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Expiratory Muscle Strength Training in Persons With Multiple Sclerosis Having Mild to Moderate Disability: Effect on Maximal Expiratory Pressure, Pulmonary Function, and Maximal Voluntary Cough

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Abstract

Objective—To determine the effect of expiratory muscle strength training (EMST) on maximal expiratory strength, pulmonary function, and maximal voluntary cough in persons with multiple sclerosis (MS) having mild to moderate disability.

Design—Before-after trial.

Setting—Assessments were completed in the privacy of the subject's home or exercise physiology laboratory.

Participants—Seventeen persons with MS were age- and sex-matched to 14 healthy controls.

Intervention—Eight weeks of EMST and 4 weeks of detraining.

Main Outcome Measures—Maximal respiratory pressures, pulmonary function, and maximal voluntary cough were assessed 3 times (pretraining, posttraining, detraining). Maximal expiratory pressure (MEP) was assessed weekly and training intensity adjusted based on the new measurement.

Results—Subjects with MS had lower MEP, decreased pulmonary function, and weaker maximal voluntary cough at each assessment. EMST increased MEP and peak expiratory flow. However, improvement in maximal voluntary cough only occurred in subjects with a moderate level of disability when the MS group was subdivided into mild and moderate disability levels based on the Expanded Disability Status Scale.

Conclusions—EMST is a viable tool to enhance the strength of the respiratory muscles. However, further work is needed to determine the best parameters to assess change in cough following EMST.

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Keywords

Cough; Multiple sclerosis; Peak expiratory flow rate; Pulmonary function tests; Rehabilitation; Respiratory muscle training.

MULTIPLE SCLEROSIS (MS) is a demyelinating disease of the central nervous system that can produce a range of respiratory dysfunctions. Most studies examining respiratory status in patients with MS reported expiratory and/or inspiratory muscle weakness only in persons with significant disability caused by paraplegia or quadriplegia.¹⁻⁹ Previous studies designed to assess the effects of expiratory and/or inspiratory muscle strength training in patients with MS with high level of disability have shown mixed results.^{3,5,7-9} Although training resulted in respiratory muscle strength gains, no change in pulmonary function was observed in some of the studies.^{3,5,7,8} In contrast, other patient populations have had improvement in pulmonary function following expiratory and/or inspiratory muscle strength training.¹⁰⁻¹²

The effectiveness of cough, an important airway defense mechanism,¹³ is dependent on the neural control influencing the strength and the velocity of airflow, so it is consistent that impaired cough has been reported in patients with MS.^{3,14-17} No objective data exist as to the effect of expiratory and/or inspiratory muscle strength training on maximal voluntary cough in patients with MS; limited data are available on the effects in healthy subjects.¹³ The primary aim of this study was to examine if expiratory muscle strength training (EMST), designed as a shorter training duration, was effective for increasing maximal expiratory pressure (MEP), pulmonary function, and maximal voluntary cough in both healthy subjects and subjects with MS. A second aim was to determine if gains would be maintained during a detraining period.

METHODS

Participants

All subjects signed an informed consent authorized by the University of Florida Health Science Center, Gainesville Florida Institutional Review Board. Seventeen subjects with MS (14 women, 3 men) were age- (± 2 y) and sex-matched to 14 healthy subjects (12 women, 2 men). We used convenience sampling to recruit both the subjects with MS and the healthy subjects through the use of fliers, presentations at MS functions including support groups and conferences for subjects with MS, and personal contact for the healthy subjects. Participants were accepted into the study if they were 20 to 59 years of age; had no cardiac, pulmonary (eg, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis), neurologic (other than MS), or orthopedic conditions that adversely effected the respiratory muscle pump; were nonsmokers or nonsmoking within the last 5 years with a forced expiratory volume in the first second (FEV₁) and forced vital capacity (FVC) greater than 75%; and had not previously participated in EMST and/or inspiratory muscle strengthening training either for research or for therapy. The subjects with MS had to have a clinically definite diagnosis of MS,^{18,19} mild to moderate disability as assessed by the Expanded Disability Status Scale (EDSS),²⁰ no exacerbation in the prior 3 months, and sufficient facial muscle strength to achieve and maintain lip closure around a circular mouthpiece.

Several subjects dropped out during the course of the study and these subjects' data were not included in the stated number of subjects presented above. One healthy subject withdrew because of conflicts with her work schedule. Of the subjects with MS, 2 were excluded before training because of exacerbation of their MS, 1 had an EDSS score that was too high

(7.5; acceptable level, ≤ 6.5), and 2 dropped out because of conflicts with work. Demographic data for the subjects are shown in table 1.

Procedures

Subjects were seen at 3 assessment sessions (pretraining, posttraining, detraining), and once a week during the training phase of the protocol. To minimize the possibility of fatigue in the subjects with MS each of the 3 main assessment sessions was completed in 2 meetings, whereas for the healthy subjects the assessments were completed in 1 session. Before entering the study, all subjects signed an informed consent form authorized by the local institutional review board.

Maximal Expiratory Pressure

MEP was assessed using a hand-held digital manometer with a small controlled leak at the exhaust port.^a Following American Thoracic Society and European Respiratory Society guidelines, each subject inhaled fully to total lung capacity, placed their mouth around the mouthpiece, with their nose closed by a nose-clip, then blew the air out as hard and fast as possible for a minimum of 1.5 seconds. The procedure was performed 3 to 10 times and the top 3 within 10% of each other were averaged for the data analysis.²¹

Pulmonary Function Test

Pulmonary function tests (PFT) for the measurement of FVC, FEV₁, and peak expiratory flow (PEF), were completed while seated using a MasterScreen PFT.^b Spirometry software provided predicted, actual, and percentage of predicted. The tests were completed 3 times and the best of the actual measurement and of the percentage of predicted were used for analysis.²²

Maximal Voluntary Cough

Maximal voluntary cough was measured using a disposable mouthpiece connected to a pneumotachometer^c in series with an ML 140 spirometer.^d Each subject took 2 normal breaths, inhaled fully, and then maximally coughed. Subjects completed at least 10 acceptable coughs. Coughs were rejected for analysis if they were performed more like a PFT maneuver or if there was a significant amount of electric noise.

The signal was low-pass filtered at 225Hz through a PowerLab data acquisition unit.^d Chart 4.0d for Macintosh was used for online data collection and offline data analysis. Cough data of interest were volume (in liters), airflow (in liters per second), rise-time (in milliseconds), compression phase time, and 3 calculated variables: cough volume acceleration (defined as peak airflow/rise-time), volume as a percentage of FVC, and airflow as a percentage of PEF. The relevant data we captured are depicted in figure 1, which is a typical cough wave form.

Training and Weekly Assessments

Subjects used a threshold trainer,^e which provided a pressure-threshold range of 16 to 160cmH₂O. Subjects trained 5 days a week—once under the supervision of one of the investigators (TC) and 4 times at home completing 4 sets of 6 repetitions a day for 8 weeks. Weekly assessments assessed training (ie, correct use of the training tool), reassessed MEP

^aMP01 mouth pressure meter; Micro Direct Inc, PO Box 239, Auburn, ME 04212-0239.

^bImpulse oscillometry and PFT MasterScreen; Jaeger Toennies, Erich Jaeger GmbH, Leibnizstr 7, D-97204 Hoechberg, Germany.

^c800 L pneumotach; Hans Rudolph, 7200 Wyandotte, Kansas City, MO 64114.

^dADInstrument, 2205 Executive Cir, Colorado Springs, CO 80906.

^ePositive Expiratory Pressure pressure-threshold trainer, Threshold PEP; Healthscan Products Inc, div of Healthdyne Technologies, 908 Pompton Ave, Cedar Grove, NJ 07009.

and adjusted the training intensity for the following week. Training intensity was controlled at a set percentage of MEP, that is, 40%, 60%, and 80% for the first, second, and the third through the eighth week, respectively. MEP was assessed identically during the 3 primary assessment sessions. The means of 3 measurements within 10% of each other were used for the adjusted intensity. Participants returned their training unit to the investigation staff at the time of their posttraining assessment and then did no training for 4 weeks. They were seen once more after the 4-week detraining for retesting.

We used a 2-way repeated-measures analysis of variance to examine the variables of MEP, PFT, and maximal voluntary cough. Regression was used to explain the variability of MEP and of the change in MEP (Δ MEP, the change in MEP between the evaluation sessions, pre- to posttraining, post- to detraining, and pre- to detraining) between evaluations as the dependent variable in relation to the independent variables of sex and age of all subjects and level of disability, years from first symptom and years from diagnosis for the subjects with MS; as well as the variables of interest for pulmonary function, maximal voluntary cough, and speech. Statistical analysis softwares used were SuperANOVA^f and Statview.^g The a priori significance level was set at .05.

RESULTS

Subjects with MS had significantly lower MEP ($F=23.93$, $P=.000$), FVC ($F=13.20$, $P=.001$), FEV₁ ($F=9.85$, $P=.004$), and PEF ($F=24.51$, $P=.000$) than the healthy subjects. MEP and PEF significantly increased following training (pretraining to post-training: MEP, $F=95.01$, $P=.000$; PEF, $F=8.03$, $P=.006$) and remained significantly above baseline following detraining (pretraining to detraining: MEP, $F=60.99$, $P=.000$; PEF, $F=7.91$, $P=.007$). Examination of MEP, as to the percentage change between the assessments found no difference between the groups; however, the percentage change in MEP between the assessment sessions was significantly greater between the pretraining to posttraining than with the post-training to detraining ($F=59.22$, $P=.000$) and between the posttraining to detraining than with the pretraining to detraining ($F=40.99$, $P=.000$). Multiple regression of Δ MEP and the independent (demographic) variables was nonsignificant ($F=2.049$, $P>.05$). See figure 2 for MEP of subjects with MS compared with healthy controls at each main assessment.

PEF, normalized to percentage of predicted PEF, was significantly less ($F=24.51$, $P=.000$) for the subjects with MS (76.47 ± 17.29) than the healthy controls (104.33 ± 15.49). After training (92.46 ± 21.87), the PEF was significantly greater ($F=8.03$, $P=.006$) compared with pretraining (83.56 ± 22.29) and remained significantly ($F=7.91$, $P=.007$) above baseline at detraining (89.62 ± 3.34). See figure 3 for PEF of subjects with MS compared with healthy controls at each main assessment.

Significant group differences in several of the maximal voluntary cough variables of interest were found between the subjects with MS and the healthy controls. Within the measured variables of interest: cough volume was significantly less (1.70 ± 0.76 and 2.17 ± 0.41 , $F=5.09$, $P=.032$) and rise time was significantly longer (73.04 ± 51.98 and 44.28 ± 27.80 , $F=5.25$, $P=.029$) in the subjects with MS than with the healthy controls. Within the derived variables of interest, the cough volume acceleration was significantly less (130.75 ± 95.0 and 217.93 ± 123.90 , $F=6.60$, $P=.016$) and the flow as a percentage of PEF was significantly greater (121.36 ± 38.10 and 100.15 ± 12.79 , $F=5.33$, $P=.028$) in the subjects with MS than with the healthy controls. No difference was found between the subjects with MS and

^fAbacus Concepts Inc, 1918 Bonita Ave, Berkeley, CA 94704-1038.

^gSAS Institute Inc, 100 SAS Campus Dr, Cary, NC 27513.

healthy controls for cough airflow ($F=1.15$, $P>.05$), cough compression time ($F=0.87$, $P>.05$; ie, the duration of the middle phase of a cough when the glottis is closed prior to the final explosive exhalation phase [see fig 1]), or volume as a percentage of FVC ($F=1.58$, $P>.05$). Following EMST group (ie, subjects with MS vs healthy controls) differences remained in the cough volume, rise time, cough volume acceleration, and flow as a percentage of PEF. Comparisons of the MS subjects with the healthy controls found group difference, but no statistically significant gains in any of the maximal voluntary cough variables of interest were found after EMST.

Maximal voluntary cough data for the subjects with MS were also examined with the subjects with MS separated as to level of disability (ie, mild: EDSS²⁰ score range, 0.0–3.5, $n=10$; moderate: EDSS score range, 4.0–6.5, $n=7$). Subjects with MS having moderate disability had a significant improvement in cough airflow after EMST (pretraining to posttraining, $F=6.35$, $P=.015$; pretraining to detraining, $F=6.23$, $P=.016$). Subjects with MS having mild disability had significantly lower ($F=17.91$, $P<.000$) cough airflow as a percentage of PEF, which returned toward baseline value during the detraining period. The Δ MEP, used as an independent variable to examine the change in cough measures, explained only the rise time at a significant level (Δ MEP $=-.848$, $R=.373$, $R^2=.139$, $F=4.686$, $P<.039$).

DISCUSSION

Subjects with MS were found to have lower MEP, FVC, FEV₁, and PEF, and weaker maximal voluntary cough than healthy subjects. EMST improved the MEP, which remained above baseline during detraining in the subjects with MS and the healthy subjects. EMST did not improve investigated components of maximal voluntary cough in the MS subjects compared with the healthy controls. However, when the subjects with MS were separated as to level of disability (ie, mild and moderate), EMST did improve the cough airflow and cough volume of the maximal voluntary cough in subjects with moderate disability due to MS.

MEP was of primary interest because maximal voluntary cough is reduced in the presence of diminished expiratory strength.^{5,15-17,21} Although we found greater MEP improvements in subjects with MS than has previously been reported, these subjects were still significantly lower than the healthy controls.^{3,5,7,8} The basis for the diminished strength of the expiratory muscles in subjects with MS may result from de-conditioning.^{7,8} Deconditioning occurs because MS subjects' usual stimulus, strenuous activity, is often severely limited because of the heat sensitivity, fatigue, general muscle weakness, or balance problems associated with MS.⁸ Expiratory muscles are skeletal muscles and respond in similar fashion to a strength-training program. The initial response to training is largely neural with changes occurring in the motor command, descending drive, muscle activation, motor unit recruitment, and sensory feedback.^{23,24} The reverse of this also holds true: neural adaptations can result from diminished muscle activity that has been seen with disuse resulting from immobilization or reduced physical activity. Many of our subjects with MS were self-reported as moderately active; therefore, we believed that reduced physical activity was not an issue. However, previous research has noted that physical activity levels in MS patients are less than healthy controls, and their activity levels did not correspond to their self-reported levels.²⁵ Other reports have noted decrements in activity and fitness in this group, and have focused on the need for MS patients to engage in more physical activity.²⁶⁻²⁸

Physical changes returned toward baseline after the training stimulus was removed, and the time frame to return varied between 2 and 4 weeks.^{29,30} The MEP of subjects with MS and healthy controls, which was reduced at detraining compared with posttraining, remained

statistically higher than at baseline. This finding is in agreement with that of investigators reporting reductions in maximal respiratory pressures that remained above baseline in subjects with MS and healthy controls following detraining periods.^{3,13} Similar to MEP, the mean PEF (percentage of predicted) of subjects with MS was significantly higher at detraining than with pretraining. Further study is warranted to examine the effect of detraining after respiratory muscle strength training on pulmonary function in patient populations and healthy subjects, as well as to determine the minimal amount of training necessary to maintain pulmonary functions.

Controversy abounds as to the effect of expiratory and/or inspiratory muscle strength training on pulmonary function. Pulmonary function in subjects with MS may be normal or reduced in the presence of weakened respiratory muscles.^{6,31} Previously, nonsignificant as well as significant gains in PEF, FVC, FEV₁, total lung capacity, and/or maximal voluntary ventilation have been reported following expiratory and/or inspiratory muscle strength training in both patient populations and healthy subjects.^{5,7,12,32-37} PEF, expressed as a percentage of predicted PEF, increased following training. The gains in PEF we observed may have occurred because our subjects had less disability than subjects with MS in previous studies in which it was recommended that training be started early in the disease process.^{3,5,7}

Explanations as to the lack of increase in FVC and FEV₁ in the presence of increased MEP are limited. First, above a certain transpulmonary pressure at a given volume, flow does not increase with driving pressure.^{38,39} It is not the effort or MEP, but the elastic recoil of the lung, determined by lung volume and properties of lung tissue, which governs the maximal expiratory flow.³⁸ Second, the intrinsic state of the lung may influence expiratory flow. If a change in the lung tissue occurs over time because of a disease process such as MS, then strengthening the respiratory muscles would have limited influence on the pulmonary function. Although there is the possibility that disuse atrophy affects connective tissue as well as muscles,⁴⁰⁻⁴² we found nothing in the literature that directly supports this concept of an effect on lung tissue.

Minimal change was found in maximal voluntary cough. Maximal voluntary cough is considered a primary airway defense mechanism and is frequently diminished in the presence of weakened respiratory muscles. Although group differences were found, EMST did not result in any significant changes in measured or calculated parameters of maximal voluntary cough in the MS subjects compared with the healthy controls. Cough volume, less in the subjects with MS than in healthy controls at each assessment, may have resulted from a decreased chest expansion seen reported in other patient populations with neurologic impairment of the inspiratory musculature.^{14,43-47} Reduced volume and flow are seen in a restricted breathing pattern, which suggests that the flow should have been reduced in persons with MS. However, we did not observe this. Although a strong, direct relation between cough peak flow rate and cough expired volume has been noted previously,⁴⁸ we observed no such relationship. We did not detect a difference in the expiratory flow in subjects with MS, even though there was an increase in volume. As has been stated, a greater inspired air volume leads to greater expired air volume and a higher peak flow rate.⁴⁹ It may be that inspiratory training in addition to expiratory training may be necessary to improve cough, at least in certain patient populations.⁵⁰

Cough volume acceleration, that is, the ratio of cough peak flow to the corresponding time to peak (rise-time) is a measure of cough intensity. It is a variant of the ratio of the integrated electromyographic activity and the time duration of the expiratory integrated electromyographic ramp during cough.^{43,44,50} In agreement with previous investigators who reported that the cough volume acceleration was significantly slower in patient populations

than healthy controls, we found that the cough volume acceleration of subjects with MS was significantly lower than healthy controls.^{43,47} Training resulted in no improvement in the cough volume acceleration possibly because of the lack of change in the flow, which showed no difference between the healthy controls and subjects with MS. Additionally, although there was a difference in rise-time between the 2 groups neither group showed improved rise-time with training. Because the training was directed at strengthening the expiratory muscles, the use of electromyography may have shown an improved intensity of the cough.

There were several limitations in this study. First, the sample size was small. Although there is a large MS population base, it was extremely difficult to recruit subjects. Conflicts between work and assessment sessions compelled 1 healthy control and 1 subject with MS to withdraw. One subject with MS was too disabled, 2 subjects appeared to be going into MS exacerbations and thus were not accepted into the study, and 1 subject with MS was starting a new job and chose not to continue. Second, although subjects' completed training logs showed greater than 90% compliance, how well each person performed the exhale breaths was not observed at each session. Because effort of one's breath is a major factor, both with the training and when performing the respiratory muscle pressure measurements as well as the PFTs, maximal effort may not have been achieved every time. Third, subjects were using an expiratory muscle trainer that is designed to strengthen the expiratory muscles, but it does not train the expiratory muscles in the pattern typically used during a cough (ie, the EMST may have lacked training specificity). Future studies may need a paradigm that truly trains the muscles as they are used during a maximal voluntary cough. Finally, further research is needed to determine which components should be measured to assess the effect of EMST and/or inspiratory muscle strength training on cough.

CONCLUSIONS

Respiratory muscle weakness may be present in subjects with MS who have mild to moderate disability. EMST, using a pressure-threshold load device, is able to improve the expiratory muscle strength as assessed by MEP. Minimal change occurs in pulmonary functions as assessed by spirometry because MS does not affect the lung tissue and airways. Based on the assessed parameters of maximal voluntary cough examined in this study, EMST is not able to improve maximal voluntary cough. Further investigation is warranted on the effect of respiratory muscle strength training on intensity and efficiency of cough because it is a primary defense mechanism of the airways.

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Fig 1.

(A) Labeled phases of cough wave: inspiratory phase, compression phase (minimal flow phase), and expiratory phase. (B) Measured components of cough wave: 1, rise-time (from the end of compression phase to the peak of expiratory flow during the expiratory phase); 2, cough expiratory airflow peak amplitude.

Fig 2.

Change in MEP from pretrain through to detrain. Significant difference was found between the MS (○) and healthy (▲) groups and across assessments: pretrain to posttrain (*) and pretrain to detrain (†). Significant at $P < .05$.

Fig 3.

Change in PEF from pretrain through to detrain. Significant difference was found between the MS (○) and healthy (▲) groups and across assessments: pretrain to posttrain (*) and pretrain to detrain (†). Significant at $P < .05$.

Table 1

Demographics of Persons With MS and Healthy Controls

Demographics	Persons With MS	Healthy Controls
Age (y)	48.9±7.61	44.1±7.64
Height (cm)	167.3±9.0	165.7±7.3
Weight (kg)	76.2±20.7	78.1±13.8

Characteristics of Persons With MS	Values
EDSS * score	3.62±1.31 (1.5–6.5)
Years from first symptom	11.76±6.56 (1.25–24.25)
Years from diagnosis	8.43±6.17 (1.25–18)

NOTE. Values are mean ± standard deviation (range).

* EDSS score range: 0=normal neurology, 10=death caused by MS.²⁰