



The Effect of Breathing Retraining Using Metronome-Based Acoustic Feedback on Exercise Endurance in COPD: A Randomized Trial

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Abstract

Background During exercise-training patients with chronic obstructive pulmonary disease (COPD) can entrain their breathing pattern to visual-feedback cues as to achieve a slower respiratory rate and prolong exhalation. The result is an improvement in exercise tolerance and a reduction in dynamic hyperinflation. Acoustic stimuli, including metronome-generated acoustic stimuli, can entrain human movements. Accordingly, we hypothesized that exercise duration and dynamic hyperinflation would be less after exercise-training plus breathing-retraining using a metronome-based acoustic-feedback system than after exercise-training alone.

Methods Of 205 patients with COPD [$FEV_1 = 44 \pm 16\%$ predicted ($\pm SD$)] recruited, 119 were randomly assigned to exercise-training plus breathing-retraining using acoustic feedback ($n = 58$) or exercise-training alone ($n = 61$). Patients exercised on a treadmill thrice-weekly for 12 weeks. Before and at completion of training, patients underwent constant-load treadmill testing with inspiratory capacity measures every 2 min.

Results At completion of training, improvements in exercise duration in the breathing-retraining plus exercise-training and exercise-training alone groups were similar ($p = 0.35$). At isotime, inspiratory capacity increased (less exercise-induced dynamic hyperinflation) by 3% ($p = 0.001$) in the breathing-retraining plus exercise-training group and remained unchanged in the exercise-alone group. The between-group change in inspiratory capacity, however, was not significant ($p = 0.08$).

Conclusions In patients with COPD, breathing-retraining using a metronome-based acoustic feedback did not result in improved exercise endurance or decreased dynamic hyperinflation when compared to exercise-training alone.

Trial registry: ClinicalTrials.gov; No.: NCT NCT01009099; URL: <http://www.clinicaltrials.gov>

Keywords COPD · Exercise · Rehabilitation

Introduction

In most patients with chronic obstructive pulmonary disease (COPD), exercise-induced dynamic hyperinflation is a major contributor to decreased exercise tolerance [1].

Dynamic hyperinflation decreases exercise tolerance through decreases in the capacity of the respiratory muscles to generate pressure [2], decreases in tidal volume (V_T), and increases in mechanical load [3] and dead-space- V_T ratio [4].

We previously reported that a ventilation-feedback system to provide visual, computerized feedback during exercise in patients with COPD decreased respiratory frequency

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(f_R) and prolonged exhalation [5, 6]. By decreasing f_R and prolonging exhalation, we were able to limit the onset and severity of exercise-induced dynamic hyperinflation and to prolong exercise duration [5–7].

Acoustic stimuli, including metronome-generated acoustic stimuli, can entrain human movements [8, 9]. Such entrainment results from an automatic synchronization between internal bodily oscillators and external rhythms [8]. Converging neurophysiological evidence suggests that brain regions underpinning movement production are also deployed during rhythm perception [8, 9]. Auditory stimuli can also modulate movement by altering output of the central pattern generators in the spinal cord. This redundancy in neural pathways explains why period shifts in music that are not consciously perceived as such can still induce entrainment of motor responses including finger tapping in patients with cerebellar lesions [9].

Bearing in mind that movements can be entrained to metronome-generated acoustic stimuli [8] and the mechanistic links between breathing-retraining and a reduction in exercise-induced dynamic hyperinflation and a prolongation in exercise duration [5–7], it would appear possible to predict that patients with COPD may be able to entrain breathing pattern to metronome-generated acoustic stimuli during exercise-training and achieve greater benefits from training that exercise alone.

The primary objective of this study was thus to explore the impact of exercise-training plus breathing-retraining using metronome-based acoustic feedback on exercise duration in patients with COPD. Specifically, we hypothesized that exercise duration would be longer after exercise-training plus breathing-retraining using acoustic feedback than after exercise-training alone.

The secondary objective of this study was to assess the impact of breathing-retraining on dynamic hyperinflation and quality of life. Specifically, we hypothesized that exercise-induced dynamic hyperinflation would be less and quality of life improved after exercise-training plus breathing-retraining than after exercise-training alone.

This is the first prospective randomized controlled trial designed to assess the impact of exercise-training plus breathing-retraining using a metronome-based acoustic feedback on exercise duration, dynamic hyperinflation, and quality of life in patients with moderate-to-severe COPD.

Methods

(See the online supplement for additional details).

Patients with moderate-to-severe COPD were recruited into the study (Table 1). Inclusion criteria were: ≥ 40 years of age, $SpO_2 \geq 90\%$ at peak exercise (with or without supplemental oxygen) [6], able to hear the metronome sounds,

Table 1 Characteristics of patients and their responses to incremental-load treadmill test at baseline

Characteristic	Exercise-training plus breathing-retraining ($n = 58$)	Exercise-training alone ($n = 61$)
Age (years)	66 \pm 8	66 \pm 8
BMI (kg/m ²)	30.0 \pm 6.7	29.3 \pm 6.2
Smoking (pack year)	58 \pm 38	49 \pm 33
FEV ₁ (L)	1.27 \pm 0.51	1.31 \pm 0.44
[% pred]	[44 \pm 15]	[44 \pm 16]
FEV ₁ /FVC %	47 \pm 13	45 \pm 12
TLC	7.19 \pm 1.89	7.47 \pm 1.49
[%pred]	[124 \pm 25]	[125 \pm 25]
RV/TLC	60 \pm 11	58 \pm 9
[%pred]	[171 \pm 30]	[168 \pm 27]
DLCO, %pred	45 \pm 23	50 \pm 23
pH	7.41 \pm 0.03	7.42 \pm 0.02
PaCO ₂ (mmHg)	41 \pm 6	42 \pm 6
PaO ₂ (mmHg)	73 \pm 12	73 \pm 10
Exercise time (min)	8.9 \pm 4.1	9.3 \pm 3.4
VO _{2peak} (mL kg ⁻¹ min ⁻¹)	15.7 \pm 3.9	16.6 \pm 3.3
V _{Epeak} (L min ⁻¹)	39 \pm 13	42 \pm 13
V _{Tpeak} (L)	1.5 \pm 0.4	1.5 \pm 0.4
f _{Rpeak} (beats min ⁻¹)	29 \pm 6	29 \pm 6
HR _{peak} (beats min ⁻¹)	119 \pm 21	123 \pm 16

Values are mean \pm standard deviation

BMI body mass index [weight (kg)/height (m)²], FEV₁ forced expiratory volume in 1 s, [% pred] percent predicted, FVC forced vital capacity, TLC total lung capacity, RV/TLC residual volume/total lung capacity, DLCO diffusing capacity, PaCO₂ partial pressure of arterial carbon dioxide, PaO₂ partial pressure of arterial oxygen, VO_{2peak} oxygen uptake at peak exercise, V_{Epeak} minute ventilation at peak exercise, V_{Tpeak} tidal volume at peak exercise; f_{Rpeak} respiratory frequency at peak exercise, HR_{peak} heart rate at peak exercise

stable clinical condition. The study was approved by the local Institutional Review Board. Written informed consent was obtained.

Patients completed the Chronic Respiratory Disease Questionnaire (CRDQ) [10] and incremental-load and constant-load treadmill tests (Fig. 1). Thereafter, using permuted block randomization, patients were assigned to breathing-retraining plus exercise-training, or exercise-training alone.

Training involved 36 sessions. Patients trained in the laboratory three times weekly. Exercise intensity was set at a percentage of peak-oxygen uptake (VO_{2peak}) recorded during the baseline incremental-load treadmill test (Supplement Fig. 1E). Patients assigned to the two groups began training on the treadmill for 25 min and progressed as tolerated up to 45 min of exercise (rest time not included). Moreover, patients randomized to breathing-retraining plus exercise-training practiced breathing-retraining with the metronome before starting exercise-training. To help patients entrain

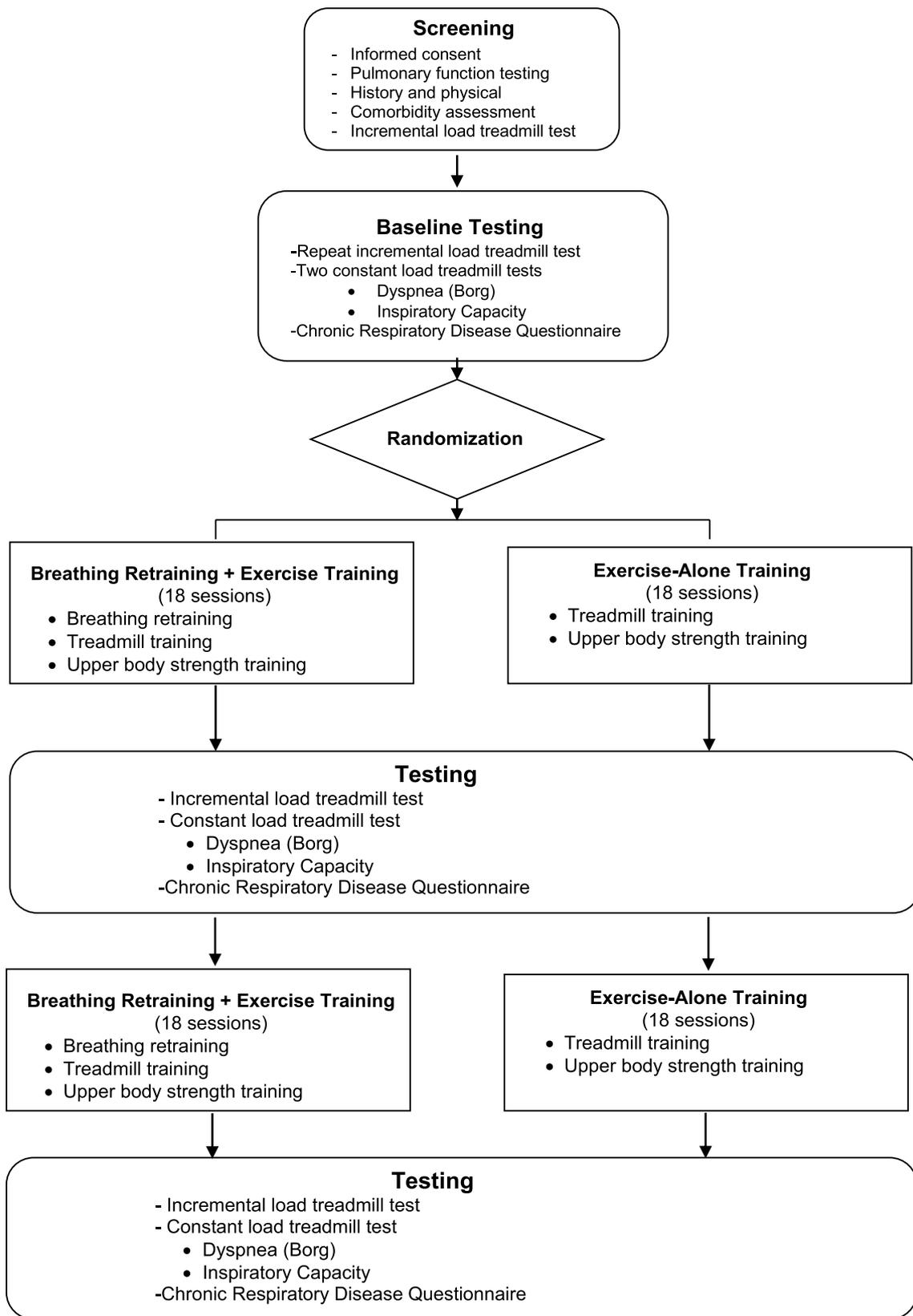


Fig. 1 Flow diagram of study design

with the metronome's acoustic cues (and to help the exercise technician monitor the patient's start and end of inhalation and exhalation) patients were instructed to inhale through the nose and exhale through the mouth with their lips pursed [11]. (See online Supplement for details.) At the start of training, the f_R goal in the breathing-retraining group was 1–2 breaths less than the f_R recorded at a similar workload during baseline exercise stress test. As training progressed, the f_R goal in this group was decreased by 1 breath min^{-1} while maintaining a 3:1 ratio of expiratory time (T_E) over inspiratory time (T_I) (Supplement Fig. 2E). Patients in the exercise-training alone were free to choose their breathing pattern.

The incremental-load treadmill-exercise test was repeated after 18 training sessions to reset exercise intensity for the remaining of the study according to changes in level of fitness (Fig. 1). To determine the value of $V_{O_{2peak}}$ at the conclusion of training, incremental-load treadmill-exercise test was repeated after the 36th training session.

The constant-load treadmill-exercise test was repeated after 18 training sessions. The results of this test were used in the intention-to-treat analysis of patients who trained for 19–35 training sessions. To determine exercise endurance, extent of exercise dynamic hyperinflation and breathing pattern at the conclusion of training, the constant-load test was repeated after the 36th session. The constant-load tests were continued until volitional exhaustion or until 60 min had elapsed. (See online supplement for details.)

Data Analysis

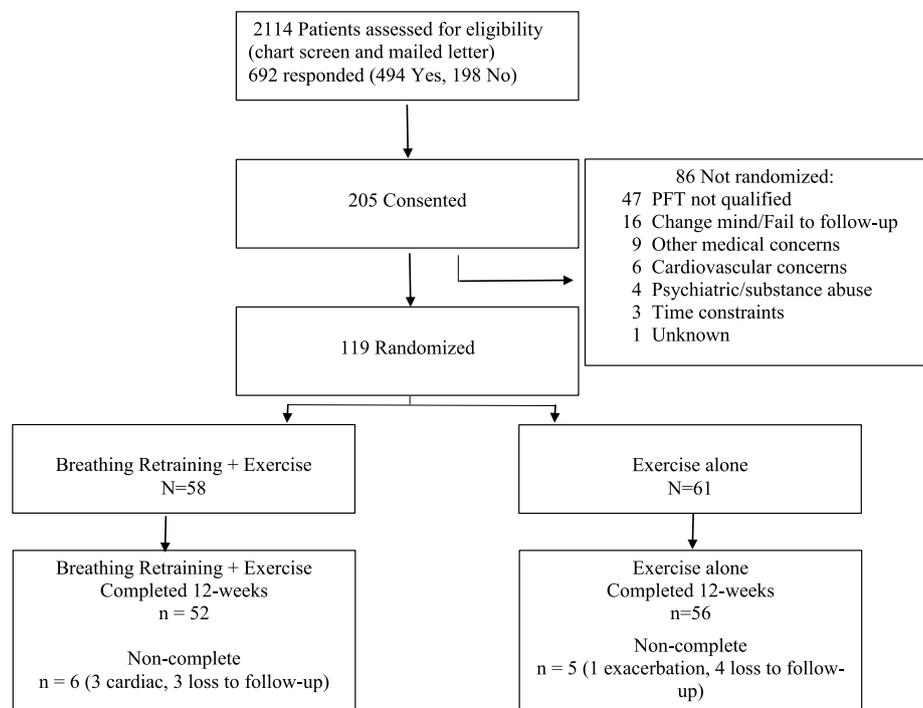
The Kolmogorow–Smirnov test was used to assess distribution of data. Normally distributed data are presented as mean \pm SD. Non-normally distributed data are presented as median and interquartile ranges (IQR).

The primary outcome variable was duration of the constant-load treadmill test after 12 weeks of training. The duration of the test between groups was compared using independent t tests (*Primary aim*). Data were analyzed with an intention-to-treat approach using the last observation carried forward [12]. Based on our previous investigation [6], to achieve 80% power to detect a difference of 8.8 min in exercise duration with a pooled standard deviation of the change of 18 min [6] (effect size = 0.49) [13], 132 patients were needed using a two-sample t test ($\alpha = 0.05$). Respiratory pattern and severity of dynamic hyperinflation recorded at isotime (the fourth minute of the constant-load test) at baseline were compared with the corresponding isotime values (the fourth minute of the constant-load test) after training using paired t tests (*Secondary aim*). Statistical tests were 2-sided, and $p \leq 0.05$ was criterion for statistical significance.

Results

Two hundred and five patients (95% male) consented to participate in the study. Eighty-six of them were not randomized due to various reasons (Fig. 2). The remaining 119 were randomized to exercise-training plus breathing-retraining

Fig. 2 Consort flowchart



using metronome-based acoustic feedback ($n = 58$) or exercise-training alone ($n = 61$) (Table 1). There were no differences in baseline characteristics between the two randomized groups.

Duration of Constant-Load Treadmill-Exercise Testing

At baseline, the median (IQR range) exercise duration on the constant-load treadmill test was 7.1 min (IQR 4.6–8.1 min) in the exercise-training plus breathing-retraining group and 6.3 min (IQR 5.5–8.0 min) in the exercise-training alone group. (These values include a 2-min warm-up completed at 2.9 km h⁻¹.) At the end of training, exercise duration increased to 9.2 min (IQR 6.0–15.0 min) in the exercise-training plus breathing-retraining group ($p < 0.001$) and it increased to 11.0 min (IQR 7.9–21.0 min) in the exercise-training alone group ($p < 0.001$). Exercise duration at the end of training was not different between the two groups of patients ($p = 0.35$).

Patients in the breathing-retraining group attended less training sessions than patients in the exercise-training alone group: 94% (IQR 77–100%) and 97% (IQR 92–100%), respectively ($p = 0.028$). To determine the independent contribution of training protocol on the duration of the constant-load treadmill test at the end of training when controlling for baseline exercise time and adherence to training, ANCOVA was conducted on all randomized patients. In this intent-to-treat analysis, duration of constant-load treadmill test at the end of training in the breathing-retraining and in the exercise-alone group were not different ($F = 1.18$, $p = 0.28$).

Midway through the training program, 93% of patients in the breathing-retraining group, and 97% in the exercise-alone group were training at Stage 2 (5-min bouts of exercise at 80–85% of $\dot{V}O_{2peak}$) or more (Supplement Fig. 1E). At the end of training, 50% patients in the breathing-retraining group, and 70% in the exercise-alone group trained at Stage 5 (15-min bouts of exercise at 80–85% of $\dot{V}O_{2peak}$). During the last week of training, patients assigned to exercise-training plus breathing-retraining trained for 42.6 ± 4.6 min and those assigned to exercise-training alone trained for 40.3 ± 6.5 min.

Isotime Exercise During Constant Work-Rate Exercise Testing

Compared to baseline, respiratory pattern at isotime in the breathing-retraining group demonstrated a magnitude of change not observed in the exercise-alone group. T_E increased by 7% (IQR 0–29%) ($p < 0.001$), f_R decreased by 9% (IQR -22 to 0%) ($p < 0.01$) and V_T increased by 4% (IQR 0–17%) with breathing-retraining. Isotime T_E , f_R and V_T did not change with exercise-alone. At isotime,

inspiratory capacity (IC) increased (less exercise-induced dynamic hyperinflation) by 3% (IQR -2 to 14%) ($p = 0.001$) with breathing-retraining and remained unchanged with exercise-alone. The percent increase in IC was not greater with breathing-retraining than with exercise-alone ($p = 0.08$).

Symptoms Experienced at the Conclusion of Constant-Load Testing

Five minutes after the constant-load tests, patients were asked, “What was the primary reason that made you stop exercising?” At baseline 48% of patients in the breathing-retraining group and 33% in the exercise-alone group stopped exercising because of dyspnea. The corresponding values after training were 31%, and 33%.

Oxygen Uptake at the Conclusion of Incremental Treadmill Tests

At baseline, $\dot{V}O_{2peak}$ in the breathing-retraining group was not different from the $\dot{V}O_{2peak}$ in the exercise-alone group ($p = 0.18$) (Table 1). At the end of training, $\dot{V}O_{2peak}$ in the breathing-retraining group and in the exercise-alone group were similar to the $\dot{V}O_{2peak}$ recorded at baseline. These results are analogous to the findings of other investigators [6, 14–18].

Health-Related Quality of Life

At the conclusion of training, dyspnea during activities of daily living, fatigue, emotional function and mastery improved in both groups of patients (Table 2). Improvements in mastery were greater in the breathing-retraining group than in the exercise-alone group ($p = 0.042$).

Table 2 CRDQ at baseline and at the end of training

	Breathing-retraining plus exercise-training $n = 58$		Exercise-training alone $n = 61$	
	Baseline	12-week	Baseline	12-week
Dyspnea	16.6 ± 4.2	21.1 ± 5.4	16.2 ± 5.4	19.4 ± 6.7
Fatigue	15.9 ± 4.0	17.7 ± 4.8	16.5 ± 4.7	18.4 ± 5.0
Emotion	33.3 ± 7.9	36.6 ± 8.6	33.6 ± 9.4	36.9 ± 9.0
Mastery*	18.8 ± 5.1	21.2 ± 5.0	19.6 ± 5.4	21.0 ± 5.3

Values are mean ± standard deviation

* $p \leq 0.042$ between groups

Discussion

This is the first randomized controlled trial designed to compare the benefits of pulmonary rehabilitation in COPD carried out with exercise-training plus breathing-retraining using metronome-based acoustic feedback, and exercise-training alone. Despite achieving changes in breathing pattern with breathing-retraining, at the end of training, improvements in exercise duration and dynamic hyperinflation with exercise-training plus breathing-retraining and with exercise-training alone were equivalent. In addition, among quality of life domains, only improvements in mastery were greater with exercise-training plus breathing-retraining than with exercise-training alone.

Training, Breathing Pattern, Exercise Duration, and Oxygen Uptake

Our investigation was based on the premises that, in patients with COPD, it is possible to retrain breathing pattern in order to limit dynamic hyperinflation and, thus, augment the effectiveness of pulmonary rehabilitation [6, 7]. As hypothesized, 12 weeks after exercise-training plus breathing-retraining using metronome feedback, patients experienced a 7% increase in T_E , 9% decrease in f_R , and 3% decrease in dynamic hyperinflation. These improvements, however, were less than the improvements we previously recorded with breathing-retraining using visual-feedback [6, 7]. In those studies, T_E increased 31–36% from baseline, f_R decreased by 19–24% and dynamic hyperinflation decreased by 9–25% [6, 7].

The modest improvements in breathing pattern achieved with breathing-retraining using the metronome-based acoustic feedback were insufficient to improve exercise endurance on the constant-load treadmill test more than exercise-training alone—this even when controlling for baseline exercise time and adherence to training. Factors that likely contributed to our negative results include: lack of real-time objective feedback of the achieved respiratory pattern, lack of post-exercise reward, distraction from the task at hand, and the type of acoustic stimulus (metronome) used to retrain breathing pattern.

By study design, breathing-retraining patients received feedback on their success (or lack thereof) with which they entrained breathing pattern with the metronome only through the verbal remarks of the exercise technician. At the end of each exercise bout, patients were not presented with objective data on how often they had been able to entrain with the metronome. In contrast, our original visual-feedback system provided real-time feedback: when patients exercised, they saw on a computer screen whether they were meeting T_i and T_e targets and adjusted their breathing pattern

accordingly [6, 7]. In addition, at the conclusion of each exercise bout, the visual-feedback system provided patient with the percentage of successfully T_i and T_e hits [6, 7]. We reason that real-time feedback (computer screen) and post-exercise reward (percent hits) contributed to the success of our visual-feedback system [6, 7] and to the modest results with our metronome-feedback system.

Breathing-retraining using our original visual-feedback system [6, 7] requires patients to pay attention to their breathing pattern while exercising. Without such real-time feedback, patients randomized to the acoustic-feedback system may not have been as focused on the task at hand—i.e., in some instances, exercise trainers had to continuously coach patients throughout the exercise sessions. Additionally, exercise trainers may have missed times when patients were not following the metronome thus failing to properly coach patients on breathing pattern.

Investigators have reported that isolated tempo or metronomic stimuli can automatically affect motor behavior [19]. For instance, despite a limited number of study participants [20, 21] and lack of a control group [21], investigators have reported positive results when using a metronome to maintain the prescribed walking speed during pulmonary rehabilitation. Temporal acoustic information alone (i.e., a metronome), however, does not always elicit behavioral changes [8]. Nittono et al. [22] found that participants' performance in a self-paced line tracing task was accelerated significantly by richer musical stimuli (fast music) but not by a similarly fast metronome.

Purse lip breathing, used to help patients retrain breathing pattern, did not augment the effectiveness of pulmonary rehabilitation. This finding is congruent with previous work demonstrating the inconsistent impact of purse lip breathing on dyspnea [23], exercise-induced dynamic hyperinflation [24] and exercise capacity [25, 26].

We considered the possibility of a type II error since we randomized 119 patients and did not reach our targeted sample size of 132. Given that the effect size of the change in exercise duration between the groups was 0.17 in favor of the exercise-alone group, we reason that such an error did not occur.

Quality of Life and Dyspnea During Activities of Daily Living

At the conclusion of training, dyspnea, fatigue, emotional function and mastery, the patient's perception of control over his/her disease, improved with exercise-alone and with exercise plus breathing-retraining. The improvement of mastery was greater with exercise plus breathing-retraining than with exercise-alone. This finding, which is consistent with the results of our previous study [7], raises the possibility of a mechanistic link between the patient's success in

retraining the pattern of breathing during exercise and the experience of having achieved a greater control over respiratory symptoms.

At the conclusion of the study, the two groups of patients reported clinically significant decreases in perceived dyspnea during activities of daily living. Improvements in dyspnea at the conclusion of the two protocols, both of which included exercise-training, support the results of earlier investigations [6, 27–29]. The similar decrease in perceived dyspnea during activities of daily living in the two groups suggests that the modest changes in respiratory pattern recorded at the conclusion of training in patients randomized to metronome plus exercise had no impact on this symptom. Alternatively, we may have underestimated the improvements in dyspnea during activities of daily living. Underestimation of the improvements may have resulted from the strategy chosen to administer the CRDQ (*see online supplement*). Unlike the procedures recommended by Guyatt et al. [10] participants in the current investigation were not informed of their previous responses. This strategy was chosen to avoid or limit any bias that might occur from the patients' desire to please the investigators with their responses. Another mechanism for this lack of statistical difference may be a type II error.

Clinical Implications/Future Directions

Solid experimental data indicate that the pattern of breathing of patients with COPD can be retrained during exercise [5–7]. The combined results of our current and prior investigations [5–7], underscore the importance of using a strong entraining signal during breathing-retraining to ensure substantial changes in breathing pattern. We reason that real-time feedback, a rewarding system and, possibly, a quiet environment contribute to the achievement of the desired breathing-retraining. Accordingly, we propose that future investigations on breathing-retraining must include a display of breathing pattern achieved by the patient. To this end, simple tools to monitor breathing pattern that do not require a mouthpiece such as piezoelectric bands [30], electrical impedance tomography [31], and respiratory inductive plethysmography [32] may be helpful.

In conclusion, in patients with moderate-to-severe COPD, improvements in exercise duration recorded at the completion of exercise-training plus breathing-retraining using a metronome-based acoustic feedback were similar to the improvements in exercise duration recorded at the completion of exercise-training alone.

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Compliance with Ethical Standards

Conflict of interest The authors have no conflicts of interest to report.

References

- O'Donnell DE, Laveneziana P (2006) The clinical importance of dynamic lung hyperinflation in COPD. *COPD* 3(4):219–232
- Sinderby C, Spahilja J, Beck J et al (2001) Diaphragm activation during exercise in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 163(7):1637–1641
- Sliwinski P, Kaminski D, Zielinski J, Yan S (1998) Partitioning of the elastic work of inspiration in patients with COPD during exercise. *Eur Resp J* 11(2):416–421
- O'Donnell DE, Reville SM, Webb KA (2001) Dynamic hyperinflation and exercise intolerance in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 164(5):770–777
- Collins EG, Fehr L, Bammert C et al (2003) Effect of ventilation-feedback training on endurance and perceived breathlessness during constant work-rate leg-cycle exercise in patients with COPD. *J Rehabil Res Dev* 40(5 Suppl 2):35–44
- Collins EG, Langbein WE, Fehr L et al (2008) Can ventilation-feedback training augment exercise tolerance in patients with chronic obstructive pulmonary disease? *Am J Respir Crit Care Med* 177(8):844–852
- Collins EG, Jelinek C, O'Connell S et al (2014) Contrasting breathing retraining and helium-oxygen during pulmonary rehabilitation in COPD: a randomized clinical trial. *Respir Med* 108(2):297–306
- Metcalfe T (2016) The contribution of different musical variables to the effect of background music on motor behavior. *Psychomusicol Music Mind Brain* 26(2):132–138
- Molinari M, Leggio MG, De Martin M, Cerasa A, Thaut M (2003) Neurobiology of rhythmic motor entrainment. *Ann N Y Acad Sci* 999:313–321
- Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW (1987) A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 42:773–778
- Faling LJ (2003) Controlled breathing techniques and chest physical therapy in chronic obstructive pulmonary disease and allied conditions. In: Casuburi R, Petty TL (eds) *Principles and practice of pulmonary rehabilitation*. W.B. Saunders, Philadelphia, pp 167–182
- Lachin JM (2000) Statistical considerations in the intent-to-treat principle. *Controlled Clin Trials* 21(3):167–189
- Cohen J (1988) *Statistical power analysis for the behavioral sciences*. Lawrence Erlbaum Associates, Inc., Hillsdale
- O'Donnell DE, McGuire M, Samis L, Webb KA (1998) General exercise training improves ventilatory and peripheral muscle strength and endurance in chronic airflow limitation. *Am J Respir Crit Care Med* 157(5 Pt 1):1489–1497
- Casaburi R, Bhasin S, Cosentino L et al (2004) Effects of testosterone and resistance training in men with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 170(8):870–878
- Ortega F, Toral J, Cejudo P et al (2002) Comparison of effects of strength and endurance training in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 166(5):669–674
- Porszasz J, Emtner M, Goto S, Somfay A, Whipp BJ, Casaburi R (2005) Exercise training decreases ventilatory requirements and exercise-induced hyperinflation at submaximal intensities in patients with COPD. *Chest* 128(4):2025–2034

18. Collins EG, Langbein WE, Fehr L, Maloney C (2001) Breathing pattern retraining and exercise in persons with chronic obstructive pulmonary disease. *AACN Clin Issues* 12(2):202–209
19. Hausdorff JM, Lowenthal J, Herman T, Gruendlinger L, Peretz C, Giladi N (2007) Rhythmic auditory stimulation modulates gait variability in Parkinson's disease. *Eur J Neurosci* 26(8):2369–2375
20. Pomidori L, Contoli M, Mandolesi G, Cogo A (2012) A simple method for home exercise training in patients with chronic obstructive pulmonary disease: one-year study. *J Cardiopulm Rehabil Prev* 32(1):53–57
21. Lee SS, Kim C, Jin YS et al (2013) Effects of home-based pulmonary rehabilitation with a metronome-guided walking pace in chronic obstructive pulmonary disease. *J Korean Med Sci* 28(5):738–743
22. Nittono H, Tsuda A, Akai S, Nakajima Y (2000) Tempo of background sound and performance speed. *Percept Mot Skills* 90(3 Pt 2):1122
23. Roberts SE, Stern M, Schreuder FM, Watson T (2009) The use of pursed lips breathing in stable chronic obstructive pulmonary disease: a systematic review of the evidence. *Phys Therapy Rev* 14(4):240–246
24. Bianchi R, Gigliotti F, Romagnoli R et al (2007) Patterns of chest wall kinematics during volitional pursed-lip breathing in COPD at rest. *Respir Med* 101(7):1412–1418
25. Nield MA, Soo Hoo GW, Roper JM, Santiago S (2007) Efficacy of pursed-lips breathing: a breathing pattern retraining strategy for dyspnea reduction. *J Cardiopulm Rehabil Prev* 27(4):237–244
26. Zhang ZQ, Chen RC, Yang QK, Li P, Wang CZ, Zhang ZH (2008) A randomized controlled trial study of pulmonary rehabilitation with respiratory physiology as the guide on prognosis in patients with chronic obstructive pulmonary disease. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue* 20(10):607–610
27. Puhan MA, Guyatt GH, Goldstein R et al (2007) Relative responsiveness of the Chronic Respiratory Questionnaire, St. Georges Respiratory Questionnaire and four other health-related quality of life instruments for patients with chronic lung disease. *Respir Med* 101(2):308–316
28. Green RH, Singh SJ, Williams J, Morgan MD (2001) A randomised controlled trial of four weeks versus seven weeks of pulmonary rehabilitation in chronic obstructive pulmonary disease. *Thorax* 56(2):143–145
29. Ferreira G, Feuerman M, Spiegler P (2006) Results of an 8-week, outpatient pulmonary rehabilitation program on patients with and without chronic obstructive pulmonary disease. *J Cardiopulm Rehabil* 26(1):54–60
30. Roca M, Mitu F, Mitu O, Roca IC, Leon MM, Mihaescu T (2015) Characteristics of respiratory mechanics in chronic obstructive pulmonary disease. *Rev Med Chir Soc Med Nat Iasi* 119(2):361–367
31. Voscopoulos C, Brayonov J, Ladd D, Lalli M, Panasyuk A, Freeman J (2013) Special article: evaluation of a novel noninvasive respiration monitor providing continuous measurement of minute ventilation in ambulatory subjects in a variety of clinical scenarios. *Anesth Analg* 117(1):91–100
32. Bernardi E, Pomidori L, Bassal F, Contoli M, Cogo A (2015) Respiratory muscle training with normocapnic hyperpnea improves ventilatory pattern and thoracoabdominal coordination, and reduces oxygen desaturation during endurance exercise testing in COPD patients. *Int J Chron Obstruct Pulmon Dis* 10:1899–1906

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