JAOA BRIEF REPORT

Effects of osteopathic manipulative treatment and concentric and eccentric maximal-effort exercise on women with multiple sclerosis: A pilot study

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The research objectives of this study were to evaluate the effects of osteopathic manipulative treatment (OMT) combined with maximal-effort exercise (MEE) on strength, coordination, endurance, and fatigue in female patients with multiple sclerosis (MS). Seven female subjects with MS participated in the 12-week study, which included intervention with OMT and MEE twice per week.

Standardized tests for progression of MS and fatigue were used. Strength (maximal effort and impulse) was measured with the IsoPump exercise machine (IsoPump USA, Cleveland, Miss) during the three phases of the exercise protocol. Significant changes occurred in all but one measure of strength and on the 25-foot walk ($P < .05$), but not on the block-and-box test. The change in fatigue scores was not significantly different.

Findings indicate that OMT combined with MEE significantly increases strength and ambulatory levels while not increasing fatigue in female patients with MS who have low to medium impairment. Qualitative data show that this intervention also produces beneficial effects in activities of daily living.

(Key words: activities of daily living, exercise, IsoPump, osteopathic manipulative treatment, multiple sclerosis, resistance training, strength training)

At present, multiple sclerosis (MS) has no cure. Treatment is often frustrating for patients and seemingly futile. The initiating cause of MS is unknown. Some evidence suggests that MS is a viral disease.[1] Another theory suggests that MS is an autoimmune disease.[2,3] Multiple sclerosis may be caused by a genetic predisposition (Northern European descent), an altered hormonal state (pituitary gland effect), or other causative factors.[3] Regardless of the cause, better treatment modalities are needed. This pilot study demonstrates a novel and effective approach to treating MS.

Koop[4] summarizes the current treatment modalities for MS, which are directed at maintaining current ability or reducing exacerbations. Recent advances have been made in relieving the disease and its symptoms. Several relatively new pharmacologic modes of therapy—including interferon β-1a (Avonex), interferon β-1b (Betaseron), and glatiramer acetate (Copaxone)—can be used to treat patients for relapsing forms of disease. These drugs have been shown in multiple studies to reduce the frequency of episodes and delay the progression of impairment in a substantial number of patients with MS.

Various treatment modalities can improve the symptoms related to MS, including muscle relaxants such as cyclobenzaprine hydrochloride, baclofen, tizanidine hydrochloride, and clonazepam. To reduce the level of fatigue in patients with MS, some physicians prescribe amantadine, an antiviral medication. Some patients are using herbal agents with mixed results—none of which have been scientifically validated. In addition, patients may be able to control pain through biofeedback or self-hypnosis.[4]

Many symptoms of MS, including those related to bladder function (eg, incontinence, incomplete emptying of the bladder—and resultant urinary tract infections), require medical supervision and intervention. Pain, especially cramping and tingling or burning sensations, along with secondary trembling and weakness is treated with antiseizure medication or low doses of antidepressants. Strong analgesics are seldom needed; narcotic analgesics are generally contraindicated, except for acute injuries. Additionally, pharmacologic modes of therapy, like antibiotics, may exacerbate the symptoms of MS.[3-5]

The cost of any one of the new single-agent pharmacologic mode of therapy for MS listed above can average $8000 to $10,000 per year, and this amount does not include the cost of other prescription and nonprescription medications.[6] The National Center for Health Statistics of the Centers for Disease Control and Prevention reported that from 1990 to 1992 (the most recent statistics available), 58% of all patients with MS and 69% of all women with MS had limitation of activity. Almost a third (30%) of all patients with MS and nearly half (47%) of

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all women with MS required hospitalization; all required physician visits.[7] These data do not account for the cost of decreased productivity, other non–MS-related healthcare costs, assistive devices, or caretaker expenses.

Information on the response of MS patients to exercise is limited, and study findings appear to be influenced by the level of physical impairment in study samples.[8,9] Exercise, and especially aerobic exercise, often leads to prolonged fatigue in patients with MS.[10] These responses have been studied by physical therapists, neurologists, and occupational therapists.[11-14]

Previous areas of study have included the response of patents with MS to exercise vis-à-vis muscle function (strength and endurance training),[9,11,14-21] cardiorespiratory response (autonomic cardiovascular regulation),[12,20,22-24] and symptom instability with thermal stress.[9,12,25] Information on the two latter areas has been obtained predominantly from research with either a medical or a neurologic perspective, and in only three studies were muscle function and cardiorespiratory response examined in relation to exercise performance.[14,18,19] These studies show that strength, cardiovascular function, and thermal tolerance can be improved, at least temporarily.[9,11,12,14-25] They serve as starting points for future research such as this project.

The most-used functional standard for evaluation of debilitated persons (eg, patients with MS) in exercise-related research is the Expanded Disability Status Scale (EDSS),[26] also known as the Kurtzke Functional System rating scale.[27] The EDSS is a global rating of neurologic impairment.

In patients with a minimal to moderate level of neurologic impairment, abnormalities in heart rate and blood pressure are seldom present, and cardiovascular response is not affected.[9] This unimpaired cardiovascular system has important safety implications in studies in which subjects attempt to exercise to maximal levels. Studies have indicated that regular exercise can change the course of life of a patient with MS by minimizing the deconditioning process and maintaining optimal levels of physical function.[11,28] Of the available research, only Kraft and Alquist,[16] Ponichtera et al,[19,29] Ponichtera-Mulcare et al,[30] and Vardy[15] had their subjects with MS exercise to a maximal level. In contrast, Schapiro et al[24] used a suboptimal effort as a maximal exercise end point. High-intensity and maximal levels of exercise at no time provoked immediate or latent MS-related symptoms.[23,30] General fatigue was common to both subjects with MS and control subjects.

Gehlsen et al,[11] Svensson et al,[14] and Ponichtera-Mulcare et al[30] used prolonged aerobic exercise with an average of 40 minutes of exertion. Gehlsen et al[11] and Basmajian et al [28] used 1-hour sessions of exercise while Svensson et al[14] and Ponichtera et al[18,19] instructed subjects to do 50 repetitions of knee extension. None of these studies evaluated fatigue in the study population. Similarly, none of these studies were followed up to evaluate prolonged effects.

Ponichtera-Mulcare et al[23] suggested that a combined arm-and-leg exercise might be more effective in eliciting truly maximal effort. The protocol in our study used a combined arm-and-leg exercise in the lunge phase.

Clinical research on the effects of osteopathic manipulative treatment (OMT) on viscerosomatic and somatic dysfunctions adds to a growing body of knowledge. The components of disease may be direct, obvious, and somatic as in musculoskeletal disease—or these components may be less obvious, viscerosomatic disorders. The results of studies of OMT on the trophic and neurotrophic function indicate that, theoretically, OMT could beneficially affect patients with MS through viscerosomatic, endocrine, and psychoimmunologic pathways.[31-37] Osteopathic manipulative treatment can provide benefits for patients with MS who suffer from somatic (musculoskeletal) dysfunctions and the ongoing compensatory problems that result from MS-related disabilities.[32]

No specific pattern of somatic dysfunction has been found in subjects—other than that which would be expected as a result of loss of strength in the lower extremities and a general loss of normal activity level due to fatigue or prolonged bed rest. The only published study on MS and OMT was a six-subject pilot study with no control group.[15] In that study, significant increases in strength were seen when both OMT and maximal-effort exercise (MEE) were done twice weekly for 12 weeks.

The emphasis of our study was to evaluate the increase in strength and function that occurs as a result of OMT when used in combination with strength training on the IsoPump exercise machine (IsoPump USA, Cleveland, Miss) using MEE. The MEE used in this study included three repetitions per session of each phase: concentric leg press, eccentric leg press, and lunge. Specifically, the research objectives of our study were to evaluate the following:

- Would female patients with MS who had a low to medium EDSS rating benefit from OMT in combination with a specialized MEE program that increases strength?
- Can strength gains be translated into improvements in coordination and endurance—as well as a decrease in perceptions of fatigue?

The research hypothesis tested was that OMT in combination with progressive, high-intensity, nonaerobic MEE has positive benefits in terms of physical performance (ie, strength, endurance, and coordination) without increasing perceived fatigue.

Methods

Seven female subjects, aged 42 to 68 years, with diagnosed MS and EDSS ratings between 2 and 6 were recruited to participate in this study. The Kirksville College of Osteopathic Medicine's institutional review board approved this study. All subjects underwent a specialized 12-week program consisting of OMT and MEE twice per week.

The MEE portion of the program was performed using the IsoPump machine (*Figure 1*). The IsoPump machine, designed by Australian physician Terence C. Vardy, provides a three-

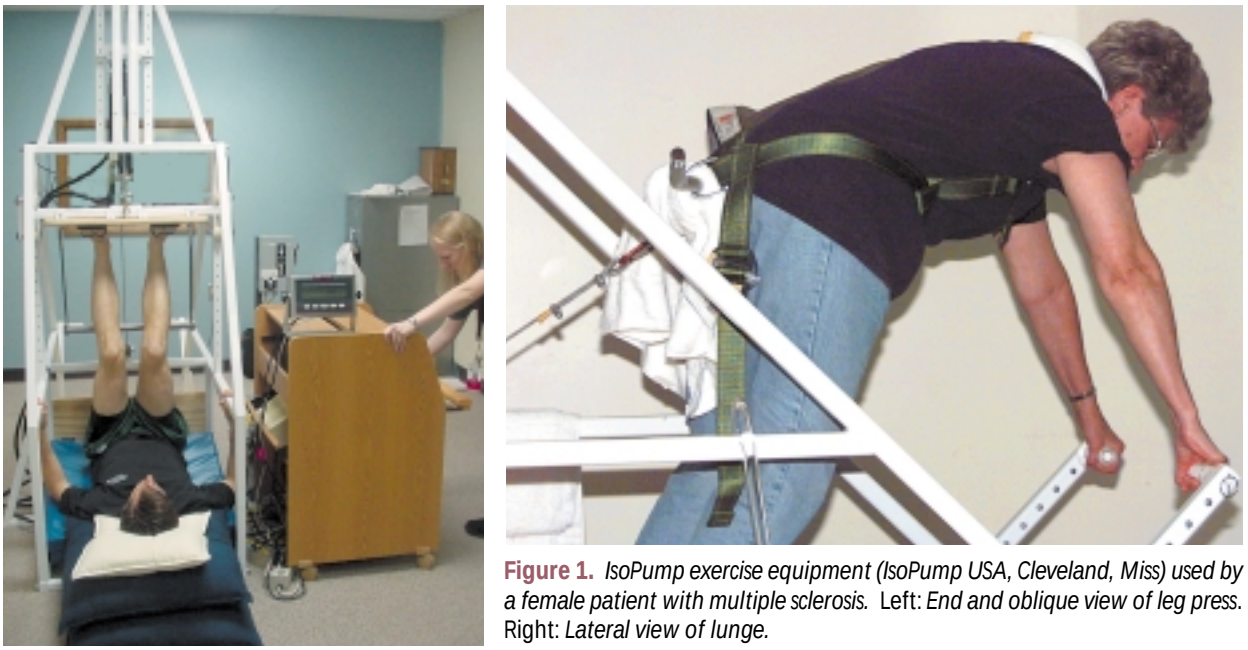


Figure 1. *IsoPump exercise equipment (IsoPump USA, Cleveland, Miss) used by a female patient with multiple sclerosis.* Left: *End and oblique view of leg press.* Right: *Lateral view of lunge.*

phase exercise protocol combining concentric and isometric vertical leg forces (concentric leg press), eccentric and isotonic vertical leg forces (eccentric leg press), and concentric and isometric semi-erect, whole-body exercise (eg, lunge). In each of these MEE phases, subjects were instructed to do a valsalva maneuver and exert maximal effort against the resistance of the IsoPump device for as long as reasonably possible (usually 5 to 30 seconds). Three MEE repetitions were completed for each phase with a 30- to 300-second subject-determined rest period between repetitions.

The OMT portion of the program was administered to patients to correct somatic (musculoskeletal) dysfunctions occurring during the study and ongoing compensatory problems resulting from MS-associated disabilities or prior traumas. Specific OMT techniques used included myofascial techniques to reduce muscle spasm and inflammation, articulatory techniques to increase restricted range of motion, and multiple types of both direct and indirect spinal and rib techniques to lessen somatic and somaticovisceral dysfunctions by enhancing beneficial trophic and neurotrophic effects on associated connective tissues.

The study used a within-subject, repeated-measures design to evaluate the effects of OMT and the exercise program over 12 weeks. All participants were required to have had a diagnosis of MS for at least 2 years, to currently be ambulatory and in remission from MS exacerbation for at least 4 months, and to have no significant spasticity or ataxia. Exclusion criteria were as follows:

- changes in MS-related prescription medicine within 1 month before the study;
- a history of lower extremity fracture or dislocation within the past year;
- clinically diagnosed moderate to severe depression;
- an inability to give informed consent;
- current bladder or lung infection;
- febrile episode at time of session (>100°F [>38°C]); and
- presence of an inguinal or abdominal hernia.

The seven subjects with chronic progressive MS completed an average of 22.2 training sessions (range, 20-24). The short duration (12 weeks) of the program was chosen to avoid maturation of the disease with exacerbations. The inclusion and exclusion factors maintained homogeneity in the sample population and allowed extrapolation to a female MS population with EDSS ratings of 2 through 6.

Strength was measured during each of the exercise sessions by attaching a Celtron load cell (STC S type 30074, Celtron Technologies Inc, Santa Clara, Calif) to the IsoPump machine. The load cell recorded the pounds of force produced by the subject every 0.25 seconds. For each repetition, two summary outcome measures were calculated: impulse generated (area) and maximum pounds of force (peak).

Area values were calculated as the sum of the pounds of force generated every 0.25 second that the subject exerted at least 50 pounds of force, divided by 4 to standardize the units of measurement (pound-seconds), which is a measure of the impulse generated. *Peak* represents the maximum effort of the subject. Exertion force measurements of less than 50 pounds were omitted to eliminate data recorded before or after the subject performed the exercise, standardizing the data collection starting point and accounting for subjects who began the exercise before or after instructed.

Overall performance was evaluated weekly. Repetitive motor coordination skills were measured in the block-and-box test (BBT),[38] endurance was measured in a 25-foot timed

Table
Summary Statistics for Analyses of Strength Data in Subjects With Multiple Sclerosis (N = 7)

Phase and outcome measure	Baseline Mean (SD)	Final Mean (SD)	*P* value*
Concentric leg press			
Area,† (pound-seconds‡)	21,187 (13,467)	45,152 (15,105)	.03
Peak,§ (pounds)	517 (191)	968 (280)	.02
Eccentric leg press			
Area (pound-seconds)	10,575 (6,714)	15,211 (3,775)	.05
Peak (pounds)	598 (219)	815 (273)	.30
Lunge			
Area (pound-seconds)	6,154 (2,956)	11,842 (3,512)	.02
Peak (pounds)	173 (70)	296 (78)	.02
Block-and-box test (No. of boxes)	61.3 (11.4)	69.1 (14.4)	.11
25-Foot walk (seconds)	10.6 (7.0)	8.2 (6.1)	.02

**P* values from Wilcoxon signed rank test comparing baseline and final sessions.
†Area, impulse generated.
‡Pound-seconds, standardized unit of measurement derived by calculating the sum of the pounds of force generated every 0.25 second that the subject is generating at least 50 pounds of force divided by 4.
§Peak, maximum pounds of force.

walk,[39] and the Subjective Perception of Fatigue Scale (SPFS)[40] provided a measure of patients' perceptions of fatigue. The SPFS is a self-reported instrument and was distributed before and after the OMT and MEE protocols.

Strength data were analyzed separately for each of the three phases: concentric leg press, eccentric leg press, and lunge. The three measurements of strength during the repetitions were averaged for the baseline and final intervention sessions. Wilcoxon signed rank tests were done to determine whether changes in coordination, endurance, or strength occurred during the study period. Data on fatigue from the SPFS were also analyzed using a Wilcoxon signed rank test to compare the baseline and final sessions on the change in perceived fatigue before and after the study protocol.

Results

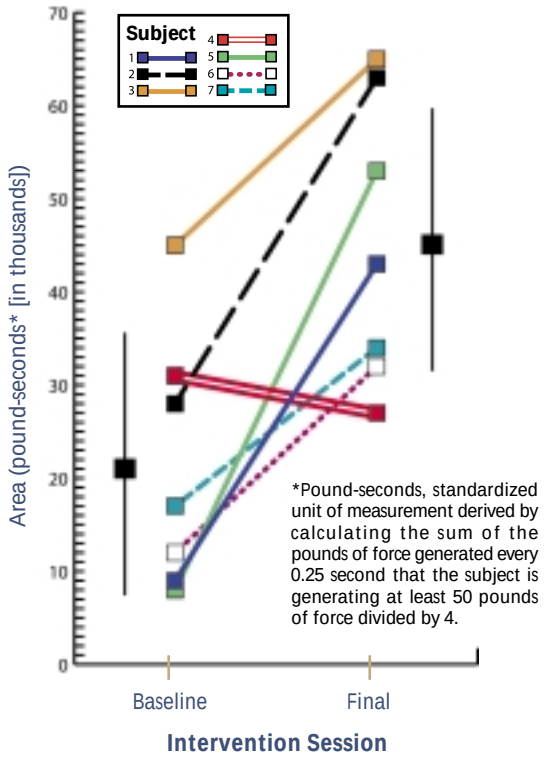
Summary statistics and *P* values from the analyses of the data on strength, BBT, and 25-foot walk are presented in the *Table*. For all three phases of the exercise protocol and both outcome measures, significant changes occurred during the intervention period (all $P \leq .05$) with the exception of the peak variable for the eccentric leg press ($P = .30$). As evidenced by the mean values (*Table*), strength was increased during the study period for all three phases and both outcome measures. The increase for the area outcome measure collected during the concentric leg press, eccentric leg press, and lunge phases of the exercise protocol is illustrated in *Figures 2*, *3*, and *4*, respectively. Corresponding illustrations for the peak outcome measure are presented in *Figure 5* through *Figure 7*. In *Figure 2* through *Figure 10*, the same color is used to identify each individual's performance.

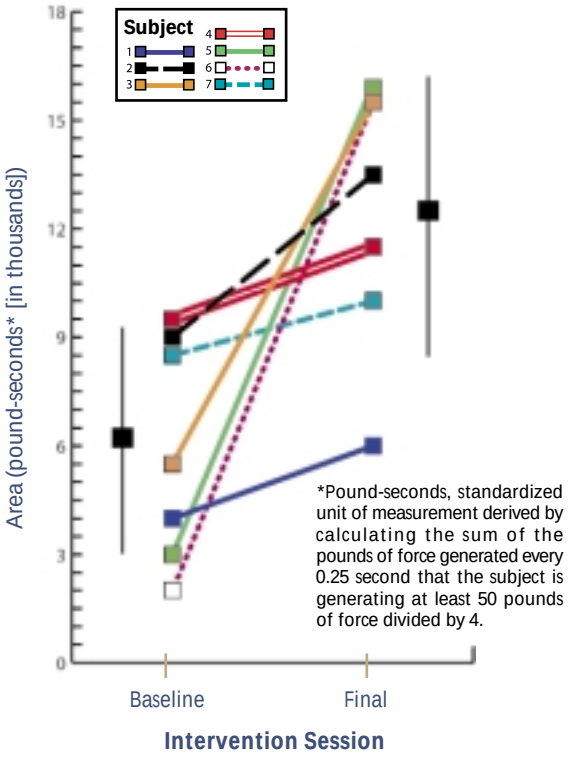
A significant change occurred during the study period on the 25-foot walk ($P = .02$) but not on the BBT ($P = .11$). Summary statistics presented in the *Table* indicate a decrease in both the time to walk 25 feet (*Figure 8*) and improved performance in the BBT (*Figure 9*), though the BBT change was not significant.

For the fatigue data, no significant difference occurred between the baseline and final sessions ($P = .06$). The mean (SD) change in SPFS score decreased from 13 (10) at baseline to 6 (5) during the final session (*Figure 10*).

Discussion

This pilot study indicates that a maximal effort concentric-eccentric exercise program combined with OMT significantly increases strength and ambulatory levels while not increasing fatigue in female patients with MS who have an EDSS rating in the low-to-medium range. However, this pilot study had a





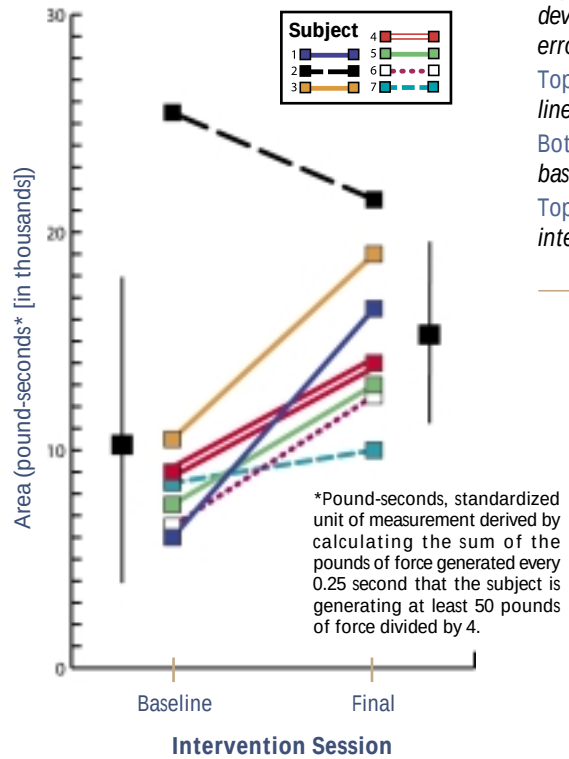


Figure 2. *Impulse generated (area). Error bars represent mean ± standard deviation. The left error bar is the baseline reading (preintervention); the right error bar is at the end of intervention (postintervention).*

Top left: *Impulse generated (area) during concentric leg press during baseline and final intervention sessions.*

Bottom left: *Impulse generated (area) during eccentric leg press during baseline and final intervention sessions.*

Top right: *Impulse generated (area) during lunge during baseline and final intervention sessions.*

within-subjects design and was not a randomized, controlled trial. In addition, the pilot study examined only the effect of the study protocol (ie, OMT and MEE) and did not address the question of whether each element of the combined intervention was effective individually. Finally, health-related quality of life was not assessed in the preliminary research protocol.

The fatigue score change from preintervention to postintervention decreased from 13 (10) at baseline to 6 (5) during the final session ($P=.06$). Although this difference was not statistically significant, five of the seven subjects showed reduced fatigue scores over the course of this study, one patient's fatigue score increased, and another patient who had little fatigue initially remained nonfatigued. The estimated effect size is 1.0, which a sample size of 11 has power of 0.8 to detect by use of a 2-tailed paired *t* test ($\alpha=.05$). This evidence of an effect

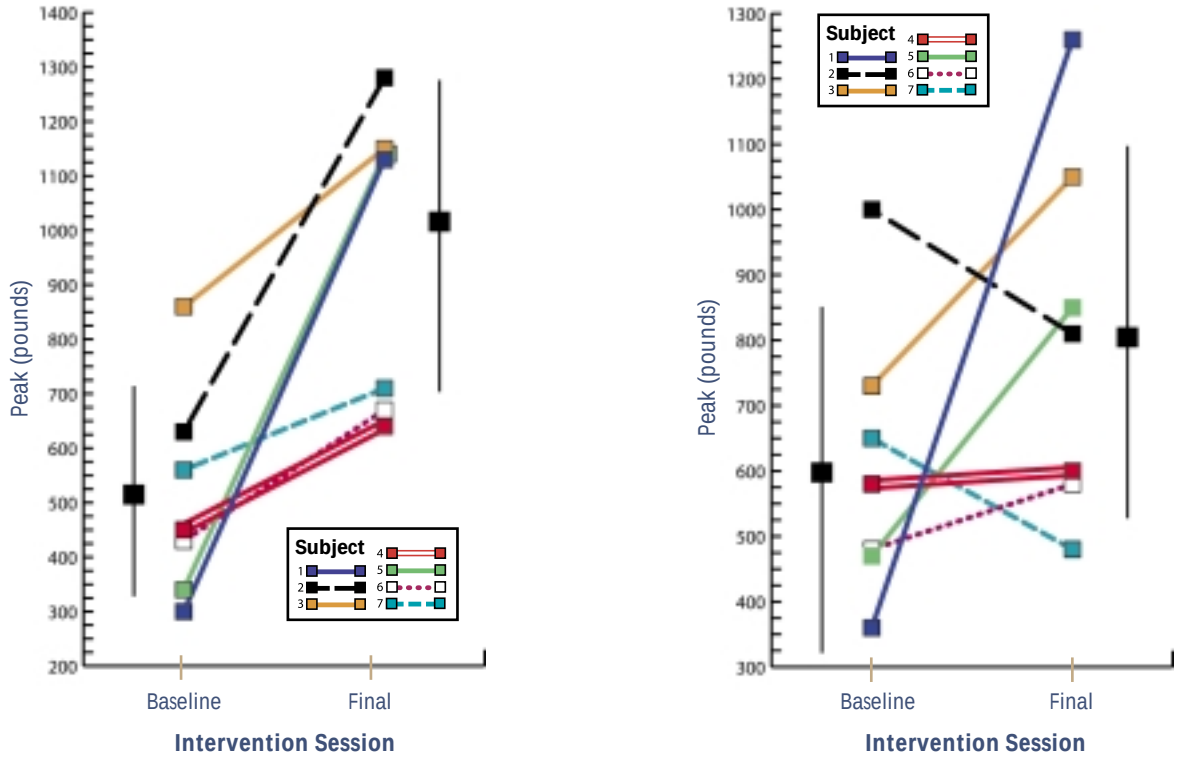


Figure 3. *Maximal force (peak). Error bars represent mean ± standard deviation. The left error bar is the baseline reading (preintervention); the right error bar is at the end of intervention (postintervention).*

Top left: *Maximal force (peak) during concentric leg press during baseline and final intervention sessions.*

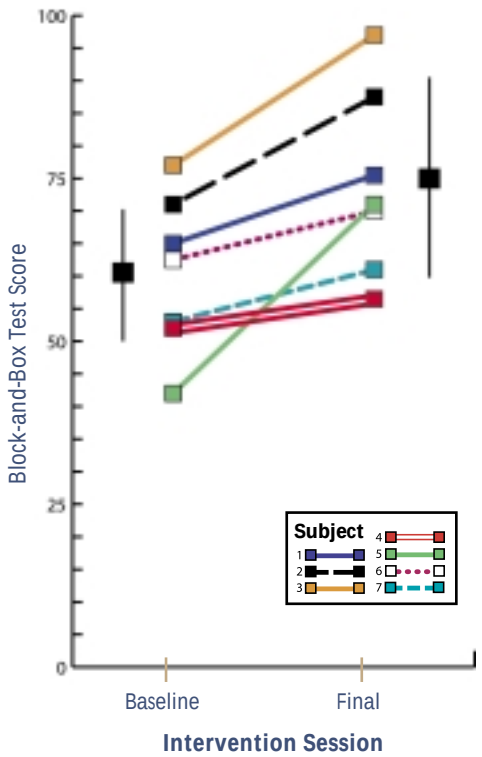
Top right: *Maximal force (peak) during eccentric leg press during baseline and final intervention sessions.*

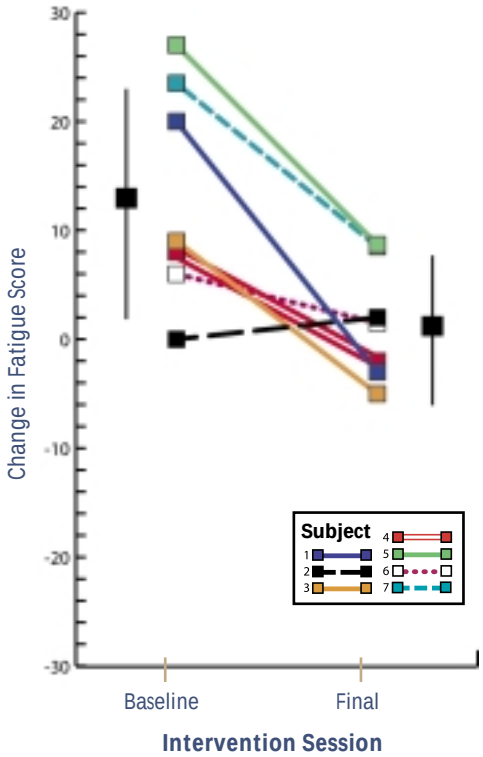
Bottom right: *Maximal force (peak) during lunge during baseline and final intervention sessions.*

needs to be evaluated in larger studies. Likewise, the results from the BBT were not statistically significant (P=.11) but may demonstrate significant improvement in larger studies. The estimated effect size is 0.7, which a sample size of 17 has power of 0.8 to detect by use of a 2-tailed paired t test (α=.05). The BBT is a test of proprioceptive coordination, an issue not addressed in the protocol. Thus, no significant improvement was expected. The improved performance on BBT may be a "learning effect" from repeating the test protocol. A larger study is necessary for the evaluation of this effect.

Other study observations that were not analyzed statistically include:

- One subject started with a walker but ended the sessions walking with one cane.
- One subject started with two canes but ended the sessions walking without assistance.





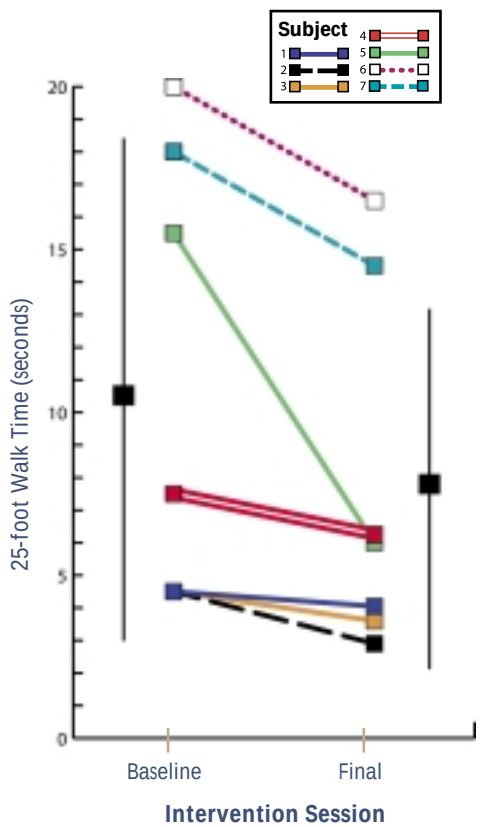


Figure 4. *Overall performance evaluations. Error bars represent mean ± standard deviation. The left error bar is the baseline reading (preintervention); the right error bar is at the end of intervention (postintervention).*

Top left: *Results of block-and-box test scores during baseline and final intervention sessions.*

Bottom left: *Results of 25-foot timed walk during baseline and final intervention sessions.*

Top right: *Results of Subjective Perception of Fatigue Scale during baseline and final intervention sessions.*

- One subject can arise from a chair without mechanical or other assistance.
- One subject improved her bowling score and was the most improved in her league.
- One subject had improved sleeping habits and a decrease in episodes and severity of irritable bowel syndrome.

Although self-reported data are not included in the study's data analysis, such information is notable as it documents subjects' improvements in the activities of daily living (ADL). Because changes in ADL are the ultimate goal of any such study, patient-reported improvements in ADL are a significant measure of success. Measurement instruments quantitatively evaluating ADL are currently being evaluated for use in future trials.

Comment

Further studies will need to measure more physiologic data and define the mechanism of the intervention and postintervention effects. Larger randomized, controlled studies will be needed to validate these data and differentiate effects on various groups of subjects with MS to ascertain the optimal training and treatment frequency and duration—as well as follow-up treatment.

Studies to evaluate the effects of this type of intervention on other deconditioning diseases such as chronic fatigue syndrome and fibromyalgia are also needed. An evaluation of the effects of this type of protocol on healthy adults—both the deconditioned and athletes—would determine the effect on their strength and performance. This type of exercise program might also aid astronauts in maintaining strength and conditioning, as well as reduce bone demineralization in weightless environments.

Our data represent a promising initial step in evaluating the effect of OMT and MEE and in determining how these interventions can affect the lives of individuals who need increased strength. The magnitude of this pilot study's importance will be seen as further experimental design protocols are tested and their results analyzed.

References

1. Johnson RT. Possible viral cause of multiple sclerosis. In: Placito M, ed. *Viral Infections of the Nervous System.* Philadelphia, Pa: Lippincott–Raven Publishers; 1998:248-258.

2. Poser CM. The pathogenesis of multiple sclerosis. Additional considerations. *J Neurol Sci.* 1993;115:S3-S15.

3. Adams RD, Victor M, Ropper AH. Multiple sclerosis and allied demyelinative diseases. In: Wonsiewicz MJ, Navrozov M, eds. *Principles of Neurology.* New York, NY: McGraw-Hill; 1997:902-927.

4. Koop CE. Multiple sclerosis: Physical findings. drkoop.com. 1998. Available at: http://www.drkoop.com/conditions/Multiple_Sclerosis/Page_14_44.asp. Accessed April 5, 2002.

5. Scientific American Medicine: IX. Demyelinating diseases. Healtheon/WebMD. 2000. Available at: http://www.samed.com/sam/forms/index.htm. Accessed April 21, 2000.

6. Mason I. Criteria for treatment of secondary progressive MS with interferon-beta-1b clarified. Reuters Health. 2000. Available at: http://www.reutershealth.com/archive/2000/05/03/mednews-priority/links/20000503clin015.html. Accessed May 3, 2000.

7. Collins JG. Vital and health statistics: Prevalence of selected chronic conditions: United States, 1990–1992. Series 10: Data from the National Health Survey. Vol 194. Hyattsville, Md: US Government Printing Office; 1997.

8. Poser CM. The epidemiology of multiple sclerosis: A general overview. *Ann Neurol.* 1994;36(suppl 2):S180-S193.

9. Ponichtera-Mulcare JA. Exercise and multiple sclerosis. *Med Sci Sports Exerc.* 1993;25:451-465.

10. Multiple Sclerosis Council. *Fatigue and Multiple Sclerosis: Evidence-Based Management Strategies for Fatigue in Multiple Sclerosis.* Washington, DC: Paralyzed Veterans of America; 1998.

11. Gehlsen GM, Grigsby SA, Winant DM. Effects of an aquatic fitness program on the muscular strength and endurance of patients with multiple sclerosis. *Phys Ther.* 1984;64:653-657.

12. Senaratne MP, Carroll D, Warren KG, Kappagoda T. Evidence for cardiovascular autonomic nerve dysfunction in multiple sclerosis. *J Neurol Neurosurg Psychiatry.* 1984;47:947-952.

13. Chen W-Y, Pierson FM, Burnett CN. Force-time measurements of knee muscle functions of subjects with multiple sclerosis. *Phys Ther.* 1987;67:934-940.

14. Svensson B, Gerdle B, Elert J. Endurance training in patients with multiple sclerosis: Five case studies. *Phys Ther.* 1994;74:1017-1026.

15. Vardy TC. Enhancing homeostasis using osteopathic techniques for multiple sclerosis. *Aust J Osteopath.* 1997;8(2):20-26.

16. Kraft GH, Alquist AD. Effect of resistive exercise on strength in patients with multiple sclerosis. In: *Rehabilitation research and development progress reports: 1995.* Baltimore, Md: VA Rehabilitation Research and Development Service, Scientific and Technical Publications Section (122), Department of Veterans Affairs; 1995;348.

17. Aitkens SG, McCrory MA, Kilmer DD, Bernauer, EM. Moderate resistance exercise program: its effect in slowly progressive neuromuscular disease. *Arch Phys Med Rehabil.* 1993;74:711-715.

18. Ponichtera JA, Glaser RM, Camaione DN, Mathews T. Physiologic responses to prolonged recumbent cycling of individuals with multiple sclerosis on land and in water. *Med Sci Sports Exerc.* 1990;22(suppl 2):S123.

19. Ponichtera JA, Mathews T, Glaser RM. Maximal aerobic power of individuals with multiple sclerosis using arm, leg, and combined arm and leg ergometer exercise. *Med Sci Sports Exerc.* 1992; 24(suppl 5):S73.

20. Ponichtera JA, Rodgers MM, Glaser RM. Mathews TA, Camaione DN. Concentric and eccentric isokinetic lower extremity strength in persons with multiple sclerosis. *J Orthopaed Sports Phys Ther.* 1992;16(3):114-122.

21. Schrag DR, Ponichtera JA, Mathews T, Glaser RM. Isokinetic upper extremity strength of persons with multiple sclerosis. *Med Sci Sports Exerc.* 1992;24(suppl 5):S34.

22. Ponichtera JA, Mathews T, Glaser RM, Ezenwa B. A test to determine dynamic exercise capacity and autonomic cardiovascular function in individuals with multiple sclerosis, In: Presperin JJ, ed. *Rehabilitation Engineering and Assistive Technology Society of North America (RESNA) International '92: Technology for Consumers. Toronto, Ontario, 6-11 June 1992.* Toronto, Ontario: RESNA Press; 1992:12-14.

23. Ponichtera-Mulcare JA, Glaser RM, Mathews T, Camaione DN. Maximal aerobic exercise in persons with multiple sclerosis. *Clin Kinesiology.* 1993:12-21.

24. Schapiro RT, Petajan JH, Kosich D, Molk B, Feeney J. Role of cardiovascular fitness in multiple sclerosis: A pilot study. *J Neurol Rehabil.* 1988;2:43-49.

25. Lai M, Hodgson T, Gawne-Cain M, Webb S, MacManus D, McDonald WI, et al. A preliminary study into the sensitivity of disease activity detection by serial weekly magnetic resonance imaging in multiple sclerosis. *J Neurol Neurosurg Psychiatry.* 1996;60:339-341.

26. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). *Neurology.* 1983;33:1444-1452.

27. Kurtzke JF. On the evaluation of disability in multiple sclerosis. *Neurology.* 1961;11:686-694.

28. Basmajian JV, Wolf SL. Multiple sclerosis and exercise. In: Butler JP, Napora L, Minkove KF, eds. *Therapeutic Exercise.* 5th ed. Baltimore, Md: Williams & Wilkins; 1990:243-244.

29. Ponichtera JA. Maximal exercise performance of individuals with multiple sclerosis: Influence of disease-related muscular- and temperature-induced dysfunction (muscular-induced dysfunction). WebSPIRS. 1989. Available at: http://webspirs4.silverplatter.com:8300/trial. Accessed March 16, 2000.

30. Ponichtera-Mulcare JA, Glaser RM. Evaluation of muscle performance and cardiopulmonary fitness in patients with multiple sclerosis: Implications for rehabilitation. *Neuro Rehabil.* 1993;3:17-29.

31. Denslow JS. Neural basis of the somatic component in health and disease and its clinical management. *J Am Osteopath Assoc.* 1972;72:149-156.

32. Kuchera WA, Kuchera ML. *Osteopathic Principles in Practice.* 2nd ed. Kirksville, Mo: Kirksville College of Osteopathic Medicine Press; 1993.

33. Peterson B, ed. *The Collected Papers of Irvin M. Korr.* Colorado Springs, Colo: American Academy of Osteopathy; 1979.

34. American Academy of Osteopathy. The central connection: Somatovisceral/viscerosomatic interaction. In: Patterson MM, Howell JN, eds. *1989 International Symposium.* Athens, Ohio: University Classics, Ltd; 1989.

35. Jackson KM, Steele TF, Dugan EP, Kukulka G, Blue W, Roberts A. Effect of lymphatic and splenic pump techniques on the antibody response to hepatitis B vaccine: A pilot study. *J Am Osteopath Assoc.* 1998;98:155-160.

36. Mesina J, Hampton D, Evans R, Ziegler T, Mikeska C, Thomas K, et al. Transient basophilia following the application of lymphatic pump techniques: A pilot study. *J Am Osteopath Assoc.* 1998;98:91-94.

37. Measel JW Jr. Introduction: Thoughts on osteopathic practice and infectious diseases. *Osteopath Ann.* 1982;10(3):92-94.

38. Goodkin DE, Hertsgaard D, Seminary J. Upper extremity function in multiple sclerosis: Improving assessment sensitivity with box-and-block and nine-hole peg tests. *Arch Phys Med Rehabil.* 1988;69:850-854.

39. Schwid SR, Goodman AD, Mattson DH, Mihai C, Donohoe KM, Petrie MD, et al. The measurement of ambulatory impairment in multiple sclerosis. *Neurology.* 1997;49:1419-1424.

40. Wenzel KC, Montgomery LD, Ku YE. The effects of cooling on performance and perceived fatigue. In: *Proceeding of the 1996 Annual Meeting of the Consortium of Multiple Sclerosis (MS) Centers, Atlanta, Ga, 27-29 September 1996.* Atlanta, Ga; 1996.