Physiological responses to moderate intensity continuous and high intensity interval exercise in persons with paraplegia

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Structured Abstract

Study Design: Randomized crossover.

Objectives: To test differences in the duration and magnitude of physiological response to isocaloric moderate intensity continuous (MICE) and high intensity interval exercise (HIIE) sessions in persons with spinal cord injury (SCI).

Setting: Academic medical center in Miami, FL, USA.

Methods: Ten adult men (mean±s.d.; 39±10 yr old) with chronic (13.2±8.8 yr) paraplegia (T2-T10) completed a graded exercise test. Then, in a randomized order, participants completed MICE and HIIE for a cost of 120 kcal. MICE was performed at 24.6% PO_{peak}. During HIIE, exercise was completed in 2 min work and recovery phases at 70%:10% PO_{peak}.

Results: MICE and HIIE were isocaloric (115.9±21.8 and 116.6±35.0 kcal, respectively; *P*=.903), but differed in duration (39.8±4.6 vs 32.2 ± 6.2 min; *P*<.001) and average respiratory exchange ratio (RER; 0.90±0.08 vs 1.01±0.07; *P*=.002). During MICE, a workrate of 24.6±6.7% PO_{peak}elicited a $\dot{V}O_2$ of 53.1±6.5% $\dot{V}O_{2peak}$ (10.1±2.2 $ml \cdot kg^{-1} \cdot min^{-1}$). During HIIE, a workrate at 70% PO_{peak} elicited 88.3±6.7% $\dot{V}O_{2peak}$ (16.9±4.2 $ml \cdot kg^{-1} \cdot min^{-1}$), and 29.4±7.7% of the session was spent at or above 80% $\dot{V}O_{2peak}$. During HIIE working phase RER declined from the first to last interval (1.08±0.07 vs 0.98±0.09; *P*<.001), reflecting an initially high but declining glycolytic rate.

Conclusion: Compared to MICE, HIIE imposed a greater physiological stimulus while requiring less time to achieve a target caloric expenditure. Thus exercise intensity might be an important consideration in the tailoring of exercise prescription to address the cardiometabolic comorbidities of SCI.

Introduction

Spinal cord injury (SCI) results in changes in bodily functions that accelerate risk for cardiometabolic disease (CMD) [1]. Specifically, SCI increases risk of cardiometabolic syndrome [2] with a clustering of component risk factors unique to this population [3]. Recently, the Consortium for Spinal Cord Medicine released the first Clinical Practice Guidelines for management of CMD in SCI which recommends ≥ 150 min of exercise per week [1]. Other recently published population-specific guidelines [4] recommend ≥ 30 min of moderate-to-vigorous intensity performed three times per week for cardiometabolic health benefits. However, current guidelines do not provide clear instruction regarding exercise intensity. Guidelines that specifically address the important role of exercise intensity would be extremely valuable, especially given the growing body of evidence demonstrating greater improvements in cardiometabolic health outcomes using high-intensity exercise compared to moderate intensity exercise [5].

High-intensity interval exercise (HIIE) is a method for structuring a session of physical activity that involves alternating the intensity of a task through routine work and recovery cycles [6]. A HIIE workout can be accomplished using any mode of rhythmic/endurance exercise. In the general population, HIIE is usually conducted with physical activities that involve large muscle groups, and heart rate (HR) is commonly used to monitor exercise intensity. However, when greater control is desired, a preferred practice is to use ergometry to prescribe HIIE relative to the peak power output (% PO_{peak}) achieved during a prior graded exercise test (GXT). Precise methods of delivering HIIE are especially important in clinical populations where pathophysiology leads to unique responses to exercise and greater exercise risks [7].

Training with HIIE (i.e., HIIT) has been prescribed for some athletes, to enhance specific adaptations related to their physical performance requirements [8], while moderate intensity continuous exercise (MICE) is recommended for the general health benefits of exercise [9]. However, the benefits of HIIE have now been realized in the context of health [7, 10-12]. Notably, to achieve some specific physiological adaptations, less time is required when using HIIE than MICE [13]. Furthermore, adaptations to HIIE better target the component risks of CMD than MICE [10-12]. While the overwhelming majority of HIIT research involves lower extremity exercise, a recent study in persons without SCI demonstrated that arm cycling HIIT induced superior fitness and performance adaptations compared to training with MICE [14]. In persons with SCI there is limited evidence suggesting superior adaptations to HIIT in SCI [5], and the few HIIT interventions in SCI are limited by small sample size [15, 16] and short training duration [17]. Furthermore, there is little evidence to guide the selection of HIIT protocol in this population. Knowledge about the acute physiological response to HIIE [18-21] in persons with SCI can inform the tailoring of HIIT protocols targeting specific components of physiological function.

There is a unique relationship between PO and oxygen consumption ($\dot{V}O_2$) during arm cycling [22] which contributes to unique physiological response to exercise in persons with SCI [23]. Quantification of exercise intensity based on $\dot{V}O_2$ has limited clinical utility and is hardly a comprehensive physiological parameter for understanding the benefits of HIIE. However, quantifying the $\dot{V}O_2$ response to HIIE allows for comparison of the physiological response between different exercise conditions and between populations. Our previous work shows that a

relatively low % PO_{peak} is required to elicit a target % $\dot{V}O_{2peak}$ compared to persons without SCI performing leg cycling [23]. For example, we previously showed that during arm ergometry 22% and 49% PO_{peak} elicited 46% and 68% $\dot{V}O_{2peak}$, respectively [23]. These data suggest that when prescribing HIIE for persons with SCI, ~70% PO_{peak} working phases will elicit $\dot{V}O_2$ excursions in intensity to the ≥90% $\dot{V}O_{2peak}$ zone. On the contrary, in persons without SCI performing lower body cycling, 95% PO_{peak} elicited a maximal 90.7% $\dot{V}O_{2peak}$ during HIIE with longer 2 min intervals [24], and one minute intervals at 90% PO_{peak} elicited responses as low as 77.3% $\dot{V}O_{2peak}$ during the entire work duration depending on the work-to-recovery ratio [25]. Thus, the delivery of HIIE in SCI is best served by a modest alteration to HIIE whereby workrate is slightly reduced compared to "standard" practice. Indeed, of the two most recent studies of acute physiological response to HIIE in SCI, one study showed that a 1 min working phase at 70% PO_{peak} elicited 86.9% $\dot{V}O_{2peak}$ during the last 15 s of work [18], and the other study showed 1 min working phases at 85% PO_{peak}, with longer recovery phases (60:120 s), elicited 86.7% $\dot{V}O_{2peak}$ during the last 15 s of work [19]. In these studies, HIIE was compared to MICE. One study was not matched for total energy expenditure [18] and the other reported no differences in duration of isocaloric bouts of MICE or HIIE [19]. Therefore, the aim of this study was to examine differences in the duration and magnitude of physiological responses to isocaloric MICE and HIIE in persons with SCI.

Methods

This study was conducted as a component of a randomized repeated measures counter-balanced study that was registered with ClinicalTrials.gov (NCT03545867). The protocol has been published in full [26], with trial enrollment and eligibility testing all conducted in accordance

with Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines [26]. All procedures were in accordance with, and approved by the Human Subjects Research Office, University of Miami Miller School of Medicine.

Participants

Ten adult males with chronic, neurologically-stable thoracic (T1 or lower) non-ambulatory (AIS A-C) SCI participated in this study. Inclusion and exclusion criteria are detailed elsewhere [26]. Descriptive characteristics and basic injury characteristics of the ten men with chronic SCI who completed the trial are presented in Table 1. Participants were of "good" cardiorespiratory fitness (19.2 ± 5.2 ml·kg^{-1}·min^{-1}) based on normative classification [27], but fitness varied within the group. Peak heart rate of 169 ± 16 min^{-1} suggests that injury did not result in disruption of sympathetic nervous system outflow to the heart.

Baseline assessments and HIIE familiarization

Participants attended two preliminary sessions including baseline assessments and a HIIE familiarization session before completing the two experimental conditions. Participants were instructed to refrain from exercise/alcohol/caffeine for 24 h prior to testing and to arrive at the laboratory normally hydrated (500 ml of water within 1 h of testing). During their first visit, participants' cardiorespiratory fitness was assessed via a GXT as previously described [26]. All exercise was conducted on a wall-mounted electronically-braked arm crank ergometer (Angio CPET, Lode B.V., Groningen, Netherlands). The GXT was conducted with 3 min stages where PO increased 20 W·stage^{-1} from a starting PO (10-40 W) estimated to elicit volitional exhaustion. During this and all subsequent arm cycling participants were advised to maintain a

cadence of ~65 rpm but could vary cadence to their liking between 40 to 90 rpm. Data from the last minute of each stage of the GXT were used to generate a PO vs $\dot{V}O_2$ linear regression equation. The data from this individualized equation were used to calculate energy expenditure [28] and thus estimate a PO during MICE that would elicit 50% $\dot{V}O_{2peak}$ for an exercise duration that would result in a total energy expenditure of 120 kcal.

During their second visit, participants completed a HIIE familiarization trial. The aim of our HIIE protocol was to elicit a physiological intensity of >80% $\dot{V}O_{2peak}$ during the working phase, with a peak intensity of ~90% $\dot{V}O_{2peak}$. The cycle ergometer was programmed to vary power output so that a warm-up and cool-down (2 min each) and the recovery phases were completed at 10% PO_{peak}, and the working phases completed at 70% PO_{peak}. The warm and cool down duration were purposefully short to reduce the contribution of these components of HIIE to the total exercise energy expenditure during HIIE, thus improving accuracy of using HIIE familiarization to estimate HIIE energy expenditure. The work and recovery phases were 2 min each. Our HIIE protocol (70:10% PO_{peak} at 2:2 min) was chosen based on previous literature [18, 19] with the intention of maximizing the time spent at/above 80% $\dot{V}O_{2peak}$ (a more detailed rational for choosing this duration is provided in the discussion). During the HIIE familiarization participants completed a warm-up, three work and recovery cycles, and a cool-down. Expired gas data from this trial were used to compute energy expenditure in order to estimate the duration of HIIE required to match the energy cost of MICE.

Experimental exercise trials

A web tool (http://www.randomization.com) was used to ensure trials were performed in a randomized order. Trails were separated by 2 to 10 days. Before exercise trials, participants were asked to abstain from strenuous exercise, caffeine, and alcohol for 24 hr. On the morning of the trials, participants were instructed to consume ~10 $ml \cdot kg^{-1}$ of water and report to the laboratory following an overnight fast (≥ 10 h). Based on the PO-$\dot{V}O_2$ regression equation, participants conducted 39.8 ± 4.6 min of MICE at 26.1 ± 7.3% PO_{peak}. Expired gas was analyzed breath-by-breath continuous during MICE and HIIE trials. HIIE was conducted in the same manner as in the HIIE familiarization trial for a duration that would elicit a total energy expenditure of 120 kcal. Calculations from the HIIE familiarization trial determined that 32.2 ± 6.2 min of HIIE (5 to 9 intervals) would be required to expend 120 kcal.

Data analysis

Expired gas data were recorded breath-by-breath and then averaged offline into 20 s windows. For HIIE, data are an average of the entire session or are an average of the last minute of the work and recovery cycles (e.g., Table 2). For the calculation of energy expenditure the appropriate stoichiometric equations [28] were applied to indirect calorimetry data. These updated equations were calibrated for high-intensity exercise where an estimated 80% of carbohydrate oxidation is attributed to intramuscular glycogen stores [28].

Statistical analysis

Statistical analysis was conducted using IBM's SPSS (v25, Chicago, IL, USA). To assess reliability of the physiological response to HIIE, intraclass correlation coefficients (ICCs; 2-way rand effect, absolute agreement [29]) and Pearson correlation coefficients were computed

comparing the HIIE familiarization and the first 3 intervals of HIIE. Because participants completed HIIE to a calorie target based, the number of intervals each participant completed was different and based on their HIIE familiarization. The differential number of intervals completed by each participant confounded the use of a repeated measures analysis of variance, and thus paired *t* tests were used to compare differences in the means between exercise conditions. Normality of distribution was checked via Shapiro-Wilks test, and data was normally distributed (average P=.505 for all comparisons reported in Table 2). For HIIE, a paired *t* test was also used to compare the first interval to the last interval. Statistical significance was set at an alpha level of $P \leq 0.05$.

Results

All participants completed all assessment and exercise sessions as required. No sessions were aborted due to exhaustion, and no adverse events were reported.

The PO-$\dot{V}O_2$ relationship calculated from the GXT was:

$$\dot{V}O_{2peak} = 9.593 \cdot PO_{peak} + 465.093$$

$$\%\dot{V}O_{2peak} = 0.726 \cdot \%PO_{peak} + 34.782$$

Correlation for the PO-$\dot{V}O_2$ and %PO-%$\dot{V}O_2$ relationships were strong (R^2 = 0.899 and 0.901, respectively). When comparing the HIIE familiarization session to the beginning of the HIIE session, the test-retest reliability of $\dot{V}O_2$ was acceptable based on ICC (mean = 0.797, range = 0.556 – 0.942) and Pearson correlation (R = 0.864).

Metabolic and Cardiovascular Response to Exercise

Physiological responses to exercise are presented in Table 2. The total caloric cost of exercise was similar between MICE and HIIE, (115.9 ± 21.8 vs 116.6 ± 35.0 kcal; *P*=.90) although MICE required more time than HIIE to reach this target (39.8 ± 4.6 vs 32.2 ± 6.2 min; *P*<.001). When averaging over the entire MICE or HIIE sessions, the relative intensity for HR (62.3 ± 7.0% vs 73.3 ± 7.7% HR_{peak}; *P*=.009) and $\dot{V}O_2$ (53.0 ± 6.6% vs 66.1 ± 5.2% $\dot{V}O_{2peak}$; *P*<.001), respiratory exchange ratio (RER; 0.90 ± 0.08 vs 1.01 ± 0.07; *P*=.002), and rate of energy expenditure (2.90 ± 0.44 vs 3.60 ± 0.66 kcal·min^{-1}; *P*=.001) were all lower in MICE than HIIE. During MICE, a 24.6 ± 6.7% PO_{peak} elicited a $\dot{V}O_2$ of 53.1 ± 6.5% $\dot{V}O_{2peak}$ (10.1 ± 2.2 ml·kg^{-1}·min^{-1}).

Figure 1 shows the time course of $\dot{V}O_2$, HR, and RER during MICE and HIIE in a representative individual. This participant's response demonstrates the steady-state physiological response during MICE. Furthermore, Figure 1 demonstrates the peaks and valleys during HIIE that correspond with working and recovery phases. The fluctuations in this representative individual were typical of the group (Figure 2 and Table 2). As a group, 70% PO_{peak} work cycle elicited a $\dot{V}O_2$ of 88.3 ± 6.7% $\dot{V}O_{2peak}$ (16.9 ± 4.2 ml·kg^{-1}·min^{-1}) during the last one minute of each interval. $\dot{V}O_2$ recovered to 49.2 ± 6.8% $\dot{V}O_{2peak}$ (9.3 ± 2.2 ml·kg^{-1}·min^{-1}), also as an average of the final minute of all recovery cycles. A total of 29.4 ± 7.7% and 33.4±25.9% of the session time was spent at or above 80% $\dot{V}O_{2peak}$ and HR_{peak}, respectively.

Figure 2 shows the change in $\dot{V}O_2$, HR, and RER from the first to last interval. The peak working phase $\dot{V}O_2$ and HR observed in any 20 s time window during HIIE occurred during the last interval. The last interval elicited higher $\dot{V}O_2$ than the first interval (Figure 2A; 18.7 ± 4.9 vs

16.2 ± 4.1 $ml \cdot kg^{-1} \cdot min^{-1}$; $P \leq .001$). Furthermore, RER during work and recovery phases was lower in the last interval compared to the first (Figure 2C).

Discussion

This study provides first evidence that when structured as described, HIIE requires less time than MICE to achieve a target energy cost in persons with SCI. In order to achieve a time-efficient and attainable session, we delivered HIIE with 2 min work and recovery phases and modestly reduced workrate (70%:10% PO_{peak}) compared to "standard" practice with leg cycling in persons without SCI (e.g., [6, 24, 25]).

The results from our graded exercise test showed that when persons with paraplegia are conducting arm cycle exercise, an increase in power by 1 W causes an increase in $\dot{V}O_2$ of 9.59±1.53 $ml \cdot min^{-1}$. Smith et al. showed that the PO-$\dot{V}O_2$ relationship during arm cycling in persons without SCI was 16.2 $ml \cdot min^{-1} \cdot W^{-1}$ [22]. The difference in these findings can be partially accounted for by differences in body mass, with participants in the current study (75.0 kg) being substantially lighter than in Smith (84.7 kg). However, after normalization of the PO-$\dot{V}O_2$ relationship to mass there is still a 39.7% difference between our findings and those of Smith et al. [22]. This difference indirectly suggests that persons with SCI are more efficient during arm cycling; corroborating our previous findings [23]. If this is true, the increased ACE efficiency is likely due to differences in arm cycling technique and/or adaptations to upper body musculature that occurs due to habitual use of upper extremities in ways uncommon in the general population.

Authoritative exercise guidelines for persons without disability state that HIIE work phases should elicit intensities between 64% to >100% $\dot{V}O_{2peak}$ [10], with health adaptation optimized by intensities >90% $\dot{V}O_{2peak}$ [6]. The HIIE protocol employed in this study achieved $\dot{V}O_2$ excursions into this target intensity zone. However, the clinical utility of $\dot{V}O_2$ measurement is limited [7], and exercise intensity during HIIE is commonly expressed as a percent of peak heart rate or percent heart rate reserve (%HRR) [11]. The HR response in the current study showed dynamic response to HIIE, with 10.5±8.6 min of the HIIE session spent above 80% HR_{peak}. Figure 1 allows for comparison of the $\dot{V}O_2$ and HR responses during HIIE from a representative individual (Participant 03 in Table 1). This participant was chosen as the representative because their characteristics are representative of the SCI community at large: they are an obese (BMI = 28.2 $kg \cdot m^{-2}$) [1] middle-aged man of "average" fitness [27]. Figure 1A and 1B show a tight coupling between $\dot{V}O_2$ and HR, with a greater dynamic fluctuation in $\dot{V}O_2$, corresponded with HIIE work and recovery phases. MICE elicited a steady state response without evidence of $\dot{V}O_2$ drift, as observed by others [30]. Figure 1A and 1B also demonstrates the gradual increase in the highest physiological response during consecutive HIIE working phases. This "treppe" phenomenon was a common feature during HIIE (Figure 2). Notable in the representative participant's response is that $\dot{V}O_2$ and HR both exceeded peak values achieved during GXT. This phenomenon was also common, with the highest $\dot{V}O_2$ and HR (observed in a 20 s window) throughout the HIIE sessions being 97.3 ± 8.8% $\dot{V}O_{2peak}$ and 91.4±9.0% HR_{peak}, respectively (Figure 2A). It should be noted that the variability in the HR response was greater than that of the $\dot{V}O_2$ response. In certain clinical populations an atypical HR response to exercise can confound the use of HR as a proxy to quantify exercise intensity [7]. Changes in left ventricular

global function [31] and the unique $\dot{V}O_2$-HR relationship during arm cycling [32] could have contributed to the greater variability of HR response to HIIE in SCI.

One of the primary benefits of HIIE is that a reduced time commitment is required to achieve a given physiological response [13]. Of the HIIE [18, 19] and sprint interval exercise (SIE; 105% to 115% PO_{peak}) [18-21] studies in SCI, ours is the first to demonstrate a reduced exercise duration required to achieve a target energy expenditure. But it is important to remember that high intensity exercise training elicits superior adaptations to moderate intensity despite substantial differences in the total work, and thus energy expenditure, completed in individual exercise sessions [13]. Thus the comparison of energy expenditure from HIIE and MICE likely overlooks the totality of the potential benefits of HIIE. Indeed, glycogen cycling and disruptions in cellular homeostasis are important considerations for the benefits of high intensity exercise [33]. These metabolic responses contribute to the energetic requirements of recovery from exercise, measured as excess post-exercise oxygen consumption (EPOC), in a manner dependent on exercise intensity [34] which might be increased in HIIE in SCI. Thus energy cost, like $\dot{V}O_2$, should be considered a useful but incomplete measurement of the physiological intensity of exercise, and other metabolic parameters should be taken into account when considering HIIE programming. Accordingly, our HIIE protocol was guided by knowledge of the heavy reliance on carbohydrates during exercise in persons with SCI [23]. Due to this heavy reliance on carbohydrates, we anticipated that a "long" [6] recovery phase would facilitate the clearance of metabolic byproducts produced during the working phase; mitigating accumulation throughout each successive interval. Examination of Figure 1C shows the coupling of RER with working and recovery phase. Furthermore, the highest RER seen during a 20 s window decreased from

303 the first to last bout (Figure 2C). This dynamic fluctuation during HIIE is common in lower
304 extremity HIIE [35], and reflects a metabolic shift likely reflective of some degree of relative
305 muscle glycogen depletion that is characteristic of HIIE [33]. The total energy expenditure in our
306 HIIE protocol is below what would likely result in relative glycogen depletion during leg
307 exercise in persons without disability. However, the arms are substantially more reliant than the
308 legs on anaerobic metabolism during exercise [36], and relatively "short" (30 min) high intensity
309 arm exercise has been shown to decrease glycogen concentrations of the triceps and deltoid
310 muscles by 83.4 and 28.0%, respectively [37]. Furthermore, training status has been shown to
311 have little effect on the high reliance on anaerobic metabolism during arm exercise [38], thus the
312 participants in our study likely experienced some degree of relative glycogen depletion. This
313 metabolic challenge, and the accompanying disruption to cellular homeostasis within skeletal
314 muscle that comes with high intensity exercise, likely has persistent metabolic effects long into
315 the post-exercise recovery period that emphasize glucose uptake and storage and fat oxidation.
316 Thus shifts in RER seen in HIIE but not MICE are reflective of physiological responses to HIIE
317 that likely confer benefits beyond the mere caloric time-efficiency of HIIE. In persons without
318 SCI adaptations to chronic HIIE training have been shown to improve the ability to use fat
319 during exercise in a variety of context [35], and if similar adaptations to HIIT interventions are
320 shown in SCI then this exercise strategy could be a promising strategy for targeting
321 cardiometabolic risks in this population [3].
322
323 Our study is subject to a number of limitations. Most importantly, we did not directly compare
324 different HIIE protocols in order to determine differences in the physiological response to
325 different HIIE paradigms. Thus, this study does not allow for conclusions to be drawn about the

optimal HIIE protocol for a target physiological response. There are limitations to using indirect calorimetry to calculate energy expenditure during exercise dominated by anaerobic metabolism [39], and some of the assumptions of the stoichiometry equations [28] were violated during certain parts of HIIE. Furthermore, matching the calorie cost of HIIE and MICE placed artificial constraints on the potential benefits of MICE. It can be argued that MICE has a greater potential capacity for energy expenditure because a greater exercise duration is possible due to the steady-state nature whereas fatigue during HIIE likely limits the capacity for total calorie cost due to exhaustion. However, it should be noted that the exercise intensity used in our study (53% $\dot{V}O_{2peak}$) was similar to other HIIE publications in SCI [19] making our data comparable to existing literature. Furthermore, long duration MICE could be considered undesirable due to the time commitment and mundane nature of the task. With respect to our population, while the participants in this study had a wide range of physical characteristics and fitness levels (Table 1), 50% of our sample had above-average cardiorespiratory fitness. Thus the results of our study may be less applicable to persons with SCI who are at the lower end of the cardiorespiratory fitness spectrum [27]. Finally, while autonomic function was not directly tested, our data (Table 1) showed that our participants had retained cardioacceleratory capacity and thus are not likely experiencing the full extent of autonomic impairment that occurs with higher level SCI. Therefore the results of this study cannot necessarily be applied to persons with higher level injuries that result in paralysis of muscles involved in arm cycling along with stark autonomic impairments that predispose an early onset of fatigue due to cardiovascular and neuroendocrine limitations.

Our study is the first to demonstrate in SCI that, when appropriately adjusted, HIIE requires less time to elicit a target calorie expenditure compared to MICE. Furthermore, fluctuations in RER

during HIIE, but not MICE, demonstrate differences in substrate partitioning between the two exercise protocols. In order to deliver this sufficiently intense and time-efficient HIIE session in SCI we used 2 min work and recovery phases prescribed at a workrate (70%:10% PO_{peak}) relatively lower than would be used in persons without disability completing leg cycling. Future studies should determine if differences in the acute physiological response to MICE and HIIE lead to differential adaptations to training interventions using these exercises to target health and fitness.

Data Archiving

The dataset generated from the current study is available from the corresponding author on reasonable request.

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Statement of Ethics

We certify that all applicable institutional and governmental regulation concerning the ethical use of human volunteers were following during the course of this research.

Conflicts of Interest

The authors have no conflicts to declare.

Author Contributions

DWM contributed to study design, data collection, data organization/analysis, and writing of the manuscript; JLM contributed to study design, data collection, and writing of the manuscript; KAJ contributed to data analysis and writing of the manuscript; MSN contributed to study design and writing of the manuscript; JLJB contributed to study design and writing of the manuscript.

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Figure Legends

Table 1: AIS=American Spinal Injury Association Impairment Scale, HR=heart rate, $\dot{V}O_2$=rate of oxygen consumption, PO=power output, RER=respiratory exchange ratio, CRF=cardiorespiratory fitness.

Table 2: Statistical results are a comparison of MICE to the average of the entire HIIE session: a=P<.001,b=.001,c=.002. Work and recovery phase HIIE data are based on the last full minute of their respective phase. HIIE=high intensity interval exercise, MICE=moderate intensity continuous exercise, HR=hear rate, $\dot{V}O_2$=rate of oxygen consumption, RER=respiratory exchange ratio.

Figure 1: A representative individual's physiological response throughout the time course of both exercise conditions. HIIE=high intensity interval exercise, MICE=moderate intensity continuous exercise, $\dot{V}O_2$=rate of oxygen consumption, HR=heart rate, RER=respiratory exchange ratio. For the HIIE condition, the grey vertical bars in the plot area represent 2 min work phases (70 $\%PO_{peak}$) and the white spaces between denote 2 min recovery phases (70 $\%PO_{peak}$). For this individual MICE was conducted at 24.2 $\%PO_{peak}$.

Figure 2: Data are the highest value in a 20 s window during the first and last interval completed during high intensity interval exercise. $\dot{V}O_2$=rate of oxygen consumption, HR=heart rate, RER=respiratory exchange ratio.

References

1. Nash MS, Groah SL, Gater DR, Jr., Dyson-Hudson TA, Lieberman JA, Myers J, et al. Identification and Management of Cardiometabolic Risk after Spinal Cord Injury: Clinical Practice Guideline for Health Care Providers. Top Spinal Cord Inj Rehabil. 2018;24(4):379-423.

2. de Groot S, Adriaansen JJ, Tepper M, Snoek GJ, van der Woude LHV, Post MWM. Metabolic syndrome in people with a long-standing spinal cord injury: associations with physical activity and capacity. Appl Physiol Nutr Me. 2016;41(11):1190-6.

3. Libin A, Tinsley EA, Nash MS, Mendez AJ, Burns P, Elrod M, et al. Cardiometabolic risk clustering in spinal cord injury: results of exploratory factor analysis. Top Spinal Cord Inj Rehabil. 2013;19(3):183-94.

4. Martin Ginis KA, van der Scheer JW, Latimer-Cheung AE, Barrow A, Bourne C, Carruthers P, et al. Evidence-based scientific exercise guidelines for adults with spinal cord injury: an update and a new guideline. Spinal Cord. 2018;56(4):308-21.

5. Nightingale TE, Metcalfe RS, Vollaard NB, Bilzon JL. Exercise Guidelines to Promote Cardiometabolic Health in Spinal Cord Injured Humans: Time to Raise the Intensity? Arch Phys Med Rehabil. 2017;98(8):1693-704.

6. Buchheit M, Laursen PB. High-Intensity Interval Training, Solutions to the Programming Puzzle. Sports Med. 2013;43(10):927-54.

7. Nash MS, Groah SL, Gater DR, Dyson-Hudson TA, Lieberman JA, Myers J, et al. Identification and Management of Cardiometabolic Risk after Spinal Cord Injury: Clinical Practice Guideline for Health Care Providers. J Spinal Cord Med. 2019:1-35.

8. Billat LV. Interval training for performance: A scientific and empirical practice - Special recommendations for middle- and long-distance running, part I: Aerobic interval training. Sports Med. 2001;31(1):13-31.

9. Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, et al. Physical-Activity and Public-Health - a Recommendation from the Centers-for-Disease-Control-and-Prevention and the American-College-of-Sports-Medicine. Jama-J Am Med Assoc. 1995;273(5):402-7.

10. Campbell WW, Kraus WE, Powell KE, Haskell WL, Janz KF, Jakicic JM, et al. High-Intensity Interval Training for Cardiometabolic Disease Prevention. Med Sci Sports Exerc. 2019;51(6):1220-6.

11. Batacan RB, Jr., Duncan MJ, Dalbo VJ, Tucker PS, Fenning AS. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. Br J Sports Med. 2017;51(6):494-503.

12. Weston KS, Wisloff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. Brit J Sport Med. 2014;48(16):1227-U52.

13. Burgomaster KA, Howarth KR, Phillips SM, Rakobowchuk M, MacDonald MJ, Mcgee SL, et al. Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. J Physiol-London. 2008;586(1):151-60.

14. Schoenmakers P, Reed K, Van Der Woude L, Hettinga FJ. High Intensity Interval Training in Handcycling: The Effects of a 7 Week Training Intervention in Able-bodied Men. Frontiers in physiology. 2016;7:638.

15. Harnish CR, Daniels JA, Caruso D. Training response to high-intensity interval training in a 42-year-old man with chronic spinal cord injury. The journal of spinal cord medicine. 2017;40(2):246-9.

16. de Groot PC, Hjeltnes N, Heijboer AC, Stal W, Birkeland K. Effect of training intensity on physical capacity, lipid profile and insulin sensitivity in early rehabilitation of spinal cord injured individuals. Spinal Cord. 2003;41(12):673-9.

17. Harnish C, Sabo R, Daniels J, Caruso D. The effects of two weeks of arm crank sprint interval training in men with chronic spinal cord injury. Int J Sports Exerc Med. 2017;3:56-9.

18. Astorino TA, Thum JS. Within-session responses to high-intensity interval training in spinal cord injury. Disabil Rehabil. 2018;40(4):444-9.

19. Astorino TA. Hemodynamic and cardiorespiratory responses to various arm cycling regimens in men with spinal cord injury. Spinal Cord Series and Cases. 2019;5:8.

20. Graham K, Yarar-Fisher C, Li J, McCully KM, Rimmer JH, Powell D, et al. Effects of High-Intensity Interval Training Versus Moderate-Intensity Training on Cardiometabolic Health Markers in Individuals With Spinal Cord Injury: A Pilot Study. Top Spinal Cord Inj Rehabil. 2019;25(3):248-59.

21. McLeod JC, Diana H, Hicks AL. Sprint interval training versus moderate-intensity continuous training during inpatient rehabilitation after spinal cord injury: a randomized trial. Spinal Cord. 2020;58(1):106-15.

22. Smith PM, Amaral I, Doherty M, Price M, Jones A. The Influence of Ramp Rate on V· O2peak and "Excess" V· O2 during Arm Crank Ergometry. International journal of sports medicine. 2006;27(08):610-6.

23. Jacobs KA, Burns P, Kressler J, Nash MS. Heavy reliance on carbohydrate across a wide range of exercise intensities during voluntary arm ergometry in persons with paraplegia. J Spinal Cord Med. 2013;36(5):427-35.

24. Zafeiridis A, Kounoupis A, Dipla K, Kyparos A, Nikolaidis MG, Smilios I, et al. Oxygen Delivery and Muscle Deoxygenation during Continuous, Long- and Short-Interval Exercise. Int J Sports Med. 2015;36(11):872-80.

25. Gosselin LE, Kozlowski KF, DeVinney-Boymel L, Hambridge C. Metabolic response of different high-intensity aerobic interval exercise protocols. J Strength Cond Res. 2012;26(10):2866-71.

26. McMillan DW, Maher JL, Jacobs KA, Mendez AJ, Nash MS, Bilzon JLJ. Influence of upper-body continuous, resistance or high-intensity interval training (CRIT) on postprandial

responses in persons with spinal cord injury: study protocol for a randomised controlled trial. Trials. 2019;20(1).

27. Simmons OL, Kressler J, Nash MS. Reference Fitness Values in the Untrained Spinal Cord Injury Population. Arch Phys Med Rehab. 2014;95(12):2272-8.

28. Jeukendrup AE, Wallis GA. Measurement of substrate oxidation during exercise by means of gas exchange measurements. Int J Sports Med. 2005;26 Suppl 1:S28-37.

29. Koo TK, Li MYJJocm. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. 2016;15(2):155-63.

30. Horiuchi M, Fukuoka Y. Absence of cardiovascular drift during prolonged arm-crank exercise in individuals with spinal cord injury. Spinal Cord. 2019;57(11):942-52.

31. Currie KD, West CR, Krassioukov AV. Differences in Left Ventricular Global Function and Mechanics in Paralympic Athletes with Cervical and Thoracic Spinal Cord Injuries. Frontiers in physiology. 2016;7:110.

32. Vokac Z, Bell H, Bautz-Holter E, Rodahl K. Oxygen uptake/heart rate relationship in leg and arm exercise, sitting and standing. J Appl Physiol. 1975;39(1):54-9.

33. Scribbans TD, Edgett BA, Vorobej K, Mitchell AS, Joanisse SD, Matusiak JB, et al. Fibre-specific responses to endurance and low volume high intensity interval training: striking similarities in acute and chronic adaptation. PloS one. 2014;9(6):e98119.

34. Børsheim E, Bahr RJSm. Effect of exercise intensity, duration and mode on post-exercise oxygen consumption. 2003;33(14):1037-60.

35. Hetlelid KJ, Plews DJ, Herold E, Laursen PB, Seiler S. Rethinking the role of fat oxidation: substrate utilisation during high-intensity interval training in well-trained and recreationally trained runners. BMJ open sport & exercise medicine. 2015;1(1):e000047.

36. Ahlborg G, Jensen-Urstad M. Metabolism in exercising arm vs. leg muscle. Clinical physiology. 1991;11(5):459-68.

37. Kiilerich K, Birk JB, Damsgaard R, Wojtaszewski JF, Pilegaard H. Regulation of PDH in human arm and leg muscles at rest and during intense exercise. American Journal of Physiology-Endocrinology and Metabolism. 2008;294(1):E36-E42.

38. Jensen□Urstad M, Ahlborg G. Is the high lactate release during arm exercise due to a low training status? Clinical physiology. 1992;12(4):487-96.

39. Scott CB, Leighton BH, Ahearn KJ, McManus JJ. Aerobic, anaerobic, and excess postexercise oxygen consumption energy expenditure of muscular endurance and strength: 1-set of bench press to muscular fatigue. J Strength Cond Res. 2011;25(4):903-8.

Figure 1. Representative physiological responses to moderate intensity continuous exercise (MICE) and high intensity interval exercise HIIE)

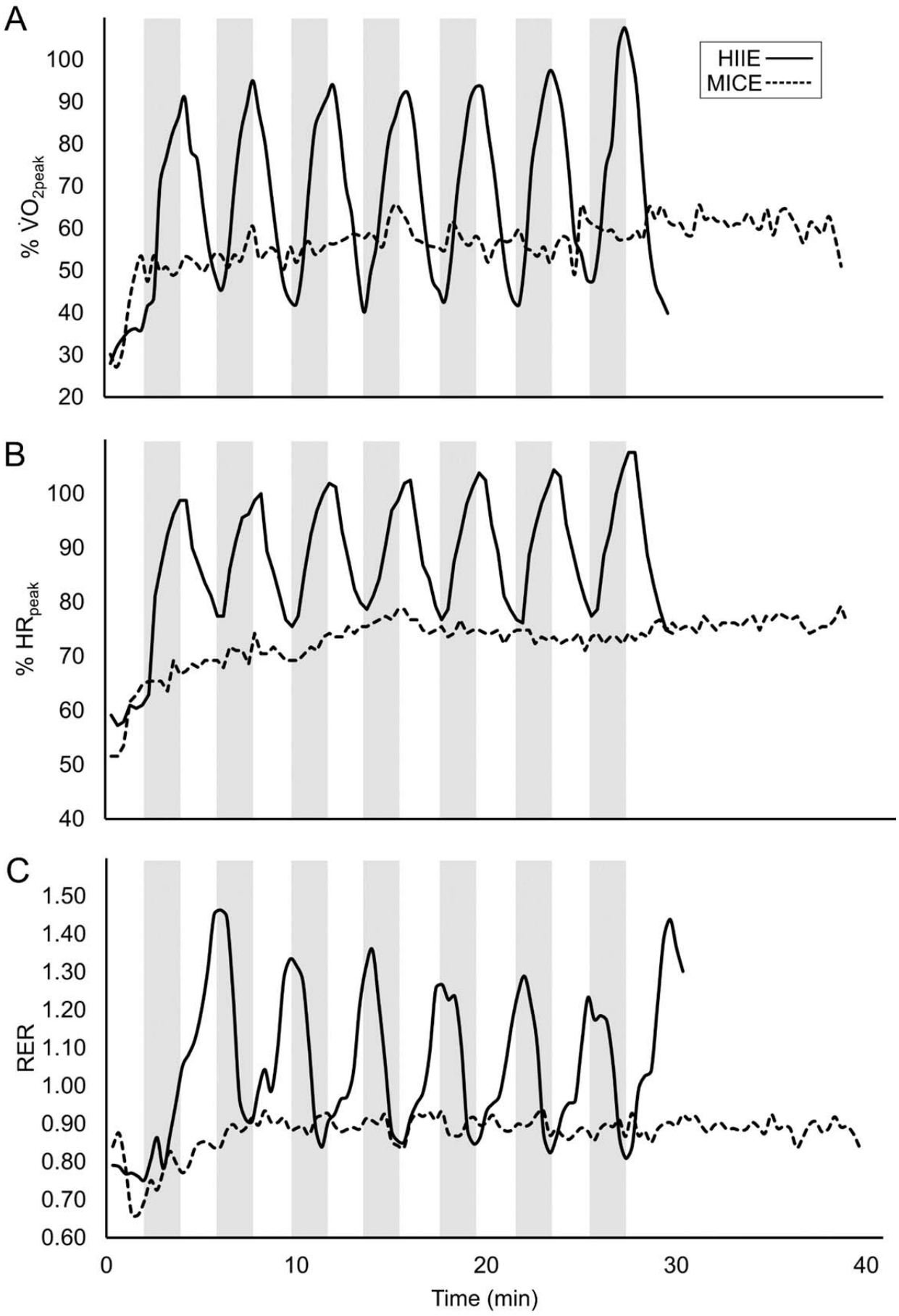

Figure 2. Peak physiological responses to first and last intervals during high intensity interval exercise

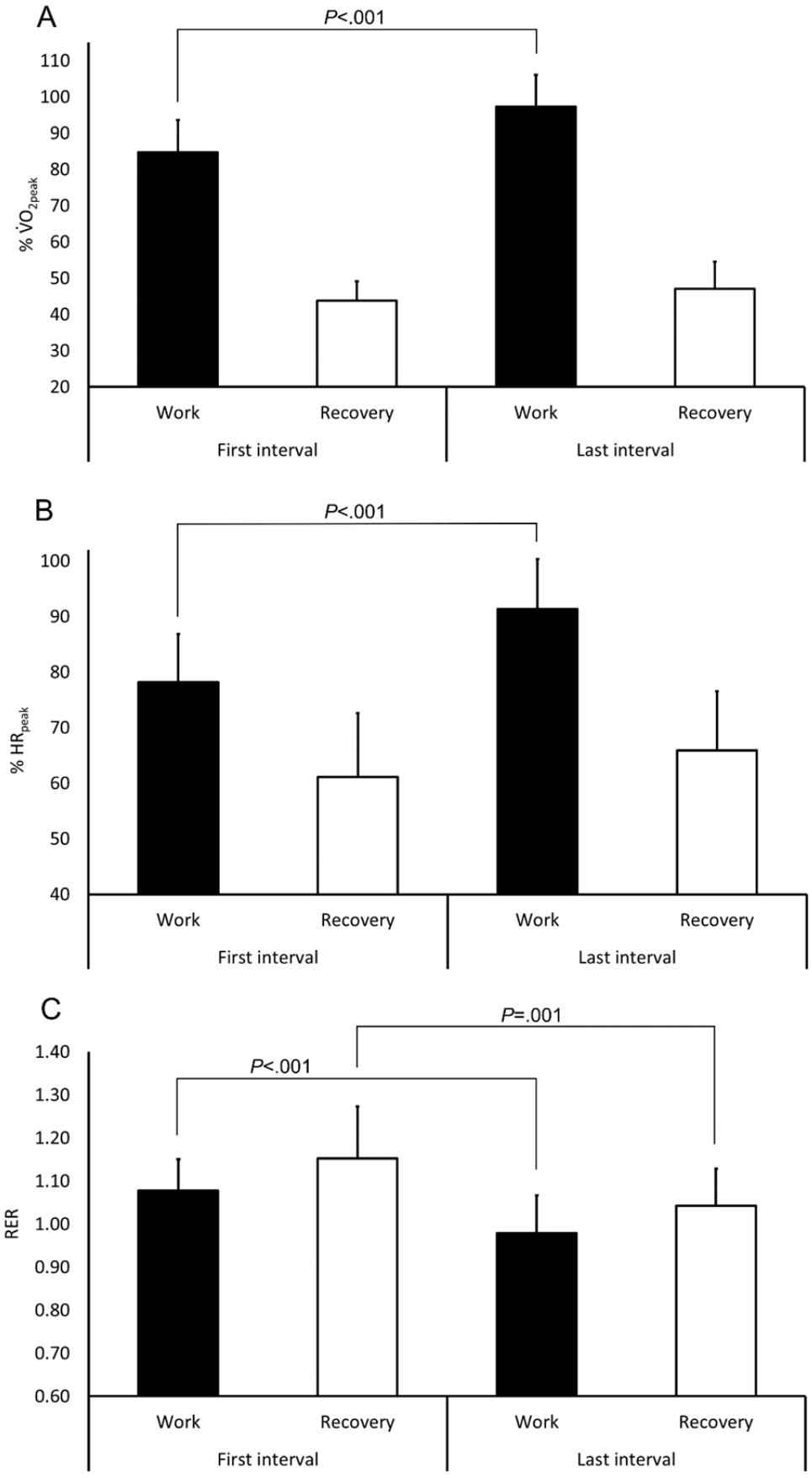

Table 1. Participant descriptive, injury, and physical fitness characteristics.

	Habitus			*Injury*			*Peak Response to GXT*				
	Age (yr)	Height (m)	Body Mass (kg)	Duration (yr)	Level of Injury	AIS	HR_{peak} (min^{-1})	$\dot{V}O_{2peak}$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	PO_{peak} (W)	RER_{peak} a.u.	CRF Classification [27]
01	28	1.68	72.6	10	T2	A	160	18.0	105	1.03	Good
02	45	1.73	78.4	16	T6	A	172	17.5	95	1.13	Good
03	37	1.88	99.5	19	T4	A	181	16.2	131	1.24	Average
04	28	1.70	51.2	8	T6	A	180	21.1	90	1.39	Good
05	51	1.65	65.6	8	T10	A	159	23.4	122	1.17	Excellent
06	32	1.83	67.6	15	T3	A	188	31.8	164	1.11	Excellent
07	35	1.78	80.8	3	T4	B	165	16.5	99	1.30	Average
08	38	1.74	106.5	13	T6	C	171	12.8	97	1.13	Fair
09	57	1.70	64.9	34	T8	B	182	17.2	81	1.08	Average
10	38	1.73	62.5	6	T9	A	134	17.7	95	1.49	Average
X±SD	39±10	1.74±0.07	75.0±17.0	13.2±8.8	N/A	N/A	169±16	19.2±5.2	108±25	1.21±0.15	N/A

Table 2. Acute physiological response to moderate intensity continuous exercise (MICE) and high intensity interval exercise (HIIE).

		Duration (min)	HR (min^{-1})	$\dot{V}O_2$ ($ml \cdot kg^{-1}min^{-1}$)	% $\dot{V}O_{2peak}$	RER	Energy Expenditure ($kcal \cdot min^{-1}$)	Energy Expenditure (kcal)
MICE	average	39.8±4.6	105±12	10.1±2.2	53.0±6.6	0.90±0.08	2.90±0.44	115.9±21.8
HIIE	average	32.2±6.2[a]	124±17[a]	12.6±3.1[b]	66.1±5.2[b]	1.01±0.07[c]	3.60±0.66[b]	116.6±35.0
	work	15.2±3.2	146±19	16.9±4.2	88.3±6.7	0.96±0.07	4.82±0.94	N/A
	recovery	13.2±3.2	115±17	9.3±2.2	49.2±6.8	1.12±0.10	2.60±0.42	N/A