muscle recruitment responses. However, given the fact that we had large increases in EMGpara activity at rest ($p=0.07$) and at relatively low absolute work rates, we think it is highly likely that EMGpara would also be contaminated in any population exercising on an upright cycle ergometer.

5. Conclusion

Our study demonstrates that EMGpara is affected by the activity of the adjacent pectoralis muscles during upright cycle exercise. Thus, EMGpara data must be interpreted with caution during cardiopulmonary cycle exercise testing. We hope that in the future a non-invasive marker of NRD for use during exercise can be obtained as the need is apparent, particularly as it relates to evaluating the mechanisms of exertional dyspnea and its response to therapy. However, at the current time, we do not believe EMGpara measured by surface electrodes during upright cycling fulfills such a role.

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Conflicts of interest

None of the authors have any conflicts of interest to report relevant to this manuscript.

References


