Aerobic Exercise in People with Multiple Sclerosis

Its Feasibility and Secondary Benefits

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The aims of this study were to explore the feasibility of structured aerobic exercise followed by a period of unstructured physical activity and determine the impact of such exercise on cognition, mood, and quality of life in people with multiple sclerosis (MS). A convenience sample of 9 individuals with relapsing-remitting MS performed 30 minutes of aerobic exercise (upper- and lower-extremity ergometry and treadmill ambulation) twice weekly for 8 weeks, followed by 3 months of unstructured physical activity. Eight participants completed the intervention and posttest; 6 returned for the 3-month follow-up. Cardiovascular fitness, cognition, mood (measured with the Beck Depression Inventory–II; BDI-II), and quality of life (measured with the Multiple Sclerosis Quality of Life–54; MSQOL-54) were assessed. Participants completed 27.9 minutes of exercise per session, with an 85.1% attendance rate. Evaluation using the Wilcoxon signed rank test revealed no deleterious effects and improved results on the BDI-II and MSQOL-54 mental subscale. Analysis of change scores using the one-sample t test revealed that the BDI-II and MSQOL-54 were changed from zero after structured exercise, but only the BDI-II maintained improvement after unstructured physical activity. Further analysis of BDI-II subscales revealed that improvement occurred only in the Somato-Affective subscale. In this study, program feasibility was demonstrated in several ways. There were no declines in cognitive function over the 5-month period. Despite unchanged cognitive function, participants may value the improved mood enough to continue both the structured and unstructured physical activity. The role of unstructured physical activity in concert with periodic structured exercise programs merits further investigation. ***Int J MS Care.*** **2013;15:138–145.**

Multiple sclerosis (MS) is a chronic immune-mediated disease with a heterogeneous course characterized by progressively diminished physical and cognitive resources, both of which may adversely affect quality of life (QOL). Historically, exercise was discouraged for people with MS for fear of possibly increasing fatigue or triggering a disease exacerbation.[1] However, the beneficial role of exercise in individuals with MS is becoming clear. For example, Rietberg et al.[2] found strong evidence of improved muscle strength, activity tolerance, and mobility in nine high-quality randomized controlled trials investigating the effects of exercise therapy for MS. In addition, the authors reported moderate evidence for the secondary benefit of improved mood.

Recently, studies have demonstrated primary exercise benefits of improved balance and increased walking capacity, with secondary benefits of reduced fatigue, enhanced mood, improved QOL, and decreased perceived disability immediately following an 8-week strength-training program[3] and an aerobic exercise intervention.[4,5] Despite the demonstrated benefits, attrition in exercise intervention studies is a concern, ranging from just over 18%[6] to 42%.[4] These high attrition rates bring into question the feasibility of exercise programs

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for people with MS regardless of any primary or secondary benefits.

In theory, the primary and secondary benefits associated with aerobic exercise may be enjoyed by the participant regardless of mode. Determining whether primary and secondary benefits associated with aerobic exercise are enjoyed regardless of mode may be valuable, because up to 75% of people with MS experience mobility and gait limitations.[7] However, no study to date has examined this assumption. The purpose of this pilot study was to explore the feasibility of physical exercise in individuals with MS and the aspects of mood affected by a structured multimodal aerobic exercise program followed by unstructured physical activity.

Methods

Instruments

This 5-month pilot study was divided into two primary components: a structured aerobic exercise program lasting 8 weeks, followed by 3 months of unstructured physical activity (Figure 1). Testing was performed at three intervals to determine baseline function (session 1), postintervention attainment (session 18), and follow-up preservation (session 19) after 3 months of self-directed exercise. Each individual underwent a standardized battery of tests to assess cardiovascular fitness, cognitive performance, and QOL during sessions 1, 18, and 19. To set the initial aerobic exercise intensity, we assessed cardiovascular function by continuously monitoring each participant's breath by breath gas analysis via a telemetry metabolic measurement system (MedGraphics VO_{2000}; MGC Diagnostics, St. Paul, MN) while performing the 6-Minute Walk (6MW) test according to American Thoracic Society guidelines.[8] Test order was standardized so as to minimize physical and mental fatigue by allowing adequate rest periods.

Cognitive performance (verbal learning and working memory domains) was assessed by selected neuropsychological measures from the Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS).[9] Verbal learning was measured using the California Verbal Learning Test, Second Edition (CVLT-II).[10] Working memory was measured by the Symbol Digit Modalities Test (SDMT)[11] and the Paced Auditory Serial Addition Test 3.0 interstimulus interval (PASAT-3).[12] Equivalent alternate versions of the CVLT-II and PASAT-3 were used during retesting to negate potential learning effects, per standard testing protocol.

Depression, fatigue, and disability are independent predictors of QOL in MS.[13] Therefore, depression was assessed by the Beck Depression Inventory–II (BDI-II),[14] which demonstrates item internal consistency for people with MS.[15] Quality of life was assessed by the Multiple Sclerosis Quality of Life–54 (MSQOL-54),[16] which reliably measures QOL in MS[17] as determined by mental and physical subscores.

Upon completion of the intervention and posttesting, each participant was encouraged to be physically active until the follow-up testing (session 19). No specific exercises or activities were provided—only the recommendation to participate in physical activity within the community.

Participants

We recruited 9 participants with a diagnosis of relapsing-remitting MS from a convenience sample in Dallas, Texas. To be eligible for this study, participants had to be ambulatory with or without an assistive device and score less than 6.5 on the Kurtzke Expanded Disability Status Scale (EDSS).[2,18] Although cognitive impairment in people with MS has been found to be more profound at EDSS stages above 4.0,[19] it may also be present during early disease stages and precede physical disability.[20] As a result, we did not set a minimum EDSS score. Individuals

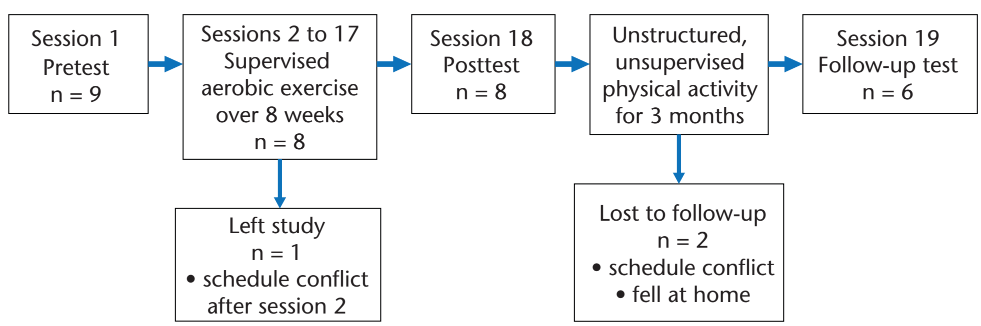

***Figure 1.* Study flow diagram**

were excluded if they had comorbid neurologic disease or conditions that would preclude participation in an exercise program, such as diagnosed cardiac or respiratory disease, an acute orthopedic condition, or gross cognitive impairment. In addition, individuals who were currently experiencing an MS exacerbation by self-report at any time during the study were excluded. Table 1 lists the participants' characteristics. No participant reported a change in medications over the course of this study.

Although 9 participants completed the baseline pretest, 8 participants completed the intervention and posttest. Only 6 participants returned to complete the 3-month follow-up (Figure 1). While there were no adverse effects from the study, one participant fell at home and sustained a fractured tibia between the posttest and follow-up time periods.

This study received approval from the institutional review board of Texas Woman's University in Dallas, Texas. Each individual provided written informed consent prior to participation.

Procedures

Sessions 2 to 17 consisted of a standardized aerobic exercise program individualized for each participant's fitness level. The 16 training sessions were conducted at Texas Woman's University two times per week for 8 weeks. Participants performed up to 30 minutes of exercise, with 15 minutes on an upper- and lower-extremity (UE/LE) ergometer and 15 minutes ambulating on a treadmill (with alternating sequence of the UE/LE ergometer and treadmill sessions) to tolerance. The initial target exercise training intensity on the UE/LE ergometer and treadmill was set at 50% to 70% of oxygen consumption achieved[21] as established by the 6MW during session 1. We conducted aerobic testing to set an appropriate exercise goal and to monitor safety of the participants during exercise. Each exercise session began with a warm-up and ended with a cooldown. To individually progress the aerobic exercise, resistance or speed of the aerobic training was adjusted to an intensity of "somewhat hard" on the Rating of Perceived Exertion (RPE) scale[22] throughout the sessions. Additionally, heart rate and exercise blood pressure were closely monitored during exercise sessions to ensure participant tolerance and safety.

Statistical Analysis

All data were analyzed using SPSS software (SPSS, Chicago, IL). Descriptive statistics were obtained for participant characteristics and the intervention. Data were analyzed with nonparametric statistics because of concerns over assumptions of normality given the small sample size. Feasibility was analyzed through descriptive analysis and the Wilcoxon signed rank test to determine the presence or absence of positive change in any of the outcome measures. We analyzed pre-post intervention differences in the dependent variables using the Wilcoxon signed rank test. One-sample t tests were also used to determine whether change scores were significantly different from zero (no change). A significant result would indicate that scores changed significantly from pretest to posttest. The alpha was set at .05 for all dependent variables in the study.

***Table 1.* Participant characteristics**

Participant	Age, y	Gender	Ethnicity	MS duration, y	EDSS score	Limb involvement	Assistive device	Exercise adherence, %
1[a]	45	M	African American	3	1.5	Right	None	N/A[a]
2	29	F	White	3	2.5	Bilateral	None	93.75
3	52	F	White	1	5.5	Bilateral	Cane, walker	100
4[b]	55	F	African American	2	2.0	Right	None	50.0
5	37	F	White	3	1.5	Left	None	100
6[c]	47	F	African American	4	6.0	Bilateral	Quad cane	93.75
7	39	F	White	4	2.5	Bilateral	None	87.5
8	47	M	White	6	3.5	Left	None	81.25
9	33	F	White	3	2.0	Bilateral	None	75.0

Abbreviations: EDSS, Expanded Disability Status Scale; F, female; M, male; MS, multiple sclerosis.
[a]Dropped from study after session 2 owing to change in work schedule.
[b]Lost at follow-up (session 19) owing to schedule conflict.
[c]Lost at follow-up (session 19) owing to fall at home resulting in tibial fracture.

Results

During the aerobic exercise intervention sessions, study participants were able to increase the treadmill speed and ergometer resistance while having a lower RPE. The characteristics of the exercise training sessions are shown in Table 2.

To be feasible, a structured aerobic exercise program should be safe and minimize anticipated deterioration of physical condition over time. Therefore, nonparametric analysis of the structured and unstructured activity effects was performed with the Wilcoxon signed rank test to determine the presence or absence of positive change in the means of all outcome measures. Neither structured nor unstructured physical activity displayed a significantly deleterious or beneficial impact on any dependent variables (Table 3). However, the MSQOL-54 mental subscale and the BDI-II demonstrated trends for improvement after the structured aerobic exercise intervention and after unstructured physical activity (Figure 2).

To examine the secondary benefits of structured aerobic exercise and unstructured physical activity, a one-sample *t* test was used to analyze change scores. The change from zero for the dependent variables is recorded in Table 3. Only one dependent variable demonstrated change from zero after structured aerobic exercise or unstructured physical activity. The BDI-II total score was significantly changed from zero, reflecting an improved mood, after the structured intervention, but this change was not sustained with unstructured physical activity.

Although a single score is commonly reported, the BDI-II has two subscales: Somato-Affective and Cognitive. A post hoc analysis was conducted to determine which BDI-II domain was affected by our intervention. We repeated the Wilcoxon signed rank test and one-sample *t* test using each subscale instead of the total BDI-II. The results are shown in Table 4. The significant changes in mood resulting from the structured aerobic exercise intervention were due to improvement in the BDI-II Somato-Affective subscale. The BDI-II Cognitive subscale demonstrated no significant changes at any point.

***Table 2.* Characteristics of initial and final exercise training sessions (sessions 2 and 17)**

Characteristic	Initial session, mean ± SD	Final session, mean ± SD
Total exercise time, min	27.34 ± 5.01	27.91 ± 3.89
HR_{max} achieved, bpm	119 ± 8.29	123 ± 15.92
% of age-predicted HR_{max}	66.99	69.25
Treadmill speed, kmph	3.32 ± 1.36	3.64 ± 1.54
U/E ergometer work, watts	51.3 ± 17.27	62.5 ± 18.32
RPE	13.1 ± 2.23	12.6 ± 2.92

Abbreviations: bpm, beats per minute; HR_{max}, maximum heart rate; kmph, kilometers per hour; RPE, Rating of Perceived Exertion; U/E, upper- and lower-extremity.

***Table 3.* Effects of the exercise intervention on cognitive performance and quality of life variables**

Variable	Pre	Post	Follow-up
PASAT-3	49.33	49.38	52.50
SDMT	51.00	50.13	55.17
CVLT-II	1.29	1.41	1.37
BDI-II[a,b]	12.89	7.875	6.167
MSQOL-p, %	59.86	68.31	68.18
MSQOL-m,[c,d] %	67.60	79.50	79.56

Abbreviations: BDI-II, Beck Depression Inventory–II; CVLT-II, California Verbal Learning Test, Second Edition; MSQOL-m, Multiple Sclerosis Quality of Life–54 scale, mental score; MSQOL-p, Multiple Sclerosis Quality of Life–54 scale, physical score; PASAT-3, Paced Auditory Serial Addition Test 3.0 interstimulus interval; SDMT, Symbol Digit Modalities Test.
Notes: Values are means. There were no significant differences between dependent variable means by time as determined by the Wilcoxon signed rank test or changes from zero as determined by the one-sample *t* test.
[a] $P = .058$ for pre-post (n = 8), $P = .058$ (n = 6) for pre–follow-up as determined by the Wilcoxon signed rank test.
[b] $P = .045$ for pre-post change from zero (n = 8), $P = .067$ (n = 6) for pre–follow-up change from zero as determined by the one-sample *t* test.
[c] $P = .069$ for pre-post (n = 8) as determined by the Wilcoxon signed rank test.
[d] $P = .094$ for pre-post change from zero (n = 8) as determined by the one-sample *t* test.

Discussion

One purpose of this study was to explore the feasibility of a structured aerobic exercise program followed by unstructured physical activity. According to Trope and Liberman,[23] feasibility and desirability are related concepts. Feasibility is the ease or difficulty of reaching the end state or goal. Desirability is the value placed on that end state. Both concepts can be considered from the perspective of the participant/patient or the researcher/physical therapist. In today's health-care environments, physical therapists desire to incorporate evidence into their decision making. However, evidence-based practice principles must balance research evidence with patient values. Therefore, physical therapists must consider both

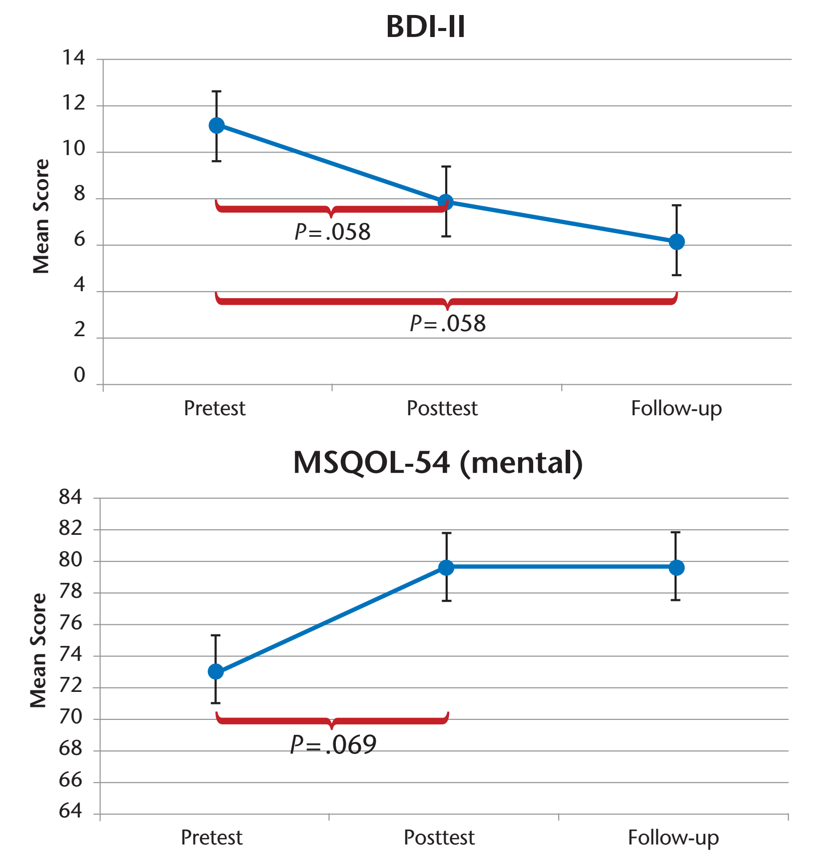

Figure 2. Mood and quality of life over time

BDI-II, Beck Depression Inventory–II; MSQOL-54, Multiple Sclerosis Quality of Life–54.

feasibility and desirability as well as evidence. Studies indicate that participants' perceived value of exercise may not exceed the associated cost of exercise. For example, earlier studies[4,6] showing statistically significant benefits in individuals with MS following exercise programs had attrition rates of up to 42%, leading one to question the feasibility or desirability of such programs. While the cost of participating in an exercise program includes dosage-dependent physical exertion, value may be found in physical attributes, cognitive factors, mood, and QOL. Our study was intended to explore feasibility through the perceived value of aerobic exercise while minimizing cost by using the minimally recommended dosage.

Adherence is one aspect of feasibility. Participants in our study attended on average 85.1% of the sessions. Further, exercise progression was well tolerated, as demonstrated by an increased workload for a longer duration with a lower overall rate of perceived exertion. Based on this finding, the least recommended dose of aerobic exercise[21] (frequency, twice per week; duration, two consecutive sessions of up to 15 minutes each; intensity, 50% to 70% of peak oxygen consumption per unit time [VO_2]; mode, UE/LE ergometer and treadmill) was well tolerated by participants, thus demonstrating feasibility. Throughout the exercise intervention, 8 of 9 participants completed the structured program, for an attrition rate of 11%. For our study, the perceived value of exercise by the majority of participants appears to have exceeded the associated cost of exercise. However, the cost of attending a follow-up testing session in our study outweighed the perceived benefits for two additional participants, for an overall attrition rate of 33%.

While our study focused on minimizing dosage to maximize feasibility, peer socialization may also improve adherence to exercise (15% attrition).[24] Although physical function was improved over the 8-week exercise intervention, no follow-up testing was performed to determine long-term adherence to exercise in the community setting.

Another aspect of feasibility is accessibility. We deliberately selected aerobic exercise interventions (walking and stationary cycling) that are easily accessible in the community. The rationale for selecting these intervention activities was to allow for an easy transition from a structured aerobic program to unstructured physical activity. Anecdotally, participants 2 and 7 reported joining a local fitness center during the unstructured physical activity interval, and participant 3 signed up to walk in a local MS awareness walk event. Though this result was unmeasured, it appears that the

Table 4. Beck Depression Inventory–II subscale analysis

	Somato-Affective subscale	Cognitive subscale
Wilcoxon (pre-post)	.026[a]	.168
Wilcoxon (pre-F/U)	.026[a]	1.000
Wilcoxon (post-F/U)	.680	.465
One-sample *t* test (pre-post)	.029[a]	.17
One-sample *t* test (pre-F/U)	.006[a]	1.000
One-sample *t* test (post-F/U)	.497	.516

Abbreviation: F/U, follow-up.
[a] $P < .05$.

tolerable structured aerobic exercise program using readily accessible interventions increased self-efficacy to pursue increased physical activity in some participants.

While the exercise program appears to be feasible, our main purpose was to explore what aspects of mood were affected by structured and unstructured activity. With this in mind, we examined secondary benefits in domains of cognitive status, mood, and QOL. We will discuss each of these in turn.

First, no improvements were observed in individual working memory or verbal learning cognitive domains. The brevity of the intervention (8 weeks) may not provide the opportunity for cognitive changes. Although Colcombe and Kramer[25] suggested that regular exercise lasting greater than 6 months is necessary for cognitive improvements, improved cognition has been observed after 3 months of exercise in frail elderly individuals,[26] people with chronic obstructive pulmonary disease (COPD),[27] and people with stroke.[28] However, in each of these studies, the exercise intervention was more intense in frequency and duration than in our study. Intensity of aerobic exercise intervention appears to be an important feature. Baker et al.[29] demonstrated improved cognitive function after 6 months, but not 3 months, of intervention because "participants had only completed 6 weeks of the program at the targeted intensity." A second explanation is that our participants may have had minimal potential to significantly improve their scores. Our participants had baseline scores approximating scores of normals in published studies[9]; thus they had minimal room for improvement. It is also possible that physical activity does not affect cognitive function in people with a compromised central nervous system regardless of dosage. For example, Ploughman et al.[30] suggested that exercise is unable to improve cognitive performance in individuals after stroke. This finding may also be true for individuals with MS. Whether or not the potential for change in cognitive function is a reflection of dosage or capability is currently unknown and merits further study.

While the exercise dosage in this study did not improve cognitive performance, an improved mood in terms of somato-affective features was observed after 8 weeks of exercise. This finding is consistent with studies involving animals,[31] healthy adults,[32] individuals needing mental health care,[33] and individuals with MS.[2] The link between participation in structured cardiovascular fitness activities and improved mood suggests that aerobic exercise may benefit individuals with MS. Furthermore, in our study, BDI-II Somato-Affective subscale scores remained improved after the 3-month period of unstructured physical activity. In the absence of gain in cognitive function, the value associated with improved mood emerges as a plausible explanation for persisting in an 8-week structured aerobic exercise program with transition to unstructured physical activity.

To gain a better understanding of the impact of physical activity on mood, we analyzed the BDI-II questionnaire's subscales (Cognitive and Somato-Affective). While an overall improved mood was not apparent on the total score, closer examination demonstrates that structured aerobic exercise affected BDI-II subscales differently. The Cognitive subscale—with salient features of pessimism, guilt, self-dislike, self-criticism, and worthlessness—was unchanged throughout the structured intervention and unstructured physical activity. However, the Somato-Affective subscale—including relevant factors of fatigue, loss of energy, changes in sleep patterns, and concentration difficulty—improved after the structured intervention and was maintained with unstructured physical activity. Fatigue, a multifactorial entity in MS with dimensions including energy loss, sleepiness, and inability to sustain activity,[34] seems to increase cognitive complaints[35] and is associated with reduced self-efficacy.[36] Although not expressly measured in this study, fatigue has been shown to be reducible with physical activity.[6] Further exploration of the relationship between somato-affective features of depression and aerobic exercise appears warranted.

We observed maintenance of an improved mood over 3 months despite the lack of a monitored or formally structured exercise program. Because temporary elimination of physical activity has been shown to worsen a depressed mood state,[37] the maintenance of improved mood may also suggest that participants wanted to continue their physical activity after the conclusion of the structured program. Inclusion of an objective monitoring tool such as a physical activity log, pedometer, or another device may have been useful in determining whether a multimodal aerobic exercise program overcomes common barriers to physical activity such as limited self-efficacy and facilitates positive coping strategies to increase physical activity.[38]

It is reasonable to consider the ethical costs associated with our program. Although the program showed little evidence of physical and cognitive changes, "keeping in good physical health is the best preventative treatment that can be offered to individuals with multiple sclerosis and the best advice for long-term, cost-effective care."[39(p1780)] Tertiary prevention as a low-cost means of managing chronic disease improves some elements of health status while reducing overall health-care costs.[40] The elements apparently improved in our sample were mood and QOL. Lorig et al. also reported that improved self-efficacy was related to decreased outpatient health-care costs. While the program was designed and conducted by a physical therapist, it was not an individualized physical therapy treatment session. The emphasis was on health promotion and wellness, and increasing physical activity in this population. To decrease costs, a physical therapist could act as a consultant and support staff could carry out the program.

Conclusion

In this study, participation in a structured aerobic exercise program two times per week for 8 weeks improved mood, with the improvement persisting over a 3-month follow-up period of unstructured physical activity. The participants' ability to complete the aerobic testing and exercise intervention and their improved mood and QOL indicate the feasibility and secondary benefits of the intervention.

Several limitations of this study may prevent the generalization of results. The small sample size contributed to the lack of statistical power, limiting the ability to draw conclusions from the results. Furthermore, the study would have benefited from a control group of either nonexercising individuals with MS or exercising individuals without MS. Several authors have noted that a minimum of 6 months of exercise is required to yield cognitive improvements in people without disease.[25] Our exercise intervention of 8 weeks may have been too brief to create positive changes in cognition despite improved mood. Additionally, failure to monitor physical activity during the 3 months between sessions 18 and 19 prevented us from fully describing the carryover impact of the structured aerobic exercise program.

Future studies should include evaluation of the role of exercise parameters in minimizing barriers to physical activity participation. Variation of dosage—including intensity, duration, frequency, and mode—may allow for a broader understanding of the feasibility of structured exercise for individuals with MS. Finally, the role of unstructured physical activity in concert with periodic structured exercise programs should be explored in order to facilitate the development of interventions that provide lasting benefits. □

PracticePoints

- Aerobic exercise performed twice per week for 30 minutes at 50% to 70% of maximal heart rate on a treadmill and stationary bicycle was feasible for study participants with MS.
- Participation in a structured 8-week aerobic exercise program improved mood in this group of individuals.
- Participation in the exercise program did not affect cognitive function in this sample.

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