Effect of Dyspnea Induced by Breath-holding on Maximal Muscular Strength of Patients with COPD

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Abstract. [Purpose] The purpose of the present study was to clarify the effect of dyspnea induced by breath-holding on maximum muscular strength of patients with COPD. [Subjects] This study recruited 14 COPD subjects via public posting. [Methods] Dyspnea was assessed by the modified Borg scale. The subject asked to stop breathing at end-expiration and to hold their breath with a nose clip for as long as possible. Both total breath-holding time and threshold time of dyspnea were measured with a chronograph. Dyspnea reserve time (DRT) was defined by subtracting the threshold time of perception dyspnea from total breath-holding time in order to calculate the 50% DRT. The muscular strengths of maximal handgrip contraction were measured at baseline, 50% threshold time of dyspnea (subliminal point of dyspnea), and the 50% DRT (supraliminal point of dyspnea). [Results] The maximal handgrip at the supraliminal point of dyspnea was significantly lower than the baseline and subliminal point of dyspnea values. There was no statistically significant difference in maximal muscular strength between baseline and the subliminal point of dyspnea value. [Conclusion] The present results demonstrate that dyspnea induced by breath-holding aggravates weakness in the maximum muscular strength of patients with COPD.

Key words: Breath-holding, Dyspnea, Muscular Strength

INTRODUCTION

Dyspnea, which is often defined as an uncomfortable awareness of difficulty in breathing, is not only a subjective sensation, but also a serious respiratory symptom in patients of Chronic Obstructive Pulmonary Disease (COPD). In particular, during acute exacerbations COPD patients experience excessive perception of dyspnea beyond normal day-to-day variations. This excessive perception of dyspnea during COPD exacerbation generally leads to limitation of weight-bearing daily activities requiring the recruitment of many motor units. Although it is known that the daily amount of weight-bearing activities is related to dyspnea and isometric muscular strength at hospital discharge1, 2), the relationship between dyspnea perception and muscular strength is not fully understood.

Respiratory sensations such as dyspnea are the result of sensory activation of subcortical and cortical neural pathways. Some of these pathways are shared across respiratory modalities while activation of some neural areas is modality specific3). Many brain imaging studies of dyspnea have been conducted using different techniques to induce dyspnea. Despite the use of different intervention techniques, a common predominant neural activity has been found in the insula, operculum, and frontal cortex areas, the anterior cingulated cortex, the posterior cingulated cortex, the cerebellum, the thalamus, and the amygdala4, 5). On the other hand, the common predominant activity during static exercise has been found in the primary motor cortex, primary sensorimotor cortex, and insular cortex6).

Since the cortical processing involved in the maximal voluntary contraction is partly consistent with that of dyspnea perception, respiratory peripheral neural afferents of perception dyspnea, activated by breath-holding, may interact with the neural circuit responsible for processing of motor output. It has been shown that pain shares several cortical cortices with dyspnea, which has been shown to attenuate pain7–9). However, whether perception of dyspnea exerts a similar inhibitory effect on maximal muscular strength has not yet been clarified.

Breath-holding is one of the most powerful methods of inducing the dyspneic sensation, and the breath-holding test can give us much information about the onset and endurance of dyspnea9). There is much evidence of the usefulness of breath-holding challenge in the various diseases10–13). Therefore, the purpose of the present study was to investigate the effect of dyspnea induced by breath-holding on the maximal muscular strength of stable COPD patients.
SUBJECTS AND METHODS

Subjects
Fourteen stable COPD subjects were recruited to investigate the effect of dyspneic sensation induced by breath-holding on maximal muscular strength. All subjects signed an informed consent form and all made aware of the physiological purpose of the study. All were regularly engaged in physical activities but not in competitive sports. Their mean age was 74.2 ± 9.4 (SD) years. The study was approved by the Ethical Committee of Tsuda Hospital.

Methods
All measurements were made while the subjects were seated in a comfortable high-backed armchair. After a 10 min rest, arterial oxyhemoglobin saturation was measured by pulse oximetry (BCI International, Waukesha, WI). Immediately after, the breath-holding test was explained. The subject was asked to stop breathing at end-expiration and to hold his or her breath with a nose clip for as long as possible without encouragement, while referring to the modified Borg scale. The end-expiration that should correspond to FRC was determined by observing the pattern of tidal breathing during at least 30 s. The breath-holding maneuver was repeated a maximum of 3 occasions separated by at least 2 min.

The subject rated sensation of dyspnea [discomfort of breathing] during breath-holding by referring to the modified Borg scale. This is a category scale in which the subject selects a number, from 0 (no dyspnea) to 10 (maximal dyspnea), describing the magnitude of the sensation of dyspnea. At the beginning of the measurement each subject was asked to rate the sensation of “kokyu-konnan” or “discomfort of breathing” while breath-holding. The term “kokyu-konnan” is an exact Japanese translation of “dyspnea” (“kokyu” means breathing or respiration and “konnan” means discomfort or difficulty). In Japan this is not a technical term, and most people understand the meaning of it. The term “kokyu-konnan”, or discomfort of breathing was not defined any further, but the subjects were instructed to avoid rating non-respiratory sensations such as headache or irritation of the pharynx.

Both the total breath-holding time and threshold time of dyspnea were measured with a chronograph. Dyspnea reserve time (DRT) was defined by subtracting the threshold time of dyspnea from total breath-holding time. After subtractions, the 50% DRT point was calculated as the sum of the threshold time of dyspnea and 50% DRT in each subject.

In a preliminary experiment, we assessed the data reproducibility of 2 consecutive breath-holding challenges, spaced 1 week apart. We obtained strong correlations for threshold time of dyspnea and total breath-holding time between the two trials (r = 0.85 p < 0.01, r = 0.83 p < 0.01, respectively).

Evaluations of maximal muscular strength were assessed by measuring the handgrip strength using the method reported by Rantanen et al. Grip strength was measured in a seated position with the elbow flexed at 90°. The baseline grip strength of each hand was measured three times.

During testing, the participant was strongly encouraged to exert the best possible force. The best measure of the stronger hand was used. All patients completed the baseline handgrip strength test. Then, they were entered into a randomized, crossover study of (3 sec) handgrip strength measurements at two points: 50% threshold time of dyspnea (subliminal point of dyspnea), and the 50% DRT point (supraliminal point of dyspnea) on different days. For each subject, to measure the maximal handgrip strength at the subliminal and supraliminal point of dyspnea, we used one-way repeated measures ANOVA. A p < 0.05 was considered significant.

RESULTS
All 14 subjects completed the experiments without any difficulty or side effects. The characteristics of the subjects are summarized in Table 1. Table 2 shows the values of muscle force and breath-holding. Table 3 shows the maximal handgrip strengths at baseline, subliminal point of dyspnea and supraliminal point of dyspnea. The maximal handgrip strength at the supraliminal point of dyspnea (25.9 ± 5.1 kg) was significantly lower than that of the baseline (28.1 ± 4.5 kg, p < 0.001) and that at subliminal point of dyspnea (27.2 ± 5.5 kg, p = 0.013). As shown in Table 3, there was no significant difference in maximal handgrip strength between baseline (28.1 ± 4.5 kg) and the subliminal point of dyspnea (27.2 ± 5.5 kg).

DISCUSSION
The novel finding of the present study is that breath-holding beyond the threshold time of dyspnea significantly attenuates the maximal handgrip force of patients with COPD. On the other hand, breath-holding under the threshold time of dyspnea did not significantly affect the maximal handgrip strength.

There is much evidence supporting the usefulness of the breath-holding challenge. In this study, the maximal Borg scale of our data is consistent with the results reported by Nannini et al. However there is a difference in breath-holding time between our data and the research of Nannini et al. Although we recruited stable COPD patients, Nannini and colleagues recruited mild to near fatal asthma patients. Since there is a difference in the mechanism of perception of dyspnea between asthma and COPD, this disagreement in breath-holding times is probably due to a disease-specific factor.

Recently, it has been recognized that physical activity of COPD patients is an independent prognostic factor of mortality and hospitalization. Hurst JR et al. reported that exacerbations of COPD are not random events but cluster together in time with a high-risk period for recurrent exacerbation in the 8-week period after an initial exacerbation. Taken together, it seems that the regular physical activity
activity after acute exacerbation is a crucial factor in the prevention of recurrent exacerbation. However, although the excessive perception of dyspnea beyond normal day-to-day variations during COPD exacerbation generally leads to limitation on weight-bearing daily activities requiring the recruitment of many motor units, the relationship between dyspnea perception and muscular strength is not fully understood. In the present study, we found that the perception of dyspnea induced by breath-holding impairs maximal muscular strength in stable COPD patients. Therefore, our data indicate that existence of perception of the dyspnea plays a crucial role in exertion of the muscular strength by patients with COPD.

One possible mechanism for this effect of dyspnea, induced by breath-holding on maximal handgrip strength, may be the interaction between brain cortical regions involved in dyspnea and those in maximal muscular strength. It has been shown that pain shares several cortical cortices with dyspnea, which has been shown to attenuate pain\textsuperscript{7, 8). In addition to these findings, coughing which shares several brain regions with dyspnea has been found to modify dyspnea\textsuperscript{18). Together taken, when two nerve impulses occur on a common neural substrate, the net resulting intensity of the response will be lower than that expected from the summation of the responses of the two separate stimuli. Despite the use of different dyspnea intervention techniques, common predominant neural activities have been found in the insula, operculum, and frontal cortex areas, the anterior cingulated cortex, the posterior cingulated cortex, the cerebellum, the thalamus, and the amygdala\textsuperscript{4, 5). On the other hand, during static handgrip, common predominant activities have been

| Table 1. Background of stable COPD patients |
|-----------------|-------|---|
| Characteristics |       |   |
| Age             | 74.2  | 9.4 |
| Height (cm)     | 162.9 | 0.1 |
| Weight (kg)     | 53.4  | 6.3 |
| BMI (kg/m\textsuperscript{2}) | 20.1 | 2.0 |
| Pulmonary function |       |   |
| FEV\textsubscript{1} (L) | 1.21 | 0.61 |
| %FEV\textsubscript{1} (%) | 44.19 | 20.91 |
| FVC (L)         | 2.42  | 0.84 |
| %FVC (%)        | 73.98 | 26.32 |
| FEV\textsubscript{1}/FVC | 44.91 | 12.93 |
| GOLD stage      |       |   |
| Stage 1         | 1     |   |
| Stage 2         | 2     |   |
| Stage 3         | 8     |   |
| Stage 4         | 3     |   |

Data are presented as mean ± SD. BMI: Body Mass Index; FVC: Forced vital capacity; FEV\textsubscript{1}: forced expiratory volume in 1 second. The staging of the disease was divided into stages I to IV based on the GOLD criteria.

| Table 2. Characteristics of muscle force and breath-holding challenge |
|-----------------|-----------------|-----------------|
| Characteristics | Muscle force | Breath-holding parameter |
|                 |               |                 |
| Handgrip strength (kg) | 28.6 ± 3.7 |                 |
| Quadriceps strength (kg) | 29.3 ± 6.6 |                 |
| Threshold time of dyspnea (sec) | 20.4 ± 7.4 | 23.5 ± 13.3 |
| Highest Borg dyspnea during breath-holding | 5.9 ± 1.9 | 9.2 ± 1.9 |
| Dyspnea reserve time (DRT), (sec) | 14.8 ± 7.4 | 34.8 ± 10.4 |
| Lowest SpO\textsubscript{2} during breath-holding (%) | 90.3 ± 3.5 | 91.2 ± 3.8 |

Data are presented as mean ± SD. Dyspnea reserve time (DRT) was calculated by subtracting the threshold time of dyspnea from total breath-holding time. The 50% DRT point was calculated as sum of the threshold time of dyspnea and 50% DRT of each subject.

| Table 3. Maximal handgrip strengths of baseline, the subliminal point of dyspnea, and the supraliminal point of dyspnea |
|-----------------|-----------------|-----------------|-----------------|
| Characteristics | Baseline (kg) | Subliminal point (kg) | Supraliminal point (kg) |
|                 | 28.1 ± 4.5 | 27.2 ± 5.5 | 25.9 ± 5.1*† |

* significant difference between the subliminal and supraliminal points (p < 0.03). † significant difference between baseline and the supraliminal point (p < 0.001).

The subliminal point is the subliminal point of dyspnea which was estimated as the 50% threshold time of dyspnea induced by breath-holding. The supraliminal point is the supraliminal point of dyspnea which was estimated as the 50% DRT point.

found in the primary motor cortex, primary sensorimotor cortex and insula cortex\textsuperscript{9). Therefore, the insular cortex, a common central processing area for dyspnea and for handgrip strength, could have contributed to the alteration in the handgrip strength observed in our stable COPD patients.

The present study shows that perception of dyspnea has an inhibitory effect on the muscular strength of stable COPD patients. Our results suggest that we should pay attention to the existence of perception of the dyspnea in order to prescribe the suitable loads for weight-bearing activities of patients with COPD.

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