Acute High-Intensity Interval Exercise in Multiple Sclerosis with Mobility Disability

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ABSTRACT

INTRODUCTION: Multiple sclerosis (MS) is an immune-mediated, neurological disease that results in physiological deconditioning with increasing disability. High-intensity interval training exercise (HIIT) has induced significant improvements in physiological conditioning in healthy and clinical populations, and might be appropriate for persons with MS who have mobility disability. The feasibility and acute effects of HIIT using recumbent stepping in persons with MS who have mobility disability are relatively unknown.

METHODS: The physiological effects of single sessions of HIIT and continuous (CON), steady-state aerobic exercise using recumbent stepping were compared in 20 persons with MS with mobility disability (i.e., EDSS of 4.0-6.5). The HIIT bout included 10 cycles of one-minute intervals at the work rate associated with 90% VO\textsubscript{2peak} followed by one-minute recovery intervals at 15W, totaling 20 minutes in length. The CON bout consisted of 20 minutes at the work rate associated with 50-60% VO\textsubscript{2peak}. Physiological (i.e., power output, oxygen consumption, carbon dioxide expiration, respiratory exchange ratio, ventilation, heart rate, and core temperature) and perceptual (i.e., ratings of perceived exertion) measures were collected across the acute sessions.

RESULTS: There were statistically significant condition × time interactions for all physiological measures and ratings of perceived exertion expressing differential patterns of change over time for HIIT versus CON (p < 0.05). The main effect of condition was significant for all physiological outcomes, except core temperature, with the HIIT condition inducing significantly higher values than CON (p < 0.05).

CONCLUSIONS: HIIT exercise taxes the cardiorespiratory system significantly more than CON, yet without deleterious effects on core temperature in persons with MS. This has important

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implications for informing an evidence-based exercise prescription that is appropriate for improving physiological conditioning in persons with MS who have mobility disabilities.

**Key Words**: high intensity interval training; neurological disorders; rehabilitation; adaptive equipment, deconditioning
INTRODUCTION

Multiple sclerosis (MS) is an immune-mediated, neurodegenerative disease of the central nervous system (CNS) with an estimated prevalence of 1 million adults in the United States and 2.5 million adults worldwide (1–3). MS is associated with physiological deconditioning, evidenced by reduced aerobic capacity (4), that worsens as a function of increasing levels of disability (5). The cycle of physiological deconditioning and worsening disability can be targeted through appropriate exercise training in MS (6), and exercise training may be a primary approach for slowing or reversing disability progression in persons with MS who have onset of mobility disability (i.e., Expanded Disability Status Scale (EDSS) score of 4.0-6.5) (7). Such exercise training must involve a stimulus and modality that can maximize adaptations and satisfy the capabilities of persons with MS (5,6).

Systematic reviews and meta-analysis support improvements in aerobic fitness, walking dysfunction and gait, balance, muscle strength and endurance, fatigue, and quality of life following exercise training in persons with mild or moderate MS characterized by minimal mobility disability (8–13). The evidence has yielded the Canadian Physical Activity Guidelines for adults with mild-or-moderate disability caused by MS (14). The guidelines, in part, recommend two-times per week of 30 minutes of moderate intensity aerobic activity (14) as part of the minimal dose necessary for improving health-related physical fitness. Of note, the aerobic activity prescription focuses on “continuous” (CON) or steady-state moderate-intensity exercise using standard equipment such as a treadmill or cycle ergometer. Although there is a vast amount of evidence to support the efficacy of CON exercise benefitting clinically-relevant outcomes in persons with MS (8–13), those with mobility disability are severely deconditioned and may be able to achieve superior benefits by engaging in high-intensity interval training (HIIT); (15–17).
Indeed, there is increasing recognition that persons with MS may experience greater benefits from higher intensity exercise (15–17), such as HIIT, as compared to moderate, continuous exercise training; yet these greater benefits could come at a cost of higher rates of adverse events (17). HIIT involves short periods of concentrated effort (e.g., 80-95% maximal heart rate) that alternate with periods of recovery (e.g., 40-50% maximal heart rate), thus maximizing overall exercise intensity (18). Some evidence suggests that HIIT is better than continuous, moderate exercise for improving aerobic capacity, increasing ventilatory threshold, and enhancing gait economy in samples of healthy people and those with heart disease (19). A recent systematic review summarizes the seven published studies on HIIT in persons with MS (15). Cycle ergometry was the exercise modality of choice, except in one case where arm ergometry was used (15). Only one study reported adverse events following HIIT (15,17). Of the six studies that reported on fitness outcomes, HIIT yielded significant improvements in cardiorespiratory fitness measured as VO$_2$peak or VO$_2$max in all but one study (15).

Three of the reviewed studies compared fitness and walking function outcomes following HIIT and continuous cycle ergometry exercise training in ambulatory persons with MS who have mild to moderate disability (15–17). One 12-week study identified significant improvements in walking function (i.e., 2-minute walk performance), yet there were more dropouts and adverse events following the HIIT program than continuous exercise program and combined program of HIIT and continuous exercise (17). The intervention-related adverse events included knee or leg pain while cycling (17), which could be considered a normal response associated with intense muscle contractions. The second study compared resistance training combined with HIIT or continuous aerobic training (16) and reported significant improvements in peak power (21±4%), time-to-exhaustion (24±5%), and peak oxygen consumption (17±5%) following the HIIT group.
only and no adverse events or dropouts(16). The most recent HIIT intervention in persons with MS directly compared HIIT to CON training over a three-week period(20). Significant group by time interactions were evident for VO_{2peak} in that those in the HIIT group had a significantly greater improvement in VO_{2peak} (~3.1 ml/kg/min) than those in the CON group(~1.4 ml/kg/min)(20). Collectively, the literature suggests a potential superiority of HIIT as compared to CON in improving physiological conditioning in a time efficient manner(20). HIIT requires a shorter period of time to achieve similar energy expenditure, likely due to an increase in Excess Post-exercise Oxygen Consumption(15). However, all of this evidence is specific to those with mild to moderate disability engaging in cycle ergometry and the feasibility and potential benefits of engaging in HIIT using recumbent stepping in persons with MS who have mobility disabilities is relatively unknown.

The application of a HIIT intervention, especially a practical, low-volume HIIT paradigm, among persons with MS who have mobility disabilities is particularly relevant in clinical practice because this population is the most deconditioned and experiences limited success with typical pharmacological methods(5,6,21). A low-volume HIIT protocol only requires 10 minutes of exercise performed over 20 minutes in a 1:1 work:rest ratio(19). In healthy populations, low-volume HIIT has provided the same benefits(e.g. rapid skeletal muscle remodeling towards a more oxidative phenotype and improved functional performance) as a work-matched, Wingate-based HIIT model, which is extremely demanding and consists of 6 all-out efforts separated by approximately four minutes of recovery on a cycle ergometer(19). As such, the low-volume HIIT protocol is proposed for the current study because it is time efficient and may be more tolerable or appealing than other HIIT protocols (19).
Many exercise interventions are designed for persons without mobility disability and use treadmill or cycle ergometers, which may not be appropriate for those with mobility disabilities(5). The American College of Sports Medicine has recommended recumbent stepping as an appropriate and viable assessment tool for evaluating aerobic fitness in neurological disorders(22) and a recent study has confirmed its efficacy for fitness assessment in MS across the disability spectrum(5). Moreover, despite kinematic differences, recumbent stepping relies on similar motor patterns as walking and it has been suggested that persons with neurological impairments may be able to increase walking performance from engaging in recumbent stepping(23).

The use of acute (i.e., single session) exercise research designs are critical for optimizing exercise protocols pragmatically, safely, efficiently, and from a sound design perspective. From a pragmatic perspective, data from acute, pilot studies can be used to develop, adapt, and identify the feasibility of the proposed methodology. Further, power analyses can utilize effect size and outcome data to generate sample sizes for larger randomized control trials. Valuable resources and time can be maximized through the implementation of an acute study to ensure the proposed methodology has a potentially large impact. The critical assumption, however, is that acute effects of single bouts of exercise are cumulative in nature resulting in an increase in aerobic fitness during longitudinal exercise studies(24). From a safety perspective, acute exercise research designs ensure the safety and feasibility for exercise within a clinical population, such as persons with moderate to severe MS, and parallel the first phase in a registered clinical trial(25). Thus, before executing a low-volume HIIT intervention in persons with MS with walking impairments, it is paramount to first ensure that the proposed recumbent stepping HIIT
prescription is safe and effective at acutely taxing the physiological systems responsible for the desired chronic adaptations (e.g., improved fitness and walking performance).

This study is the first to examine the acute effects of low-volume HIIT as compared to the CON with the explicit, long-term purpose of assessing the HIIT protocol’s potential for improving physiological and clinically relevant outcomes in persons with MS with mobility disability using adaptive equipment (i.e., a recumbent stepper). To do so, we compared the feasibility and within-session effects of acute sessions of HIIT and CON aerobic exercise performed on a recumbent stepper in persons with MS who had significant mobility disabilities based on standard clinical metrics (i.e., EDSS of 4.0-6.5). We hypothesized that all participants would complete both the HIIT and CON exercise sessions as prescribed. We further hypothesized that the HIIT condition would induce oscillating, yet significantly higher overall, patterns of physiological stress (i.e., VO$_2$, VCO$_2$, RER, VE, and HR) and perceived tolerance (i.e., RPE) data as compared with the relatively stable data from the CON condition. We further hypothesized that core temperature would increase significantly more during the HIIT condition as compared to the CON condition.

METHODS

Setting & Participants

The present study was approved by a University Institutional Review board and was performed within a university laboratory in the Midwest of the United States. Participants were recruited through online advertisements and through a database of past research participants expressing interest in research opportunities related to exercise and MS. Participants who met the following criteria were included: (a) age 18-64 years; (b) diagnosis of MS; (c) Patient
Determined Disability Steps (PDSS) scale score between 3.0 and 7.0; (d) relapse free in past 30 days; (e) willing and able to visit the laboratory on three testing occasions; (f) asymptomatic status for maximal exercise testing; and (g) physician approval for undertaking exercise testing.

**Design Overview**

The present study used a within-subjects, repeated measures design. All participants provided written informed consent upon arrival to the laboratory. There were three testing sessions: one baseline session followed by two exercise sessions. Each session was separated by at least 48 hours, and the order of the two sessions following the baseline session was randomized and counter-balanced. The baseline session lasted approximately 90 minutes. All HIIT and CON control sessions lasted approximately 120 minutes. Participants received $20 remuneration for completing each testing session for a total of $60.

**Baseline Session**

The baseline session included a neurological exam by a Neurostatus Level C examiner for generation of an EDSS score, administration of a demographic scale, and an incremental cardiopulmonary exercise test (CPET) to assess peak aerobic capacity and power using a recumbent stepper (NuStep T5\text{XR} recumbent stepper; NuStep Inc, Ann Arbor, MI, USA). The NuStep T5\text{XR} is intended for use in professional or commercial areas and is classified as accuracy Class A under the European Committee for Standardization’s EN ISO 20957-8:2017 standard. According to these standards, the NuStep T5\text{XR}’s determined power does not exceed ±5W up to 50W and ±10% over 50 W and is categorized as highly accurate. Participants were initially fitted to the recumbent stepper and subsequently read standardized instructions for completing the
maximal aerobic capacity test. Expired gases were collected using a 2-way non-rebreathing valve (Hans Rudolph, Kansas City, MO, USA) and oxygen consumption was continuously measured using an open circuit spirometry system (TrueOne, Parvo Medics, Sandy, UT, USA). Participants completed a 1-minute warm-up at 15W. The initial work rate was set to 15W and was gradually increased until the participant reached volitional fatigue. The work rate was increased by 10W per minute for participants with moderate disability (i.e., EDSS of 4.0-6.0) and 5W per minute for participants with severe disability (i.e., EDSS of 6.5). Heart rate (Polar FT1 Heart Rate Monitor, Polar Electro Inc., Bethpage, NY, USA), and Ratings of Perceived Exertion (RPE) via the Borg Rating of Perceived Exertion Scale were recorded every minute(27). The highest recorded 30-second rate of oxygen consumption value \( (V_O_2) \) was recorded as peak oxygen consumption \( (V_O_2\text{peak}) \), expressed in mL/kg/min, when at least 1 of the following criteria was satisfied: (1) respiratory RER 1.10 or greater; (2) peak heart rate within 10 beats per minute of age-predicted maximum (i.e., 220-age); or (3) RPE 17 or greater. The highest recorded power achieved was recorded as peak power output \( (W_{\text{peak}}) \). This CPET protocol has been validated in persons with MS previously(5).

**Aerobic Exercise Sessions**

Participants underwent single sessions of either HIIT or CON aerobic exercise on the recumbent stepper. The HIIT and CON exercise protocols were matched for total work duration and active exercise lasted for 20 minutes each (Figure 1). Both aerobic exercise sessions on the recumbent stepper were preceded by a 5-minute warm up and followed by a 5-minute cool down, making each session 30 minutes in duration. During the exercise sessions, participants were encouraged to maintain a stepping rate of 60-70 steps per minute throughout the exercise session.
The prescribed exercise intensity for each aerobic exercise session was calculated by first multiplying the desired percentage (i.e., .90 for HIIT and .50 and .60 for CON) by each participant’s recorded VO$_2$peak value. The within-exercise VO$_2$ measurements were graphed versus the incremental watt ranges achieved during the CPET. The VO$_2$ measurements were averaged over 30s and graphed along the x-axis. The associated watt values were plotted on the y-axis. A line of best fit was calculated using Microsoft Excel (Microsoft, Redmond, WA, USA) and used to predict the wattage associated with 90% and between 50% and 60% of VO$_2$peak.

**HIIT.** The HIIT protocol included 60 seconds of stepping at the workload associated with 90% of VO$_2$peak from the incremental CPET protocol followed by 60 seconds of active recovery at 15W. The bursts of vigorous exercise were interspersed with periods of active recovery for 10 cycles, yielding an active exercise duration of 20 minutes.

**CON.** The continuous aerobic exercise using the recumbent stepper consisted of 20 minutes of exercise at the workload associated with 50-60% of VO$_2$peak. This intensity level matches that recommended from the Canadian Guidelines for Physical Activity for Adults with MS(14).

**Outcome Variables**

**Cardiorespiratory Outcomes:** Volumes of oxygen consumption (VO$_2$, mL/kg/min), carbon dioxide production (VCO$_2$, L/min), ventilation (VE, L/min), and respiratory exchange ratio (RER) were measured continuously by the open-circuit spirometry system and expressed as 1-minute averages during all exercise sessions.

During the HIIT and CON sessions, VO$_2$, VCO$_2$, VE, and RER were recorded every minute, and the highest 30-second averaged values of VO$_2$, VCO$_2$, VE, and RER were recorded.
as $W_{\text{peak}}$, $\text{VO}_{2\text{peak}}$, $\text{VCO}_{2\text{peak}}$, $\text{VE}_{\text{peak}}$, and $\text{RER}_{\text{peak}}$, respectively. Power output data was collected from the recumbent stepper every minute following the warm-up until termination. The highest recorded power achieved was recorded as peak power output ($W_{\text{peak}}$).

**Heart Rate.** Heart rate was measured continuously during all exercise sessions and expressed as 1-minute averages during all sessions using a Polar FT1 heart rate monitor.

**Core Temperature.** All participants were given ingestible and disposable core temperature sensors in capsules (CorTrack II system, HQ Inc., FL, USA) after the baseline session as a measure of core body temperature (CTemp). Participants were asked to swallow one capsule 6-12 hours before each session, and refrain from eating or drinking alcohol or caffeine at least 3 hours prior to each session. The ingestible sensor capsules wirelessly transmitted CTemp ($^\circ$C) to a wireless physiological data recorder while traveling through the digestive tract. CTemp was recorded every minute throughout the HIIT and CON sessions.

**Ratings of Perceived Exertion.** Overall Ratings of Perceived Exertion (RPE) were measured using the Borg RPE scale(27). This scale ranges from 6 to 20, representing no exertion to maximal exertion. RPE data were collected from the participant every minute following the warm-up until termination during CPET and all HIIT and CON sessions.

**Statistical Analyses**

All data were analyzed using SPSS software version 24(IBM corporation, Armonk, NY). The data were assessed for normality violations, outliers, and errors. Significant differences between the HIIT and CON protocols were determined using a repeated-measures, 2-factor analysis of variance (RM ANOVA) with condition (HIIT, CON) and time as within subject factors. The within-session measure (i.e., cardiorespiratory outcomes, heart rate, CTemp, and
RPE) had 30 time-points. Overall effect sizes from the RM ANOVAs were expressed as partial eta-squared. Small, medium, and large effects were interpreted as partial eta-squared values of 0.01, 0.06, and 0.14, respectively(28). Paired samples \( t \)-tests compared the peak and average physiological and perceptual tolerance outcomes between the HIIT and CON conditions. Effect sizes were expressed as Cohen’s \( d \). Small, medium, and large effects were interpreted as Cohen’s \( d \) values of 0.2, 0.5, and 0.8, respectively(29). All statistical tests utilized an alpha level of 0.05(29). According to an \textit{a priori} power analysis(30,31) for a 2×30 repeated measures ANOVA with seven comparisons (VO\(_2\), VCO\(_2\), RER, VE, HR, CTemp, RPE) using reported effect sizes (i.e., ~.55-.65) for detecting a difference between exercise intensities from research on acute physiological and perceptual responses to three varying intensities of exercise in MS(32), a total sample size of 18 participants was needed to detect large effects (1 – \( \beta \)=0.8) with an alpha at 0.05.

**RESULTS**

**Participant Characteristics**

Twenty participants were enrolled in the study. The characteristics of the sample are listed in Table 1. On average, participants were 55.1(7.4) years of age, mostly female (85%), had some college (35%) or were college graduates (30%), and were unemployed (90%). RRMS was the dominant disease type (65%), but progressive MS was represented in the sample (35%). Participants had an average disease duration of 17.2 (10.3) years. The median (IQR) EDSS score was 6.0 (1.0), indicating a sample with ambulatory impairment(33). The sample had a mean aerobic capacity of 14.7 (5.2) ml/kg/min, which is comparable to other samples of person’s MS with mobility disability(i.e., EDSS of 4.0-6.5; (5).
Feasibility & Training Session Compliance

No adverse events occurred during the exercise sessions. Of the 20 participants enrolled in the study, only one participant was unable to complete the HIIT session as prescribed; this participant was unable to meet the wattage prescribed and volitionally discontinued the HIIT session after five interval cycles. This participant’s data were removed from the data analyses. All participants completed the CON sessions as prescribed. The mean prescribed power outputs for the overall sample were 68.3 (25.0) W and 29.6 (13.6) W for the 90% HIIT intervals and CPAG sessions, respectively. The mean power outputs for the 90% HIIT intervals and CPAG conditions were 72.7 (26.7) W and 32.5 (15.1) W, respectively. A paired samples t-test indicated that there was a statistically significant difference in prescribed (~68 W) and actual power output (~73 W) for the 90% HIIT intervals; t(19) = 9.26, p < .001, indicating that participants during the high-intensity intervals were working at a statistically significant higher power than prescribed. A paired samples t-test indicated that there was no significant difference in prescribed (~30 W) and actual power output (~33 W) for the CPAG exercise session; t(19) = -1.54, p = .14, indicating that participants were working within the prescribed power range. The HIIT and CON training session compliance rates were 95% and 100%, respectively. CTemp data were included for only 16 participants due to equipment error and incomplete data.

Power Output

The mean (SD) work rates for the 90% HIIT intervals and CON conditions were 72.7 (26.7) W and 32.5 (15.1) W, respectively. The 2 × 30 repeated measures ANOVA indicated an overall large, statistically significant condition × time interaction on power output, F (29,522) = 79.72, p < .001, ηp^2 = .82. As prescribed, the pattern for HIIT was periodic with
peaks and valleys based on high-intensity and recovery intervals; whereas the pattern for the CON condition was relatively stable (Figure 2, Tables 2-3).

**Cardiorespiratory Outcomes and Heart Rate**

Results for the 19 subjects with complete cardiorespiratory data are presented in Figure 3 and Tables 2-3. The $2 \times 30$ repeated measures ANOVAs for all cardiorespiratory outcomes indicated overall large, statistically significant condition $\times$ time interactions ($p < .001$, $\eta^2_p$ ranged from .44 - .55). The significant interactions were likely due to the pattern of higher VO$_2$, VCO$_2$, RER, VE, and HR for the active exercise during the HIIT session, which was significantly higher, on average, than during the CON session ($p < .05$). Average and peak oxygen consumption during active HIIT exercise were 75.1% (9.1%) and 91.2% (10.9%) of VO$_{2\text{peak}}$, respectively. Average and peak oxygen consumption during active CON exercise were 63.1% (8.2%) and 73.8% (10.5%) of VO$_{2\text{peak}}$, respectively. Average and peak heart rate during active HIIT exercise were 82.9% (5.9%) and 92.6% (5.9%) of HR$_{\text{peak}}$, respectively. Average and peak heart rate during active CON exercise were 78.5% (5.9%) and 81.5% (5.9%) of HR$_{\text{peak}}$, respectively. There were no significant differences between conditions for any of the cardiorespiratory outcomes during the warm-up. VO$_2$ and VCO$_2$ levels converged during the cool-down, whereas RER, VE, and HR levels remained significantly higher during cool-down in the HIIT condition than CON ($p < .05$).

**Core Temperature**

Figure 3F and Tables 2-3 illustrate the acute effects of HIIT and CON NuStep aerobic exercise sessions on CTemp for the 16 participants with complete data. The CTemp receiving
device did not collect complete minute-by-minute data for 3 participants. Thus, we removed these CTemp data from the analyses. The $2 \times 30$ repeated measures ANOVA indicated an overall large, statistically significant condition \times time interaction, $F(29,435) = 2.68$, $p < .001$, $\eta_p^2 = .15$, on CTemp. There was a statistically significant, large, main effect of time, $F(29,522) = 7.85$, $p < .001$, $\eta_p^2 = .34$, on CTemp. The main effect of condition, $F(1,16) = 0.27$, $p = .61$, $\eta_p^2 = .02$, on CTemp was not statistically significant. The significant interaction indicates a differential pattern of CTemp over time in the HIIT versus CON condition. The significant interaction effect likely occurred at minute 16, where CTemp appears to be significantly higher for the HIIT condition than the CON condition. However, upon formal follow-up using a paired samples $t$-test for minute 16, there were no significant differences between conditions; $t(15) = 1.43$, $p = .17$. Over time, CTemps rose from warm-up to cool-down for both the HIIT and CON exercise conditions. On average, CTemp was not significantly different between conditions ($p > .05$). CTemp significantly increased $0.31 \, ^\circ \text{C}$ and $0.53 \, ^\circ \text{C}$ from minute 1 to minute 31 ($p < .05$) during the CON and HIIT exercise sessions, respectively.

**Ratings of Perceived Exertion**

Figure 3G and Tables 2-3 illustrate the acute effects of HIIT and CON NuStep aerobic exercise sessions on RPE for the 19 participants with complete data. The $2 \times 30$ repeated measures ANOVA for the RPE outcome indicated an overall large, statistically significant condition \times time interaction($F(29,522) = 10.03$, $p < .001$, $\eta_p^2 = .36$). Participants rated their perceived exertion as higher during the CON warm-up as compared to the HIIT-warm-up. Perceived exertion oscillated up and down consistently with the high-intensity and recovery intervals during the active exercise of the HIIT session, with a slightly increasing trend of perceived exertion during the exercise session until the cool-down. The interaction effects
evident for perceived exertion are likely due to the HIIT recovery RPE at minutes 6, 8, 10, 18, 20, and 22 and the HIIT high-intensity RPE at minutes 11 and 13. The data did not indicate a significant difference in RPE between conditions during the cool-down.

**DISCUSSION**

The present study examined the feasibility and acute effects of HIIT exercise compared with CON using adaptive equipment on physiological outcomes in persons with MS who have mobility disabilities. The HIIT exercise session was feasible and safe as evidenced by the lack of adverse events and 19 out of 20 participants successfully completing the sessions as prescribed. Given that one participant did not complete the HIIT session as prescribed, a stimulus with decreased interval cycles could still be included in a future intervention, and this modified stimulus might be delivered such that a participant does fewer intervals over time until adaptations permit a full training stimulus. The HIIT exercise session significantly increased the physiological (i.e., W, VO$_2$, VCO$_2$, RER, VE, HR) and perceptual (i.e., RPE) demands of exercise more than the CON session, except in the cases of CTemp where there were no significant differences between conditions. Collectively, the data indicate that even though the HIIT exercise session was more intense and required more overall work, the HIIT exercise session was well tolerated and there were no untoward findings relative to the CON exercise session. Recurrent exposure to appropriately curated acute exercise sessions that yield preferred physiological responses are required to stimulate the desired chronic exercise adaptations. The present results may support the development of an optimal HIIT exercise stimulus for incorporation in a randomized control trial (RCT) for improving overall fitness and physiological conditioning in persons with MS who have mobility disabilities. HIIT using adaptive equipment
might be particularly beneficial for improving fitness and functional capacity in persons with MS who exhibit mobility disabilities and subsequent physiological deconditioning.

As hypothesized, the HIIT condition induced significantly higher and oscillating patterns of physiological and perceived exertion training session data as compared to the relatively stable data from the CON exercise session. On average, participants’ VO$_2$, VCO$_2$, RER, VE, and HR were significantly higher during the HIIT session as compared to the CON session (Table 2, Figure 3A-E). The majority of the physiological outcomes (i.e., VCO$_2$, RER, VE, and HR) during the HIIT session oscillated above those from the CON session during both the high-intensity and recovery intervals. However, the pattern of VO$_2$ in the HIIT session did not follow an oscillating pattern as expected based on previous acute data in stroke patients(34). Perhaps the deconditioned nature of the current participants induced an aerobic response similar to the post-exercise excess oxygen consumption typical at the end of an exercise session(35), causing their oxygen use to stay elevated even during the recovery periods. Perceptually, differential effects by condition for RPE were evident, wherein participants felt that they were exerting themselves more during the high-intensity minutes and less during the recovery minutes in the HIIT session as compared to the corresponding time points during the CON session.

Interestingly, the current data did not support the hypothesis that the HIIT condition would induce significantly higher CTemp data as compared to the CON exercise session. Although a significant condition \times time interaction effect was evident for CTemp, this interaction effect was likely due to minute 16, where the CTemp was higher in the HIIT condition than the CON condition (Figure 3F). The CTemp data indicated significant increases in temperature during the exercise sessions, but temperatures did not differ based on condition. Although some researchers suggest minimizing exercise intensity due to possible decrements in walking
performance or perceived severity of symptoms with increasing temperatures (36–38), the present data are encouraging as they indicate no differential effects on temperature between the varying intensities of the HIIT and CON exercise conditions, which replicates previous research in persons with MS (17). It is important to note that we only had reliable data for 16 participants, which is below the sample size calculated via an *a priori* power analysis. This decrease in data points was due to CTemp receiving device error. Thus, these data suggest that CTemp rises from pre- to post-exercise, regardless of exercise condition, and these increases are safe and tolerable in a sample of persons with MS with mobility disabilities; however, more research is needed to ensure that the CTemp recording device and result is reliable in a larger sample size.

Collectively, these physiological and perceptual tolerance data essentially inform the development of an appropriate exercise prescription for a RCT in persons with MS with mobility disabilities based on the American College of Sport Medicine’s (ACSM) principals of exercise prescription (39,40). This intervention could utilize the current prescribed intensity (i.e., the individualized wattage associated with 90% of VO\textsubscript{2peak}), time (i.e., 20-minutes of active exercise with a 5-minute warm-up and cool-down) and exercise modality type (i.e., aerobic exercise performed on a recumbent stepper). To complete the ACSM’s principles of exercise prescription (39,40), such an intervention might include a frequency of two-to-three times per week, exercise volume of greater than or equal to 500-1000 MET-minutes per week, and a progression in exercise frequency (i.e., increasing the number of days per week of exercise), or intensity (i.e., increasing the prescribed wattage to be associated with 100%-120% of baseline VO\textsubscript{2peak}) over a 12-week period. The current results are particularly intriguing because they suggest that if the effects of this properly curated acute HIIT exercise paradigm are indeed cumulative, persons with MS with mobility disabilities could accrue greater fitness benefits in a
more time-efficient manner following a longitudinal HIIT intervention as compared to traditional aerobic exercise. Indeed, the results from two previous cycling-based HIIT interventions in persons with MS with mild disability indicated significant improvements in peak oxygen consumption(16,20), peak power(16), time-to-exhaustion(16), Type II and Type IIa cross-sectional area(16), lean tissue mass(16), and isometric knee flexion strength(16) over and above those in the continuous aerobic training group in 3-(20) and 12-weeks of time(16).

The current study replicated previous studies identifying acute effects of HIIT on various physiological and outcomes in neurological populations(32,41). Research involving acute HIIT exercise protocols in stroke patients identified training session tolerance ranges between 61%-83% and significant increases in oxygen consumption (range 63.3%-70.9% VO$_{2\text{peak}}$) and heart rate (range 63.1%-76.1% HRR)(41). The present data replicate these results with 95% of participants successfully completing the HIIT protocol as prescribed based on wattage with peak oxygen consumption and heart rate exercise intensities reaching 91.2% (10.9%) VO$_{2\text{peak}}$ and 92.6% (5.9%) HR$_{\text{peak}}$, respectively. In a previous acute research study involving persons with MS with mild disability, protocols involving continuous cycling at 60% of VO$_{2\text{peak}}$ and intermittent cycling at 90% VO$_{2\text{peak}}$ yielded similar increases in tympanic temperature, but higher increases in HR and leg and breathing RPE during the continuous cycling session as compared to the intermittent session(32). The present results replicate and extend these temperature data utilizing more robust CTTemp methods with increases from 37.2 (0.5) °C pre-session to 37.7(0.7) °C post-session in the HIIT condition and increases from 37.2(0.6) °C to 37.5(0.6) °C in the CON condition. However, the current HIIT paradigm yielded significantly higher cardiorespiratory outcomes and heart rate as compared to the CON session, which is the opposite result to this previous acute study in persons with MS(32). This discrepancy may be due to the prescribed
work performed during each session. Total work calculations based on average power output for the two sessions revealed that total work was 1.4 times higher during the HIIT session as compared to the CON session. The previous study indicated that their continuous exercise session was 1.3 times more total work(32). Moreover, the current results extend these data through the addition of more objective cardiorespiratory measures (i.e., VCO₂, RER, and VE) to better conceptualize the physiological nature of an acute HIIT exercise session.

The current research involved several strengths including a within-subjects, randomized and counterbalanced design and the use of a novel approach using adaptive aerobic equipment (i.e., recumbent stepping) for improving fitness in people with MS with mobility disabilities. However, the present study is not without limitations. The HIIT and CON exercise sessions were not designed on a matched-work basis. In order to match work, the CON session needed to be extended in duration, which would have increased the time burden on participants and decreased the ecological validity of such an exercise session. The HIIT and CON sessions were matched on exercise duration in order to meet the current Canadian Physical Activity Guidelines for Adults with MS and to keep the time burden to a minimum. Future research should utilize a matched work design in order to identify if the same amount of work in HIIT and CON sessions would cause similar physiological stress. The sample also included mostly participants with relapsing-remitting MS (65%), but representation from persons with progressive MS was evident (35%). The representation of persons with progressive MS could be improved and would be beneficial to the literature due to the relative dearth of research involving persons with progressive MS(42). Finally, the current data analysis did not control for age, sex, disability status, or aerobic capacity; however, the within-subjects, repeated measures design called for all participants to
serve as their own control. Thus, variability due to individual differences was likely minimized from the error term (43).

Nonetheless, recent evidence suggests that HIIT is safe and efficacious, and perhaps better, at inducing a higher cardiorespiratory response in persons with MS with mild disability(16,17). The current results support the viability and safety of a recumbent stepping-based, HIIT exercise session. These results are exciting because they represent the next step in developing a RCT utilizing HIIT for benefitting physiological and functional outcomes in persons with MS who have mobility disabilities. Future research should implement such a RCT to identify any possible benefits above and beyond the CON for persons with MS who have mobility disabilities.
ACKNOWLEDGEMENTS

The authors would like to acknowledge and thank all participants who contributed to this study.

CONFLICTS OF INTEREST AND SOURCE OF FUNDING

The authors do not have any conflicts of interest. There are no funding sources for the present study. The results of the present study do not constitute endorsement by the ACSM. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.
REFERENCES


18. Roy BA. High-Intensity Interval Training: Efficient, Effective, and a Fun Way to Exercise. 
ACSMs Health Fit J. 2013;17(3):3.

19. Gibala MJ, Little JP, MacDonald MJ, Hawley JA. Physiological adaptations to low-volume, 

exercise improves cognitive performance and reduces matrix metalloproteinases-2 serum 
levels in persons with multiple sclerosis: A randomized controlled trial. Mult Scler J. 2018 
Oct 1;24(12):1635–44.


22. Durstine JL, American College of Sports Medicine, American College of Sports Medicine, 
editors. ACSM’s exercise management for persons with chronic diseases and disabilities. 

23. Stoloff RH, Zehr EP, Ferris DP. Recumbent stepping has similar but simpler neural control 
compared to walking. Exp Brain Res. 2007 Apr 1;178(4):427–38.

24. Haskell W l. Health consequences of physical activity: understanding and challenges 
regarding dose-response. / Consequences sur la sante de l ’ activite physique: 
Comprehension et mise en question de la relation entre la dose et la reponse. Med Sci 


FIGURE DESCRIPTIONS

Figure 1. Acute Exercise Session Protocol Schematics.

Figure 2. Actual power output during the bouts of acute HIIT and CON NuStep-based aerobic exercise in 19 persons with MS.

Figure 3. Acute effects of HIIT and CON NuStep-based aerobic exercise on within-session oxygen consumption (A), carbon dioxide expiration (B), respiratory exchange ratio (C), minute ventilation (D), heart rate (E), core temperature (F), and ratings of perceived exertion (G), including error bars, in 19 persons with MS with mobility disability.
Figure 1

[Diagram showing HIIT and CON training programs with detailed time and wattage breakdowns]
Figure 2

Power Output

---

CON  
HII T

Watts (W)

Time (minutes)
Figure 3

A) Relative Volume of Oxygen Consumption

B) Volume of Carbon Dioxide Expiration

C) Respiratory Exchange Ratio

D) Minute Ventilation

E) Heart Rate

F) Core Temperature (n=16)

G) Ratings of Perceived Exertion

---

CON  HIIT
Table 1. 

*Descriptive characteristics of the sample of persons with MS (N=20).*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.1 (7.4)</td>
</tr>
<tr>
<td>Sex (n, % female)</td>
<td>17 (85%)</td>
</tr>
<tr>
<td>Clinical Disease Course (n, % RRMS)</td>
<td></td>
</tr>
<tr>
<td>RRMS (n, %)</td>
<td>13 (65%)</td>
</tr>
<tr>
<td>Progressive MS (n, %)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Disease Duration (years)</td>
<td>17.2 (10.3)</td>
</tr>
<tr>
<td>EDSS (median, interquartile range)</td>
<td>6.0 (1.0)</td>
</tr>
<tr>
<td>Assistive Device</td>
<td></td>
</tr>
<tr>
<td>None (n, %)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Cane (n, %)</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>Walker (n, %)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>VO$_{2peak}$ (ml/kg/min)</td>
<td>14.7 (5.2)</td>
</tr>
</tbody>
</table>

*Note.* All data are presented as mean (SD) unless otherwise noted (e.g. percentages, median, etc);

RRMS = Relapsing-Remitting Multiple Sclerosis; EDSS = Expanded Disability Status Scale; PDDS = Patient Determined Disease Steps; VO$_{2peak}$ = peak aerobic capacity.
Table 2

Average primary physiological and exercise tolerance outcomes during the HIIT and CON exercise sessions exclusive of warm-up and cool-down in the sample of persons with MS (N = 19).

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIIT</th>
<th>CON</th>
<th>df</th>
<th>t</th>
<th>p</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power (W)</td>
<td>43.9 (13.3)</td>
<td>32.5 (15.1)</td>
<td>18</td>
<td>8.66</td>
<td>&lt;.001</td>
<td>0.82***</td>
</tr>
<tr>
<td>VO(_2) (ml/kg/min)</td>
<td>11.0 (3.6)</td>
<td>9.3 (3.2)</td>
<td>18</td>
<td>8.72</td>
<td>&lt;.001</td>
<td>0.51***</td>
</tr>
<tr>
<td>VCO(_2) (L/min)</td>
<td>0.8 (0.3)</td>
<td>0.7 (0.2)</td>
<td>18</td>
<td>8.40</td>
<td>&lt;.001</td>
<td>0.40***</td>
</tr>
<tr>
<td>RER (units)</td>
<td>1.0 (0.0)</td>
<td>0.9 (0.1)</td>
<td>18</td>
<td>5.26</td>
<td>&lt;.001</td>
<td>1.45***</td>
</tr>
<tr>
<td>VE (L/min)</td>
<td>29.9 (8.8)</td>
<td>24.1 (6.8)</td>
<td>18</td>
<td>7.24</td>
<td>&lt;.001</td>
<td>0.76***</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>112.5 (16.0)</td>
<td>106.5 (15.2)</td>
<td>18</td>
<td>3.46</td>
<td>&lt;.01</td>
<td>0.40**</td>
</tr>
<tr>
<td>CTemp (°C, N=16)</td>
<td>37.4 (0.6)</td>
<td>37.3 (0.6)</td>
<td>15</td>
<td>0.63</td>
<td>.54</td>
<td>0.17</td>
</tr>
<tr>
<td>RPE (units)</td>
<td>10.7 (2.5)</td>
<td>10.8 (3.7)</td>
<td>18</td>
<td>-0.29</td>
<td>.77</td>
<td>-0.03</td>
</tr>
</tbody>
</table>

*Note.* All data are presented as mean (SD) unless otherwise noted (e.g. percentages, median, etc); CTemp data include only 16 persons with MS; * p < .05 (two-tailed); ** p < .01 (two-tailed); *** p < .001 (two-tailed); HIIT = High-Intensity Interval Training; CON = Continuous, steady-state aerobic exercise; VO\(_2\) = oxygen consumption; VCO\(_2\) = carbon dioxide expiration; RER = respiratory exchange ratio; VE = minute ventilation; HR = heart rate; CTemp = core temperature.
Table 3

Peak primary physiological and exercise tolerance outcomes during the HIIT and CON exercise sessions in the sample of persons with MS (N = 19).

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIIT</th>
<th>CON</th>
<th>df</th>
<th>t</th>
<th>p</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power&lt;sub&gt;peak&lt;/sub&gt; (W)</td>
<td>80.2 (30.0)</td>
<td>36.1 (16.3)</td>
<td>18</td>
<td>10.88</td>
<td>&lt;.001</td>
<td>1.88***</td>
</tr>
<tr>
<td>VO&lt;sub&gt;2peak&lt;/sub&gt; (ml/kg/min)</td>
<td>13.4 (4.7)</td>
<td>11.0 (4.2)</td>
<td>18</td>
<td>8.49</td>
<td>&lt;.001</td>
<td>0.55***</td>
</tr>
<tr>
<td>VCO&lt;sub&gt;2peak&lt;/sub&gt; (L/min)</td>
<td>1.0 (0.3)</td>
<td>0.7 (0.2)</td>
<td>18</td>
<td>9.48</td>
<td>&lt;.001</td>
<td>1.21***</td>
</tr>
<tr>
<td>RER&lt;sub&gt;peak&lt;/sub&gt; (units)</td>
<td>1.1 (0.1)</td>
<td>1.0 (0.1)</td>
<td>18</td>
<td>7.00</td>
<td>&lt;.001</td>
<td>1.03***</td>
</tr>
<tr>
<td>VE&lt;sub&gt;peak&lt;/sub&gt; (L/min)</td>
<td>35.6 (13.1)</td>
<td>27.0 (9.2)</td>
<td>18</td>
<td>6.84</td>
<td>&lt;.001</td>
<td>0.78***</td>
</tr>
<tr>
<td>HR&lt;sub&gt;peak&lt;/sub&gt; (bpm)</td>
<td>126.5 (24.0)</td>
<td>110.7 (16.5)</td>
<td>18</td>
<td>5.11</td>
<td>&lt;.001</td>
<td>0.79***</td>
</tr>
<tr>
<td>CTemp&lt;sub&gt;peak&lt;/sub&gt; (°C)</td>
<td>37.9 (0.9)</td>
<td>37.6 (0.6)</td>
<td>15</td>
<td>1.41</td>
<td>.18</td>
<td>0.41</td>
</tr>
<tr>
<td>RPE&lt;sub&gt;peak&lt;/sub&gt; (units)</td>
<td>14.5 (3.5)</td>
<td>12.7 (4.1)</td>
<td>18</td>
<td>2.52</td>
<td>.02</td>
<td>0.49**</td>
</tr>
</tbody>
</table>

*Note.* All data are presented as mean (SD) unless otherwise noted (e.g. percentages, median, etc); CTemp data include only 16 persons with MS; * p < .05 (two-tailed); ** p < .01 (two-tailed); *** p < .001 (two-tailed); HIIT = High-Intensity Interval Training; CON = Continuous, steady-state aerobic exercise; VO<sub>2</sub> = oxygen consumption; VCO<sub>2</sub> = carbon dioxide expiration; RER = respiratory exchange ratio; VE = minute ventilation; HR = heart rate; CTemp = core temperature.