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The Effects of M2M and Adapted Yoga on Physical and **Psychosocial Outcomes in People With Multiple Sclerosis**

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Abstract

Objective: To investigate the effects of two 12-week exercise training interventions, movementto-music (M2M) and adapted yoga (AY), on physical and psychosocial outcomes in people with multiple sclerosis (MS).

Design: Three-arm randomized controlled proof-of-concept trial.

Setting: A community-based fitness facility.

Participants: Participants (N = 81) with MS (Patient Determined Disease Steps [PDDS] selfreported disease status scores: 0-6) between ages of 18 and 65 years were randomized to M2M (n=27), AY (n=26), or waitlist control (n=28).

Interventions: Both M2M and AY completed three 60-minute exercise sessions per week for 12 weeks. Waitlist controls received biweekly newsletters via mail that contained educational information on living with MS.

Main Outcome Measures: Primary measures were timed Up and Go (TUG, s) test, 6-minute walk test (6MWT, m), and 5 times sit-to-stand test (FTSST, s). Secondary measures were self-reported outcomes assessed using Patient-Reported Outcomes Measurement Information System Fatigue and Pain Interference Short Form 8a. Participants were evaluated at baseline and postintervention. Primary analyses were performed using an intent-to-treat mixed model analysis of covariance.

Results: Comparisons across all 3 groups revealed significant group differences in TUG and 6MWT. Post hoc analyses indicated significant improvements in TUG (least square mean

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Suppliers

difference [95% confidence interval] = -1.9s [-3.3 to -0.5], P=.01, d=0.7 and 6MWT (41.0m [2.2-80.0], P=.04, d=0.6; controlled for PDDS) in M2M compared to controls, while no significant differences were observed when compared AY to controls. No significant group differences were found in FTSST, fatigue, and pain interference.

Conclusions: M2M may be a useful and enjoyable exercise form for people with MS in improving mobility and walking endurance and merits long-term study in larger study populations.

Keywords

Dancing; Exercise; Multiple sclerosis; Rehabilitation

Multiple sclerosis (MS) is characterized by demyelination and axonal loss of the central nervous system, which progressively results in neurologic dysfunction¹ and is often accompanied by mobility limitations, reduced fitness, and increased risk of falls.^{2,3} Regular exercise has been recognized as an important health behavior in the general population.^{4,5} For people with MS, numerous studies have shown the benefits of exercise on muscle strength,^{6,7} aerobic fitness,⁸ pain,⁹ fatigue,¹⁰ fall risk,¹¹ and other secondary conditions.¹² However, evidence suggests that people with MS are much less physically active than the general population.¹³⁻¹⁶ Engaging in regular exercise can be challenging. Asano et al¹⁷ surveyed 417 people with MS and found "dislike exercise" and "find exercise boring" common reasons for not exercising. Developing alternative exercise forms, thus, becomes critical in helping people find activities that fit their interests and needs.

A critical aspect of an exercise intervention is to ensure that it is enjoyable so that individuals are more likely to remain active over time. Traditional exercises such as treadmill walking or stationary cycling can often be perceived as boring, because these exercises usually involve repetitive, continuous movements. ¹⁸ In addition, outdoor activities may be difficult for people with MS due to mobility deficits and potential disease exacerbation when exposed to heat and humidity. ¹⁹⁻²¹ Alternative exercise forms such as yoga have become increasingly popular among people with MS. ²²⁻³³ In a systematic review of 7 randomized controlled trials, Cramer et al ³⁴ reported positive short-term effects of yoga on fatigue and mood in people with MS.

In designing exercise interventions to address MS symptoms, incorporating music into movement-based programs can potentially lead to greater enjoyment and serve as an adjunct to standard rehabilitation.^{3,35} In fact, evidence has suggested dance as a promising intervention for improving physical functions in people with Parkinson disease, ^{36,37} stroke, ³⁸ and other disabling conditions. ³⁸⁻⁴¹ To date, there are only 3 studies that have examined the effects of dance on mood, self-esteem, mobility, gait, balance, and physical activity in people with MS. ^{2,35,42}

There is a need to provide alternative, more enjoyable forms of exercise that can positively affect the physical function and health of people with MS. Thus, the purpose of this study was to examine the effects of 2 exercise interventions, a novel dance-based program termed movement-to-music (M2M), and an adapted yoga (AY) program, on the physical (mobility

and balance, walking endurance and lower extremity functional strength) and psychosocial (fatigue and pain interference) outcomes in people with MS.

Methods

Study design

This study was designed as a 3-arm randomized controlled trial comparing the effects of M2M, AY, and a waitlist control (WC). Eligible participants who provided informed consent and completed baseline testing were randomly assigned to M2M, AY, or WC using computer-generated randomization by a statistician who was not involved with the interventions. Assignments were sealed in opaque envelopes opened by each participant. Although participants and study staff who supervised intervention delivery were not blinded to group assignments, all outcomes measures were administered by blinded assessors. Participants in WC were offered a 12-week home-based M2M posttesting, which is a separate ongoing study.

Participants

Potential participants were identified from the membership database of a community-based health and fitness facility for individuals with physical disabilities, physician referrals, flyers, informational mailings, and word of mouth. A sample size of 60 was determined for purpose of estimating effect sizes for future studies.⁴³ Interested participants were enrolled if they self-reported a diagnosis of MS, with a Patient Determined Disease Steps (PDDS) score between 0 and 6. The PDDS is an ordinal scale ranging from 0 (normal) to 8 (bedridden). It is a simple and practical tool for measuring self-reported disability status⁴⁴⁻⁴⁶ and has a strong correlation (rs=0.8) with the Expanded Disability Status Scale. 44 Additional inclusion criteria included ages of 18-65 years, ability to exercise with arms and/or legs, and physician clearance. Exclusion criteria included participation in a similar intervention in the last 6 months, use of tobacco products in the last 6 months, unstable weight, cognitive impairment (Mini-Mental State Exam score <24), active pressure ulcer, and any contraindications to exercise based on the American College of Sports Medicine guidelines.⁴⁷ Four types of adverse events (AEs), as defined by the Behavior Change Consortium of the National Institutes of Health, ⁴⁸ that were monitored are as follows: falls, cardiovascular-related episodes, musculoskeletal-related events, and health care use. The study was approved by the Institutional Review Board of the institution and was conducted in accordance with a clinical trial protocol registered at ClinicalTrials.gov.

Interventions

Both M2M and AY consisted of three 60-minute sessions per week for 12 weeks. All 36 sessions for both interventions took place in an exercise room of the fitness facility. Resting blood pressure, a resting heart rate, and oxygen saturation were recorded before and after class. Participants also reported rating of perceived exertion at the end of each class. For safety purposes, exercise heart rate was monitored during class to ensure that it did

a. Fingertip pulse oximeter \mbox{Spo}_2 PR monitor; ChoiceMMed.

b. MDF 840 professional blood pressure monitor; MDF Instruments Direct, Inc.

not exceed 80% of age-predicted maximal heart rate. Make-up classes were offered when needed.

Movement-to-music—The M2M intervention aimed to progressively improve mobility using combinations of movement forms that were structured to target 3 fitness components: strength, cardiorespiratory endurance, and balance. Table 1 highlights the general structure of M2M. Each class was choreographed by an experienced dance instructor and incorporated multiple movement routines accompanied with music. Every routine specifically targeted a fitness component, with the movements and tempo adapted to participants' functional level. For example, standing routines were adapted to seated versions for participants who experienced excessive fatigue during prolonged standing. Each class began with a warm-up routine that focused on upper and lower extremity range of motions performed in a seated position, followed by upper extremity muscle strengthening, cardiorespiratory endurance, lower extremity muscle strengthening, and balance routines performed either seated or standing with or without support of a dance barre. The class ended with a cool-down routine that emphasized breathing and mindfulness. Equipment included chairs, wrist weights, TheraBands, exercise balls, and ribbons.

Adapted yoga—The AY intervention was taught by yoga instructors who were YogaFit level 1 certified and had experience adapting yoga for people with disabilities. The intervention was delivered in the Iyengar approach to Hatha yoga.^{29,31} Each class consisted of a series of stationary poses that used isometric contraction and relaxation techniques to obtain specific body alignments, which were performed either seated or standing. Classes were based on the 3-Mountain format, which included a warm-up phase (Mountain 1), work phase (Mountain 2), and cool-down phase (Mountain 3). This format provided consistency between classes while progressively introducing new and advanced poses to participants. The class was adapted for participants with limited flexibility and/or strength by using props (ie, chairs, straps) to help with performing poses. Each class ended with relaxation.

Waitlist control—WC participants received biweekly newsletters that provided educational information on living with MS. Information was obtained through the National Center on Health, Physical Activity and Disability. ⁴⁹ Participants were instructed to maintain usual activities.

Outcome measures

All participants completed a baseline demographic and health history questionnaire that included age, sex, race, health history, and PDDS. Anthropometric measures included height, weight, and body mass index. Primary and secondary outcomes were assessed by qualified exercise physiologists who were trained to administer the measures with a standardized testing protocol at baseline and postintervention.

Primary outcomes—The primary outcomes were changes in mobility and balance, walking endurance, and lower extremity functional strength. Mobility and balance were

c. BiohamessTM 3; Zephyr Technology.

assessed with the timed Up and Go (TUG) test. The TUG was recorded as the time required to rise from a chair, walk to a 3-m mark, turn around, walk back to the chair, and sit down. ^{50,51} Walking endurance was measured using the 6-minute walk test (6MWT), where distance walked over 6 minutes was documented in meters. ^{52,53} The 5 times sit-to-stand test (FTSST) was used to measure lower extremity functional strength and was recorded as the time required to stand up and sit down (seat height=47.5cm) as quickly as possible 5 times without assistance. ⁵⁴ The FTSST is commonly referred to as a *functional strength* test because it is a common activity of daily living. ⁵⁴⁻⁵⁷

Secondary outcomes—The secondary outcomes were changes in self-reported scores for fatigue and pain interference over the past 7 days. Fatigue was assessed with the Patient-Reported Outcomes Measurement Information System (PROMIS)⁵⁸ Fatigue-Short Form 8a (adult v1.0),⁵⁹ which contains 8 items on a 5-point Likert scale, ranging from *never* to *always*. The influence of pain on performing daily activities was assessed with the PROMIS Pain Interference-Short Form 8a (adult v1.0),⁵⁹ which contains 8 items with 5 response options ranging from *not at all* (1) to *very much* (5). Both forms have raw scores range from 8 to 40, with higher scores indicating more fatigue or pain interference.

Program adherence was calculated as a percentage of the number of classes offered (36) to the number of classes attended.

Statistical analysis

Descriptive statistics were used to summarize participant baseline characteristics. Data were presented as means \pm SD (n). Baseline variables were compared between groups using 1-way analysis of variance to test for homogeneity. When PROMIS short-form items were unanswered, a total prorated raw score was approximated using the following formula if minimum number of items required by the instrument were answered:

 $\frac{Total \ pro-rated \ score =}{(Raw \ sum \times \ x \ number \ of \ items \ on \ the \ short \ form)}{Number \ of \ items \ that \ were \ actually \ answered}$

The total raw or prorated score was translated into a T score for analyses. 60

Our primary and secondary analyses focused on comparing outcomes between M2M, AY, and WC. Primary analyses were performed using an intent-to-treat mixed model analysis of covariance, with the corresponding baseline measure and intervention group as covariates, and the intervention wave (study delivered in five 3mo intervention waves) as random effect. Secondary analyses were conducted with PDDS as an additional covariate. Post hoc analyses were performed to identify differences between groups when the global test for the intervention term in analysis of covariance was significant. Least square mean (LSM) differences with 95% confidence interval (CI) and corresponding effect sizes (Cohen's *d*) were estimated for each outcome. All analyses were performed using Statistical Analysis System version 9.4. Statistical significance was accepted at *P*<.05.

d. Statistical Analysis System, version 9.4; SAS Institute, Inc.

Results

There were 171 individuals approached between December 2014 and August 2016, with 81 enrolled in the study (n=27 in M2M; n=26 in AY; n=28 in WC). Figure 1 provides the CONSORT diagram showing participant flow through the study.

Participant baseline characteristics are presented in table 2. There were no statistical differences between groups with respect to all baseline characteristics and measures for primary and secondary outcomes.

Primary outcomes

Table 3 displays all descriptive and statistical indices for TUG, 6MWT, and FTSST. A group difference in TUG change score was found statistically significant ($F_{(2,57)}$ =3.7; P=.03). Post hoc analyses revealed that TUG time was significantly lower in M2M compared to WC postintervention (LSM difference [95% CI]=-1.9s [-3.3 to -0.5], P=.01, d=0.7). No significant TUG improvement was found in AY compared to WC.

There was a significant group difference in 6MWT after accounting for PDDS ($F_{(1,51)}$ =4.5; P=.04). Post hoc analyses revealed that 6MWT distance increased significantly in M2M compared to WC (LSM difference [95% CI])=41.0m [2.2-80.0], P=.04, d=0.6), whereas no significant improvement was observed in AY compared to WC.

For FTSST, no statistically significant group difference was observed postintervention $(F_{(2.47)}=0.9; P=.41)$. The difference remained nonsignificant after controlling for PDDS.

Secondary outcomes

All descriptive and statistical indices for fatigue and pain interference are presented in table 3. There was no statistically significant group difference in change in fatigue ($F_{(2,47)}$ =1.61; P=.21), but when controlling for PDDS, the difference approached significance ($F_{(1,47)}$ =3.22; P=.08). Figure 2 illustrates the distribution of fatigue data at baseline and postintervention by study group. Post hoc analyses revealed a trend in fatigue reduction in M2M compared to WC (LSM difference [CI] = -3.6 [-7.9 to 0.7], P=.09, d=0.5). There was no statistically significant group difference in change in pain interference postintervention ($F_{(2,53)}$ =0.36; P=.70), and this remained nonsignificant after controlling for PDDS.

Adherence and AEs

Average attendance was 53.7% for M2M and 67.7% for AY, with an average of 7 makeup classes offered per wave. An overview of study-related and nonstudy-related AEs are presented in table 4.

Discussion

The primary findings of this proof-of-concept study are that, compared to controls who were instructed to maintain usual activities, M2M participants showed statistically significant improvements in mobility and walking endurance after 12-week intervention. On the other

hand, evidence from comparing AY and WC indicated that AY participants had improved mobility that was not statistically significant and had no change in walking endurance postintervention.

The significant findings of the present study on TUG and 6MWT improvements in M2M agree with previous studies in MS³⁵ and Parkinson disease. 41,62,63 Mandelbaum et al³⁵ examined effects of a 4-week salsa dance intervention and reported a significant TUG improvement in 8 participants with MS. In our study, we observed moderate effect sizes for TUG and 6MWT between M2M and WC. However, the improvements observed in M2M (1.3s for TUG and 33.7m for 6MWT) did not reach the minimal important difference of TUG (10.6s) and 6MWT (76.2m) reported by Learmonth et al⁶⁴ in people with MS. One possible explanation is that participants in the study by Learmonth had a higher severity and narrower range of disability status (average Expanded Disability Status Scale score=6.0 [range: 5.0-6.5]) compared to our participants (average PDDS=2.4 [range: 0-6]). The minimal important difference values, thus, might not be appropriate for interpreting clinical significance of outcome improvements in participants with less severity and a wider range of disability status. Nevertheless, Sosnoff et al⁶⁵ suggested that decreased balance and walking endurance were associated with greater risk of falls in people with MS. The TUG and 6MWT improvements observed in M2M provide promising preliminary data for future investigation on preventing falls using M2M in this population. More studies are needed to examine the clinical difference of including participants with a similar range of disability severity in M2M.

Interestingly, no significant FTSST improvement was observed in M2M participants compared to controls, despite the significant findings in TUG and 6MWT. A possible explanation for this nonsignificant result is that a sit-to-stand motion requires different kinematics and greater muscle strength compared to walking. ^{66,67} Although M2M involved sit-to-stand motions during movement transitions, the focus was to enhance mobility so the intervention may not have been of sufficient training intensity to improve this specific motion. Future studies should consider incorporating specific training routines for improving the sit-to-stand motion in people with MS.

There was no statistically significant improvement in all physical outcomes observed in AY compared to controls. Previous studies on yoga and MS have mainly focused on its psychosocial benefits. Rogers et al⁶⁸ suggested that more research is needed to determine its effects on MS symptoms including impaired mobility. The effect sizes observed in the present study for AY on TUG (d=0.5), 6MWT (d=0.3), and FTSST (d=0.3) thus add to the current MS literature. It is logical to postulate that M2M would result in better mobility outcomes because it involves more dynamic movements while AY consists of more stationary poses. Further investigation is required to examine specific elements of M2M that lead to these physical improvements.

Fatigue is one of the most common MS symptoms.⁶⁹ In this study, participants in all 3 groups had an average baseline self-reported PROMIS fatigue score that was approximately 1 SD higher than the average of US general population (T score of 50),⁷⁰ suggesting higher fatigue levels in this population.⁶⁹ Our data also indicate a wide fatigue score distribution

at baseline and postintervention among the 3 groups. The broad MS severity range of our participants could potentially explain the varying fatigue levels observed. In addition, fatigue in MS is multifactorial in nature and can be caused by different mechanisms, which could also contribute to the observed variability. Future investigation should distinguish mechanisms and causes that lead to fatigue in people with a range of MS severity and examine potential influences of M2M and AY on different types of fatigue.

Rhythmic-based M2M offers a unique and enjoyable way to obtain regular exercise. It may serve as a viable adjunct to other forms of exercise that may be less appealing to some or many people with MS. The M2M intervention was designed to target mobility through enhancing range of motion, muscular strength, endurance, and balance through routines that can be adapted for individuals with a wide range of physical function. It is currently unknown if a greater training effect can be achieved when classes are offered for participants with similar functional levels. This remains an area for future research.

Finally, it is important to recognize that M2M is not limited to 1 dance style (eg, ballet, jazz, salsa), because its goal is to use various rhythmic movements to target different fitness components. Care should be taken when extrapolating the results of this study to other specific types of dance interventions.

Study limitations

Our study had limitations. First, we did not identify the types of MS (eg, relapsing-remitting, secondary-progressive), which could have influenced how participants responded to assigned interventions. Second, although exercise adaptations were provided in both interventions, participants with higher functional levels may have had a lower training effect than participants with lower functional levels. Third, activity level of the WC participants was not monitored so we could not objectively confirm that they maintained usual activities during the study period. Fourth, similar to exercise studies in other disability groups, 72 our study experienced barriers including transportation, scheduling conflicts, and effects of weather on MS symptoms. Finally, the present study included participants with a wide range of MS severity so the observed results should be interpreted with caution. Considerations for overcoming these limitations should be incorporated into future research.

Conclusions

Findings from this proof-of-concept study suggest that a 12-week M2M intervention may be effective in improving mobility and walking endurance in participants with MS while no significant improvements were observed in participants undergoing a 12-week AY intervention. Future studies should examine specific intervention elements as well as the physiological mechanisms that contributed to the functional improvements observed in M2M.

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List of abbreviations:

AE adverse event

AY adapted yoga

CI confidence interval

FTSST five times sit-to-stand test

LSM least square mean

M2M movement-to-music

MS multiple sclerosis

6MWT 6-minute walk test

PDDS Patient Determined Disease Steps

PROMIS Patient-Reported Outcomes Measurement Information System

TUG timed up and go

WC waitlist control

References

- 1. Compston A, Coles A. Multiple sclerosis. Lancet 2008;372:1502–17. [PubMed: 18970977]
- 2. Salgado R, Paula Vasconcelos LA. The use of dance in the rehabilitation of a patient with multiple sclerosis. Am J Dance Ther 2010; 32:53–63.
- 3. Dhami P, Moreno S, DeSouza JFX. New framework for rehabilitation–fusion of cognitive and physical rehabilitation: the hope for dancing. Front Psychol 2014;5:1478. [PubMed: 25674066]
- 4. Cress ME, Buchner DM, Questad KA, Esselman PC, deLateur BJ, Schwartz RS. Exercise: effects on physical functional performance in independent older adults. J Gerontol A Biol Sci Med Sci 1999;54:M242–8. [PubMed: 10362007]
- 5. Howe TE, Rochester L, Neil F, Skelton DA, Ballinger C. Exercise for improving balance in older people. Cochrane Database Syst Rev 2011;(11):CD004963. [PubMed: 22071817]
- 6. Dalgas U, Stenager E, Jakobsen J, et al. Resistance training improves muscle strength and functional capacity in multiple sclerosis. Neurology 2009;73:1478–84. [PubMed: 19884575]
- 7. Moradi M, Sahraian MA, Aghsaie A, et al. Effects of eight-week resistance training program in men with multiple sclerosis. Asian J Sports Med 2015;6:e22838. [PubMed: 26448834]
- 8. Gallien P, Nicolas B, Robineau S, Pétrilli S, Houedakor J, Durufle A. Physical training and multiple sclerosis. Ann Réadapt Méd Phys 2007;50:373–6. [PubMed: 17482708]
- 9. Motl RW, McAuley E, Snook EM, Gliottoni RC. Physical activity and quality of life in multiple sclerosis: intermediary roles of disability, fatigue, mood, pain, self-efficacy and social support. Psychol Health Med 2009;14:111–24. [PubMed: 19085318]
- Pilutti LA, Greenlee TA, Motl RW, Nickrent MS, Petruzzello SJ. Effects of exercise training on fatigue in multiple sclerosis: a meta-analysis. Psychosom Med 2013;75:575–80. [PubMed: 23788693]

11. Freeman J, Gear M, Pauli A, et al. The effect of core stability training on balance and mobility in ambulant individuals with multiple sclerosis: a multi-centre series of single case studies. Mult Scler 2010;16:1377–84. [PubMed: 20699285]

- 12. Snook EM, Motl RW. Effect of exercise training on walking mobility in multiple sclerosis: a meta-analysis. Neurorehabil Neural Repair 2008;23:108–16. [PubMed: 18948413]
- White LJ, Dressendorfer RH. Exercise and multiple sclerosis. Sports Med 2004;34:1077–100.
 [PubMed: 15575796]
- 14. Motl RW, McAuley E, Snook EM. Physical activity and multiple sclerosis: a meta-analysis. Mult Scler 2005;11:459–63. [PubMed: 16042230]
- Beckerman H, de Groot V, Scholten MA, Kempen JC, Lankhorst GJ. Physical activity behavior of people with multiple sclerosis: understanding how they can become more physically active. Phys Ther 2010;90:1001–13. [PubMed: 20508028]
- Motl RW, Goldman M. Physical inactivity, neurological disability, and cardiorespiratory fitness in multiple sclerosis. Acta Neurol Scand 2011;123:98–104. [PubMed: 21108624]
- 17. Asano M, Duquette P, Andersen R, Lapierre Y, Mayo NE. Exercise barriers and preferences among women and men with multiple sclerosis. Disabil Rehabil 2013;35:353–61. [PubMed: 23347461]
- 18. Bartlett JD, Close GL, Maclaren DP, Gregson W, Drust B, Morton JP. High-intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: implications for exercise adherence. J Sports Sci 2011;29:547–53. [PubMed: 21360405]
- 19. Syndulko K, Jafari M, Woldanski A, Baumhefner RW, Tourtellotte WW. Effects of temperature in multiple sclerosis: a review of the literature. Neurorehabil Neural Repair 1996;10:23–34.
- Simmons RD, Ponsonby A-L, Mei IAvd, Sheridan P. What affects your MS? Responses to an anonymous, Internet-based epidemiological survey. Mult Scler 2004;10:202–11. [PubMed: 15124768]
- Guthrie TC, Nelson DA. Influence of temperature changes on multiple sclerosis: critical review of mechanisms and research potential. J Neurol Sci 1995;129:1–8.
- Guclu-Gunduz A, Citaker S, Irkec C, Nazliel B, Batur-Caglayan HZ. The effects of pilates on balance, mobility and strength in patients with multiple sclerosis. NeuroRehabilitation 2014;34:337–42. [PubMed: 23949064]
- Marandi SM, Nejad VS, Shanazari Z, Zolaktaf V. A comparison of 12 weeks of pilates and aquatic training on the dynamic balance of women with mulitple sclerosis. Int J Prev Med 2013;4(Suppl 1): S110–7. [PubMed: 23717760]
- 24. van der Linden ML, Bulley C, Geneen LJ, Hooper JE, Cowan P, Mercer TH. Pilates for people with multiple sclerosis who use a wheelchair: feasibility, efficacy and participant experiences. Disabil Rehabil 2014;36:932–9. [PubMed: 23957639]
- Azimzadeh E, Hosseini MA, Nourozi K, Davidson PM. Effect of Tai Chi Chuan on balance in women with multiple sclerosis. Complement Ther Clin Pract 2015;21:57–60. [PubMed: 25534298]
- Burschka JM, Keune PM, Oy UH, Oschmann P, Kuhn P. Mindfulness-based interventions in multiple sclerosis: beneficial effects of Tai Chi on balance, coordination, fatigue and depression. BMC Neurol 2014;14:165. [PubMed: 25145392]
- 27. Ahmadi A, Nikbakh M, Arastoo A, Habibi A-H. The effects of a yoga intervention on balance, speed and endurance of walking, fatigue and quality of life in people with multiple sclerosis. J Hum Kinet 2010;23:71–8.
- 28. Doulatabad SN, Nooreyan K, Doulatabad AN, Noubandegani ZM. The effects of pranayama, hatha and raja yoga on physical pain and the quality of life of women with multiple sclerosis. Afr J Tradit Complement Altern Med 2013;10:49–52.
- 29. Frank R, Larimore J. Yoga as a method of symptom management in multiple sclerosis. Front Neurosci 2015;9:133. [PubMed: 25983675]
- 30. Guner S, Inanici F. Yoga therapy and ambulatory multiple sclerosis assessment of gait analysis parameters, fatigue and balance. J Bodyw Mov Ther 2015;19:72–81. [PubMed: 25603746]
- 31. Oken B, Kishiyama S, Zajdel D, et al. Ramdomized controlled trial of yoga and exercise in multiple sclerosis. Neurology 2004; 62:2058–64. [PubMed: 15184614]

32. Rahnama N, Namazizadeh M, Etemadifar M, Bambaeichi E, Arbabzadeh S, Sadeghipour HR. Effects of yoga on depression in women with multiple sclerosis. J Isfahan Med Sch 2011;29: 483–90.

- 33. Salgado BC, Jones M, Ilgun S, McCord G, Loper-Powers M, van Houten P. Effects of a 4-month Ananda Yoga program on physical and mental health outcomes for persons with multiple sclerosis. Int J Yoga Therap 2013;(23):27–38.
- 34. Cramer H, Lauche R, Azizi H, Dobos G, Langhorst J. Yoga for multiple sclerosis: a systematic review and meta-analysis. PLoS One 2014;9:e112414. [PubMed: 25390344]
- 35. Mandelbaum R, Triche EW, Fasoli SE, Lo AC. A pilot study: examining the effects and tolerability of structured dance intervention for individuals with multiple sclerosis. Disabil Rehabil 2016;38: 218–22. [PubMed: 25875049]
- 36. Hackney ME, Earhart GM. Recommendations for implementing tango classes for persons with Parkinson disease. Am J Dance Ther 2010;32:41–52. [PubMed: 30369677]
- 37. Hackney ME, Earhart GM. Effects of dance on gait and balance in Parkinson's disease: a comparison of partnered and nonpartnered dance movement. Neurorehabil Neural Repair 2010;24:384–92. [PubMed: 20008820]
- 38. Hackney M, Hall C, Echt K, Wolf S. Application of adapted tango as therapeutic intervention for patient with chronic stroke. J Geriatr Phys Ther 2012;35:206–17. [PubMed: 22143597]
- 39. Hokkanen L, Rantala L, Remes AM, Härkönen B, Viramo P, Winblad I. Dance and movement therapeutic methods in management of dementia: a ramdomized, controlled study. J Am Geriatr Soc 2008;56:771–2. [PubMed: 18380687]
- 40. Abreu M, Hartley G. The effects of Salsa dance on balance, gait, and fall risk in a sedentary patient with Alzheimer's dementia, multiple comorbidities, and recurrent falls. J Geriatr Phys Ther 2013;36:100–8. [PubMed: 22955042]
- 41. Hackney ME, Earhart GM. Effects of dance on movement control in Parkinson's disease: a comparison of Argentine tango and American ballroom. J Rehabil Med 2009;41:475–81. [PubMed: 19479161]
- 42. Charlton ME, Gabriel KP, Munsinger T, Schmaderer L, Healey KM. Program evaluation results of a structured group exercise program in individuals with multiple sclerosis. Int J MS Care 2010;12:92–6.
- 43. Teare MD, Dimairo M, Shephard N, Hayman A, Whitehead A, Walters SJ. Sample size requirements to estimate key design parameters from external pilot randomised controlled trials: a simulation study. Trials 2014;15:264. [PubMed: 24993581]
- 44. Learmonth YC, Motl RW, Sandroff BM, Pula JH, Cadavid D. Validation of patient determined disease steps (PDDS) scale scores in persons with multiple sclerosis. BMC Neurol 2013;13:37. [PubMed: 23617555]
- 45. Hohol MJ, Orav EJ, Weiner HL. Disease steps in multiple sclerosis: a longitudinal study comparing disease steps and EDSS to evaluate disease progression. Mult Scler 1999;5:349–54. [PubMed: 10516779]
- 46. Hohol MJ, Orav EJ, Weiner HL. Disease steps in multiple sclerosis: a simple approach to evaluate disease progression. Neurology 1995;45:251–5. [PubMed: 7854521]
- 47. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. 9th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2014.
- 48. Ory M, Resnick B, Jordan PJ, et al. Screening, safety, and adverse events in physical activity interventions: collaborative experiences from the behavior change consortium. Ann Behav Med 2005;29:20–8. [PubMed: 15921486]
- 49. National Center on Health, Physical Activity and Disability (NCHPAD). (2018). NCHPAD Building Inclusive Communities. Available at: http://www.nchpad.org/. Acessed June 13, 2018.
- 50. Sebastião E, Sandroff BM, Learmonth YC, Motl RW. Validity of the timed up and go test as a measure of functional mobility in persons with multiple sclerosis. Arch Phys Med Rehabil 2016;97:1072–7. [PubMed: 26944709]
- 51. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. J Am Geriatr Soc 1991; 39:142–8. [PubMed: 1991946]

52. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111–7. [PubMed: 12091180]

- 53. Goldman MD, Marrie RA, Cohen JA. Evaluation of the six-minute walk in multiple sclerosis subjects and healthy controls. Mult Scler 2008;14:383–90. [PubMed: 17942508]
- 54. Møller AB, Bibby BM, Skjerbæk AG, et al. Validity and variability of the 5-repetition sit-to-stand test in patients with multiple sclerosis. Disabil Rehabil 2012;34:2251–8. [PubMed: 22612360]
- 55. Bohannon RW, Bubela DJ, Magasi SR, Wang Y-C, Gershon RC. Sit-to-stand test: performance and determinants across the age-span. Isokinet Exerc Sci 2010;18:235–40. [PubMed: 25598584]
- 56. Mong Y, Teo TW, Ng SS. 5-repetition sit-to-stand test in subjects with chronic stroke: reliability and validity. Arch Phys Med Rehabil 2010;91:407–13. [PubMed: 20298832]
- 57. Duncan RP, Leddy AL, Earhart GM. Five times sit-to-stand test performance in Parkinson's disease. Arch Phys Med Rehabil 2011;92:1431–6. [PubMed: 21878213]
- 58. Ader DN. Developing the Patient-Reported Outcomes Measurement Information System (PROMIS). Med Care 2007;45:S1–2. [PubMed: 18027399]
- Senders A, Hanes D, Bourdette D, Whitham R, Shinto L. Reducing survey burden: feasibility and validity of PROMIS measures in multiple sclerosis. Mult Scler 2014;20:1102–11. [PubMed: 24402035]
- 60. Reeve BB, Teresi JA. Overview to the two-part series: measurement equivalence of the Patient Reported Outcomes Measurement Information System (PROMIS) short forms. Psychol Test Assess Model 2016;58:31–5.
- 61. Meier U A note on the power of Fisher's least significant difference procedure. Pharm Stat 2006;5:253–63. [PubMed: 17128424]
- 62. de Natale ER, Paulus KS, Aiello E, et al. Dance therapy improves motor and cognitive functions in patients with Parkinson's disease. NeuroRehabilitation 2017;40:141–4. [PubMed: 27814308]
- 63. McNeely ME, Mai MM, Duncan RP, Earhart GM. Differential effects of Tango versus dance for PD in Parkinson disease. Front Aging Neurosci 2015;7:239. [PubMed: 26733865]
- 64. Learmonth YC, Paul L, McFadyen AK, Mattison P, Miller L. Reliability and clinical significance of mobility and balance assessments in multiple sclerosis. Int J Rehabil Res 2012;35:69–74. [PubMed: 22315143]
- 65. Sosnoff JJ, Socie MJ, Boes MK, et al. Mobility, balance and falls in persons with multiple sclerosis. PLoS One 2011;6:e28021. [PubMed: 22132196]
- 66. Rodosky MW, Andriacchi TP, Andersson GB. The influence of chair height on lower limb mechanics during rising. J Orthop Res 1989;7: 266–71. [PubMed: 2918425]
- 67. Ploutz-Snyder LL, Manini T, Ploutz-Snyder RJ, Wolf DA. Functionally relevant thresholds of quadriceps femoris strength. J Geront A Biol Sci 2002;57:B144–52.
- 68. Rogers KA, MacDonald M. Therapeutic yoga: symptom management for multiple sclerosis. J Altern Complement Med 2015;21: 655–9. [PubMed: 26270955]
- 69. Krupp LB, Alvarez LA, LaRocca NG, Scheinberg LC. Fatigue in multiple sclerosis. Arch Neurol 1988;45:435–7. [PubMed: 3355400]
- 70. Cella D, Riley W, Stone A, et al. Initial adult health item banks and first wave testing of the Patient-Reported Outcomes Measurement Information System (PROMISTM) Network: 2005–2008. J Clin Epidemiol 2010;63:1179–94. [PubMed: 20685078]
- 71. Braley TJ, Chervin RD. Fatigue in multiple sclerosis: mechanisms, evaluation, and treatment. Sleep 2010;33:1061–7. [PubMed: 20815187]
- 72. Rimmer JH, Riley B, Wang E, Rauworth A, Jurkowski J. Physical activity participation among persons with disabilities: barriers and facilitators. Am J Prev Med 2004;26:419–25. [PubMed: 15165658]

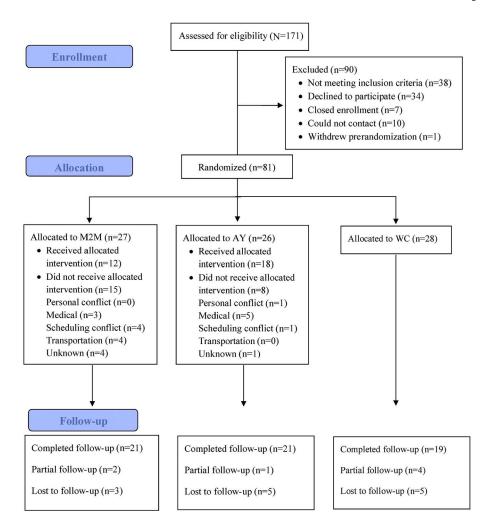


Fig 1.CONSORT diagram reflecting flow of participants through the study. Partial follow-up indicates participants did not complete entire set of postintervention assessments.

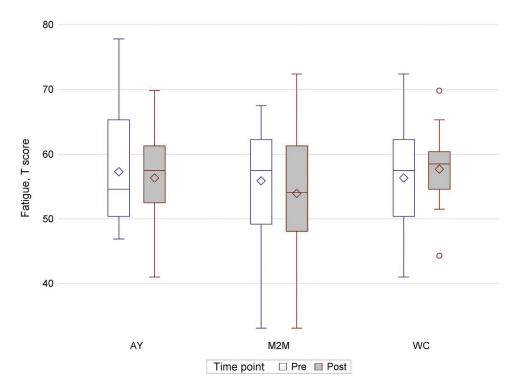


Fig 2. Box plot illustrating the distribution of fatigue data at baseline and postintervention, separated by the 3 study groups.

Table 1

Overall structure of M2M

Training Component/Week 1 2 3 4 5 6 7 8 9 10 Warm up (range of motion) Cupper body 5 5 5 4 4 4 4 4 3 3 3 Lower body 3 5 5 6 6 7 7 8 3 4 3 4						直	ıratio	Duration (Min)	n)				lι
orday 5 5 5 4 4 4 4 4 3 body 5 5 5 5 4 4 4 4 4 3 3 tody 3 4 4 4 4 4 <td< th=""><th>Training Component/Week</th><th>1</th><th>7</th><th>3</th><th>4</th><th>w</th><th>9</th><th>7</th><th>œ</th><th>6</th><th>10</th><th>11</th><th>12</th></td<>	Training Component/Week	1	7	3	4	w	9	7	œ	6	10	11	12
body 5 5 5 4 4 4 4 4 3 rbody 3 5 5 5 4 4 4 4 4 3 rbody 3 <t< td=""><td>Warm up (range of motion)</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>	Warm up (range of motion)												
thody determity muscle strength determity muscle strength 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	Upper body	S	S	S	S	4	4	4	4	8	∞	3	8
veody 3 <td>Lower body</td> <td>5</td> <td>S</td> <td>5</td> <td>5</td> <td>4</td> <td>4</td> <td>4</td> <td>4</td> <td>33</td> <td>33</td> <td>3</td> <td>33</td>	Lower body	5	S	5	5	4	4	4	4	33	33	3	33
body 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 4	Upper extremity muscle strength												
body 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	Upperbody	33	33	33	33	33	33	ω	3	3	33	3	3
simagery 5 6 6 7 7 8 8 9 9 xtremity muscle strength 10 10 8 8 8 8 8 9 9 9 mic 5 4 4 3 3 2 5 1 1 mic 0 1 2 3 4 5 6 7 8 nm 5	Lower body	7	2	2	7	2	7	7	2	2	7	2	2
imagery 5 6 6 7 7 8 8 9 9 9 xtremity muscle strength 10 10 8 8 8 6 6 6 6 7 8 9 <	Cardio	5	5	9	9	7	7	∞	∞	6	6	10	10
Autremity muscle strength 10 8 8 8 8 6 7 8 7 8 7 8 7 8 9 </td <td>Cardio + imagery</td> <td>S</td> <td>S</td> <td>9</td> <td>9</td> <td>7</td> <td>7</td> <td>∞</td> <td>∞</td> <td>6</td> <td>6</td> <td>10</td> <td>10</td>	Cardio + imagery	S	S	9	9	7	7	∞	∞	6	6	10	10
mic 0 1 2 3 4 4 3 3 2 2 1 1 1 wn 5 5 5 5 5 5 5 5 5 5 inutes 45 45 46 47 47 48 48 49 49	Lower extremity muscle strength	10	10	∞	∞	∞	∞	9	9	9	5	4	4
5 4 4 3 3 2 2 1 1 1 1 1 2 3 4 5 6 7 8 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	Balance												
0 1 2 3 4 5 6 7 8 5 5 5 5 5 5 5 5 5 5 45 46 46 47 47 48 48 49	Static	5	4	4	33	33	2	7	-	-	-	0	0
5 5 5 5 5 5 5 5 5 5 5 5 45 45 46 47 47 48 48 49	Dynamic	0	_	2	3	4	5	9	7	∞	6	10	10
45 45 46 46 47 47 48 48 49	Cool down	5	5	5	5	5	5	5	5	5	5	5	5
	TotaL minutes	45	45	46	46	47	47	48	48	49	49	50	50

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Baseline characteristic of the participants

	M2M (n=27)	Yoga (n=26)	Control (n=28)	P Value
Age, y (n)	49.67±9.40 (27)	48.35±9.95 (26)	47.29±10.33 (28)	19:
Sex, % (n)				.71
Men	18.5 (5)	23.1 (6)	14.3 (4)	
Women	81.5 (22)	76.9 (20)	85.7 (24)	
Ethnicity, % (n)				5.
White	44.4 (12)	57.7 (15)	60.7 (17)	
Black	55.6 (15)	34.6 (9)	39.3 (11)	
Other	0.0 (0)	7.7 (2)	0.0(0)	
PDDS, % (n)	2.37±2.13 (27)	1.58 ± 1.90 (26)	2.57±2.01 (28)	68:
0	29.6 (8)	46.2 (12)	21.4 (6)	
1	11.1 (3)	11.5 (3)	14.3 (4)	
2	14.8 (4)	15.4 (4)	14.3 (4)	
3	14.8 (4)	7.7 (2)	14.3 (4)	
4	7.4 (2)	7.7 (2)	17.9 (5)	
ν.	11.1 (3)	7.7 (2)	7.1 (2)	
9	11.1 (3)	3.8 (1)	10.7 (3)	
Duration of diagnosis, y (n)	13.56±8.26 (27)	10.98 ± 5.57 (24)	13.38 ± 8.50 (28)	.41
Height, cm (n)	168.14±8.47 (27)	166.94±7.65 (24)	167.34±9.62 (28)	88.
Weight, kg (n)	84.34±22.42 (27)	88.23±19.97 (25)	86.38±23.33 (28)	.82
BMI, kg/m ² (n)	29.88±7.50 (27)	31.68±6.49 (24)	31.01 ± 8.98 (28)	.71

NOTE. Data reported as mean \pm SD (n) or % (n).

Abbreviation: BMI, body mass index.

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Table 3

Descriptive and ANCOVA statistics for primary and secondary outcomes

		p		0.71	0.46	1.38	0.59	0.32	1.34	0.38	0.28	0.53	0.49	0.11	
		P		*10.	60:	.33	* 40.	.25	.34	.20	.34	69:	60:	.70	
	Post Hoc Pairwise Comparisons	Differences of LSM (95% CI)		-1.89 (-3.30 to -0.48)	-1.20 (-2.58 to 0.18)	0.69 (-0.71 to 2.08)	40.98 (2.21-79.75)	22.83 (-16.67 to 6.2)	-18.15 (-56.36 to 20.05)	-1.00 (-2.58 to 0.55)	-0.70 (-2.17 to 0.77)	0.30 (-1.21 to 1.82)	-3.60 (-7.90 to 0.71)	0.83 (-5.17 to 3.51)	2.77 (-1.37 to
ANCOVA		Groups		M2M- WC	AY-WC	AY-M2M	M2M- WC	AY-WC	AY-M2M	M2M- WC	AY-WC	AY-M2M	M2M- WC	AY-WC	
	Secondary Analysis Covariates: Baseline Score+ Intervention+ PODS	P		.37			* 40.			1.00			80:		
	Sec Ar Cov Bs Sc	Ħ		0.81			4.49			0.00			3.22		
	Primary Analysis Covariates: Baseline Score+ Intervention	Ь		.03			.12			.41			.21		
	Pri An Covi Ba Sc Sc	Į		3.69			2.25			06.0			1.61		
	M2M (n=27) AY (n=26) WC (n=28)	Post		12.8 \pm 11.7 (22)			310.7 ± 130.8 (19)			$11.6\pm 3.6 \\ (19)$			57.7±5.9 (18)		
		Baseline		15.6 ± 22.4 (28)			302.2±152.8 (28)			12.7±3.8 (24)			56.3 ± 8.0 (27)		
roup		Post		10.6 ± 12.7 (24)			421.7 ± 159.2 (21)			10.6 ± 5.1 (21)			56.3±7.6 (21)		
Study Group		Baseline		$11.1\pm 10.8 \\ (26)$			407.3±152.4 (25)			11.6 ± 5.9 (21)			57.3±8.8 (23)		
		Post		12.2 ± 14.1 (20)			383.9 ± 134.1 (20)			$12.5\pm 4.5 (18)$			53.9±10.2 (22)		
		Baseline		12.3 ± 12.4 (26)			341.7 ± 110.1 (26)			12.5±5.1 (22)			comes 55.9 ± 9.2 (23)		
			Primary outcomes	TUG, s			6MWT, m			FTSST, s			Secondary outcomes Fatigue, T 55		

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	l	p	0.13	0.25	0.61
		P	99.	.40	99.
	Post Hoc Pairwise Comparisons	Differences of LSM (95% CI)	1.06 (-3.70 to 5.83)	2.06 (-2.80 to 6.92)	0.10 (-3.59 to 5.59)
ANCOVA		Groups	M2M- WC	AY-WC	AY-M2M
Ì	Secondary Analysis Covariates: Baseline Score+ Intervention+ PODS	Ь	.95		
	Sec A A A B B B B S S S S S S S S S S S S S	F	.70 0.00		
	Primary Analysis Covariates: Baseline Score+ Intervention	Ь	07.		
	Pri An Cova Ba Sc Inter	ম	0.36		
	WC (n=28)	Post	51.7±9.0 (17)		
	WC	Baseline	52.9±9.8 (27)		
Study Group	AY (n=26)	Post	53.3±8.3 (21)		
Study	AX	Baseline	52.7 ± 9.1 (23)		
	M2M (n=27)	Post	53.1±10.4 (22)		
	MZM	Baseline	52.3±9.7 (24)		
			Pain interference, T score		

NOTE. Data reported as mean \pm SD (n). Post hoc pairwise comparisons were reported based on primary analysis for TUG and secondary analysis for 6MWT. When the global test for the intervention term in ANCOVA was not significant, post hoc analyses were also reported to provide more information for future investigation.

Abbreviation: ANCOVA, analysis of covariance.

* P value <.05.

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Table 4

Overview of study- and nonstudy-related adverse events

	M2M (n=27)	Yoga (n=26)	Control (n=28)
AEs related to the study (n)			
Falls	0	0	0
Cardiovascular-related episodes	0	0	0
Musculoskeletal-related events	1	0	0
Muscle strain	1*	0	0
Health care use	0	0	0
AEs not related to the study (n)			
Falls	0	0	0
Cardiovascular-related episodes	0	1	0
Stroke	0	1	0
Musculoskeletal-related events	2	0	0
Stress fracture	1	0	0
Knee pain	1	0	0
Health care use	0	0	0

^{*} The 1 study related musculoskeletal-related event (muscle strain) was treated with rest and ice prior to the participant returning to the intervention.