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1   Physiological responses to moderate intensity continuous and high intensity interval exercise in

2   persons with paraplegia

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29 **Structured Abstract**

30 **Study Design**: Randomized crossover.

31 **Objectives**: To test differences in the duration and magnitude of physiological response to

32 isocaloric moderate intensity continuous (MICE) and high intensity interval exercise (HIIE)

33 sessions in persons with spinal cord injury (SCI).

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

35 **Methods**: Ten adult men (mean±s.d.; 39±10 yr old) with chronic (13.2±8.8 yr) paraplegia (T2-

36 T10) completed a graded exercise test. Then, in a randomized order, participants completed

37 MICE and HIIE for a cost of 120 kcal. MICE was performed at 24.6% PO_{peak}. During HIIE,

38 exercise was completed in 2 min work and recovery phases at 70%:10% PO_{peak}.

39 **Results**: MICE and HIIE were isocaloric (115.9±21.8 and 116.6±35.0 kcal, respectively;

40 P=.903), but differed in duration (39.8±4.6 vs 32.2 ± 6.2 min; P<.001) and average respiratory

41 exchange ratio (RER; 0.90±0.08 vs 1.01±0.07; P=.002). During MICE, a workrate of 24.6±6.7%

42 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}). During HIIE, a workrate at

43 70% PO_{peak} elicited 88.3±6.7% $\dot{V}O_{2peak}$ (16.9±4.2 ml·kg^{-1}·min^{-1}), and 29.4±7.7% of the session

44 was spent at or above 80% $\dot{V}O_{2peak}$. During HIIE working phase RER declined from the first to

45 last interval (1.08±0.07 vs 0.98±0.09; P<.001), reflecting an initially high but declining

46 glycolytic rate.

47 **Conclusion**: Compared to MICE, HIIE imposed a greater physiological stimulus while requiring

48 less time to achieve a target caloric expenditure. Thus exercise intensity might be an important

49 consideration in the tailoring of exercise prescription to address the cardiometabolic

50 comorbidities of SCI.

51

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 $\geq$ 150 min of exercise per week [1]. Other recently published population-specific guidelines [4] recommend $\geq$ 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].

3

75

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.

91

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

98   relatively low % PO_{peak} is required to elicit a target % $\dot{V}O_{2peak}$ compared to persons without SCI

99   performing leg cycling [23]. For example, we previously showed that during arm ergometry 22%

100   and 49% PO_{peak} elicited 46% and 68% $\dot{V}O_{2peak}$, respectively [23]. These data suggest that when

101   prescribing HIIE for persons with SCI, ~70% PO_{peak} working phases will elicit $\dot{V}O_2$ excursions

102   in intensity to the $\geq$90% $\dot{V}O_{2peak}$ zone. On the contrary, in persons without SCI performing lower

103   body cycling, 95% PO_{peak} elicited a maximal 90.7% $\dot{V}O_{2peak}$ during HIIE with longer 2 min

104   intervals [24], and one minute intervals at 90% PO_{peak} elicited responses as low as 77.3% $\dot{V}O_{2peak}$

105   during the entire work duration depending on the work-to-recovery ratio [25]. Thus, the delivery

106   of HIIE in SCI is best served by a modest alteration to HIIE whereby workrate is slightly

107   reduced compared to "standard" practice. Indeed, of the two most recent studies of acute

108   physiological response to HIIE in SCI, one study showed that a 1 min working phase at 70%

109   PO_{peak} elicited 86.9% $\dot{V}O_{2peak}$ during the last 15 s of work [18], and the other study showed 1

110   min working phases at 85% PO_{peak}, with longer recovery phases (60:120 s), elicited 86.7%

111   $\dot{V}O_{2peak}$ during the last 15 s of work [19]. In these studies, HIIE was compared to MICE. One

112   study was not matched for total energy expenditure [18] and the other reported no differences in

113   duration of isocaloric bouts of MICE or HIIE [19]. Therefore, the aim of this study was to

114   examine differences in the duration and magnitude of physiological responses to isocaloric

115   MICE and HIIE in persons with SCI.

116

117   **Methods**

118   This study was conducted as a component of a randomized repeated measures counter-balanced

119   study that was registered with ClinicalTrials.gov (NCT03545867). The protocol has been

120   published in full [26], with trial enrollment and eligibility testing all conducted in accordance

121 with Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines

122 [26]. All procedures were in accordance with, and approved by the Human Subjects Research

123 Office, University of Miami Miller School of Medicine.

124

125 *Participants*

126 Ten adult males with chronic, neurologically-stable thoracic (T1 or lower) non-ambulatory (AIS

127 A-C) SCI participated in this study. Inclusion and exclusion criteria are detailed elsewhere [26].

128 Descriptive characteristics and basic injury characteristics of the ten men with chronic SCI who

129 completed the trial are presented in Table 1. Participants were of "good" cardiorespiratory fitness

130 (19.2 ± 5.2 ml·kg^{-1}·min^{-1}) based on normative classification [27], but fitness varied within the

131 group. Peak heart rate of 169 ± 16 min^{-1} suggests that injury did not result in disruption of

132 sympathetic nervous system outflow to the heart.

133

134 *Baseline assessments and HIIE familiarization*

135 Participants attended two preliminary sessions including baseline assessments and a HIIE

136 familiarization session before completing the two experimental conditions. Participants were

137 instructed to refrain from exercise/alcohol/caffeine for 24 h prior to testing and to arrive at the

138 laboratory normally hydrated (500 ml of water within 1 h of testing). During their first visit,

139 participants' cardiorespiratory fitness was assessed via a GXT as previously described [26]. All

140 exercise was conducted on a wall-mounted electronically-braked arm crank ergometer (Angio

141 CPET, Lode B.V., Groningen, Netherlands). The GXT was conducted with 3 min stages where

142 PO increased 20 W·stage^{-1} from a starting PO (10-40 W) estimated to elicit volitional

143 exhaustion. During this and all subsequent arm cycling participants were advised to maintain a

144   cadence of ~65 rpm but could vary cadence to their liking between 40 to 90 rpm. Data from the

145   last minute of each stage of the GXT were used to generate a PO vs $\dot{V}O_2$ linear regression

146   equation. The data from this individualized equation were used to calculate energy expenditure

147   [28] and thus estimate a PO during MICE that would elicit 50% $\dot{V}O_{2peak}$ for an exercise duration

148   that would result in a total energy expenditure of 120 kcal.

149

150   During their second visit, participants completed a HIIE familiarization trial. The aim of our

151   HIIE protocol was to elicit a physiological intensity of >80% $\dot{V}O_{2peak}$ during the working phase,

152   with a peak intensity of ~90% $\dot{V}O_{2peak}$. The cycle ergometer was programmed to vary power

153   output so that a warm-up and cool-down (2 min each) and the recovery phases were completed at

154   10% PO_{peak}, and the working phases completed at 70% PO_{peak}. The warm and cool down

155   duration were purposefully short to reduce the contribution of these components of HIIE to the

156   total exercise energy expenditure during HIIE, thus improving accuracy of using HIIE

157   familiarization to estimate HIIE energy expenditure. The work and recovery phases were 2 min

158   each. Our HIIE protocol (70:10% PO_{peak} at 2:2 min) was chosen based on previous literature [18,

159   19] with the intention of maximizing the time spent at/above 80% $\dot{V}O_{2peak}$ (a more detailed

160   rational for choosing this duration is provided in the discussion). During the HIIE familiarization

161   participants completed a warm-up, three work and recovery cycles, and a cool-down. Expired

162   gas data from this trial were used to compute energy expenditure in order to estimate the duration

163   of HIIE required to match the energy cost of MICE.

164

165   *Experimental exercise trials*

166 A web tool (http://www.randomization.com) was used to ensure trials were performed in a

167 randomized order. Trails were separated by 2 to 10 days. Before exercise trials, participants were

168 asked to abstain from strenuous exercise, caffeine, and alcohol for 24 hr. On the morning of the

169 trials, participants were instructed to consume ~10 ml·kg^{-1} of water and report to the laboratory

170 following an overnight fast ($\geq$ 10 h). Based on the PO-$\dot{V}O_2$ regression equation, participants

171 conducted 39.8 ± 4.6 min of MICE at 26.1 ± 7.3% PO$_{peak}$. Expired gas was analyzed breath-by-

172 breath continuous during MICE and HIIE trials. HIIE was conducted in the same manner as in

173 the HIIE familiarization trial for a duration that would elicit a total energy expenditure of 120

174 kcal. Calculations from the HIIE familiarization trial determined that 32.2 ± 6.2 min of HIIE (5

175 to 9 intervals) would be required to expend 120 kcal.

176

177 *Data analysis*

178 Expired gas data were recorded breath-by-breath and then averaged offline into 20 s windows.

179 For HIIE, data are an average of the entire session or are an average of the last minute of the

180 work and recovery cycles (e.g., Table 2). For the calculation of energy expenditure the

181 appropriate stoichiometric equations [28] were applied to indirect calorimetry data. These

182 updated equations were calibrated for high-intensity exercise where an estimated 80% of

183 carbohydrate oxidation is attributed to intramuscular glycogen stores [28].

184

185 *Statistical analysis*

186 Statistical analysis was conducted using IBM's SPSS (v25, Chicago, IL, USA). To assess

187 reliability of the physiological response to HIIE, intraclass correlation coefficients (ICCs; 2-way

188 rand effect, absolute agreement [29]) and Pearson correlation coefficients were computed

189 comparing the HIIE familiarization and the first 3 intervals of HIIE. Because participants

190 completed HIIE to a calorie target based, the number of intervals each participant completed was

191 different and based on their HIIE familiarization. The differential number of intervals completed

192 by each participant confounded the use of a repeated measures analysis of variance, and thus

193 paired t tests were used to compare differences in the means between exercise conditions.

194 Normality of distribution was checked via Shapiro-Wilks test, and data was normally distributed

195 (average $P=.505$ for all comparisons reported in Table 2). For HIIE, a paired t test was also used

196 to compare the first interval to the last interval. Statistical significance was set at an alpha level

197 of $P \leq 0.05$.

198

199 **Results**

200 All participants completed all assessment and exercise sessions as required. No sessions were

201 aborted due to exhaustion, and no adverse events were reported.

202

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

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

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

206

207 Correlation for the PO-$\dot{V}O_2$ and $\%PO$-$\%\dot{V}O_2$ relationships were strong ($R^2 = 0.899$ and 0.901,

208 respectively). When comparing the HIIE familiarization session to the beginning of the HIIE

209 session, the test-retest reliability of $\dot{V}O_2$ was acceptable based on ICC (mean = 0.797, range =

210 $0.556 - 0.942$) and Pearson correlation ($R = 0.864$).

211

212 *Metabolic and Cardiovascular Response to Exercise*

213 Physiological responses to exercise are presented in Table 2. The total caloric cost of exercise

214 was similar between MICE and HIIE, (115.9 ± 21.8 vs 116.6 ± 35.0 kcal; *P*=.90) although MICE

215 required more time than HIIE to reach this target (39.8 ± 4.6 vs 32.2 ± 6.2 min; *P*<.001). When

216 averaging over the entire MICE or HIIE sessions, the relative intensity for HR (62.3 ± 7.0% vs

217 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

218 exchange ratio (RER; 0.90 ± 0.08 vs 1.01 ± 0.07; *P*=.002), and rate of energy expenditure (2.90

219 ± 0.44 vs 3.60 ± 0.66 $kcal·min^{-1}$; *P*=.001) were all lower in MICE than HIIE. During MICE, a

220 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 $ml·kg^{-1}·min^{-1}$).

221

222 Figure 1 shows the time course of $\dot{V}O_2$, HR, and RER during MICE and HIIE in a representative

223 individual. This participant's response demonstrates the steady-state physiological response

224 during MICE. Furthermore, Figure 1 demonstrates the peaks and valleys during HIIE that

225 correspond with working and recovery phases. The fluctuations in this representative individual

226 were typical of the group (Figure 2 and Table 2). As a group, 70% PO_{peak} work cycle elicited a

227 $\dot{V}O_2$ 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

228 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

229 the final minute of all recovery cycles. A total of 29.4 ± 7.7% and 33.4±25.9% of the session

230 time was spent at or above 80% $\dot{V}O_{2peak}$ and HR_{peak}, respectively.

231

232 Figure 2 shows the change in $\dot{V}O_2$, HR, and RER from the first to last interval. The peak

233 working phase $\dot{V}O_2$ and HR observed in any 20 s time window during HIIE occurred during the

234 last interval. The last interval elicited higher $\dot{V}O_2$ than the first interval (Figure 2A; 18.7 ± 4.9 vs

235   16.2 ± 4.1 ml·kg^{-1}·min^{-1}; $P \leq .001$). Furthermore, RER during work and recovery phases was

236   lower in the last interval compared to the first (Figure 2C).

237

Discussion

239   This study provides first evidence that when structured as described, HIIE requires less time than

240   MICE to achieve a target energy cost in persons with SCI. In order to achieve a time-efficient

241   and attainable session, we delivered HIIE with 2 min work and recovery phases and modestly

242   reduced workrate (70%:10% PO$_{peak}$) compared to "standard" practice with leg cycling in persons

243   without SCI (e.g., [6, 24, 25]).

244

245   The results from our graded exercise test showed that when persons with paraplegia are

246   conducting arm cycle exercise, an increase in power by 1 W causes an increase in $\dot{V}O_2$ of

247   9.59 ± 1.53 ml·min^{-1}. Smith et al. showed that the PO-$\dot{V}O_2$ relationship during arm cycling in

248   persons without SCI was 16.2 ml·min^{-1}·W^{-1} [22]. The difference in these findings can be

249   partially accounted for by differences in body mass, with participants in the current study (75.0

250   kg) being substantially lighter than in Smith (84.7 kg). However, after normalization of the PO-

251   $\dot{V}O_2$ relationship to mass there is still a 39.7% difference between our findings and those of

252   Smith et al. [22]. This difference indirectly suggests that persons with SCI are more efficient

253   during arm cycling; corroborating our previous findings [23]. If this is true, the increased ACE

254   efficiency is likely due to differences in arm cycling technique and/or adaptations to upper body

255   musculature that occurs due to habitual use of upper extremities in ways uncommon in the

256   general population.

257

258 Authoritative exercise guidelines for persons without disability state that HIIE work phases

259 should elicit intensities between 64% to >100% $\dot{V}O_{2peak}$ [10], with health adaptation optimized

260 by intensities >90% $\dot{V}O_{2peak}$ [6]. The HIIE protocol employed in this study achieved $\dot{V}O_2$

261 excursions into this target intensity zone. However, the clinical utility of $\dot{V}O_2$ measurement is

262 limited [7], and exercise intensity during HIIE is commonly expressed as a percent of peak heart

263 rate or percent heart rate reserve (%HRR) [11]. The HR response in the current study showed

264 dynamic response to HIIE, with 10.5±8.6 min of the HIIE session spent above 80% HR_{peak}.

265 Figure 1 allows for comparison of the $\dot{V}O_2$ and HR responses during HIIE from a representative

266 individual (Participant 03 in Table 1). This participant was chosen as the representative because

267 their characteristics are representative of the SCI community at large: they are an obese (BMI =

268 28.2 $kg \cdot m^{-2}$) [1] middle-aged man of "average" fitness [27]. Figure 1A and 1B show a tight

269 coupling between $\dot{V}O_2$ and HR, with a greater dynamic fluctuation in $\dot{V}O_2$, corresponded with

270 HIIE work and recovery phases. MICE elicited a steady state response without evidence of $\dot{V}O_2$

271 drift, as observed by others [30]. Figure 1A and 1B also demonstrates the gradual increase in the

272 highest physiological response during consecutive HIIE working phases. This "treppe"

273 phenomenon was a common feature during HIIE (Figure 2). Notable in the representative

274 participant's response is that $\dot{V}O_2$ and HR both exceeded peak values achieved during GXT. This

275 phenomenon was also common, with the highest $\dot{V}O_2$ and HR (observed in a 20 s window)

276 throughout the HIIE sessions being 97.3 ± 8.8% $\dot{V}O_{2peak}$ and 91.4±9.0% HR_{peak}, respectively

277 (Figure 2A). It should be noted that the variability in the HR response was greater than that of

278 the $\dot{V}O_2$ response. In certain clinical populations an atypical HR response to exercise can

279 confound the use of HR as a proxy to quantify exercise intensity [7]. Changes in left ventricular

280 global function [31] and the unique $\dot{V}O_2$-HR relationship during arm cycling [32] could have

281 contributed to the greater variability of HR response to HIIE in SCI.

282

283 One of the primary benefits of HIIE is that a reduced time commitment is required to achieve a

284 given physiological response [13]. Of the HIIE [18, 19] and sprint interval exercise (SIE; 105%

285 to 115% PO_{peak}) [18-21] studies in SCI, ours is the first to demonstrate a reduced exercise

286 duration required to achieve a target energy expenditure. But it is important to remember that

287 high intensity exercise training elicits superior adaptations to moderate intensity despite

288 substantial differences in the total work, and thus energy expenditure, completed in individual

289 exercise sessions [13]. Thus the comparison of energy expenditure from HIIE and MICE likely

290 overlooks the totality of the potential benefits of HIIE. Indeed, glycogen cycling and disruptions

291 in cellular homeostasis are important considerations for the benefits of high intensity exercise

292 [33]. These metabolic responses contribute to the energetic requirements of recovery from

293 exercise, measured as excess post-exercise oxygen consumption (EPOC), in a manner dependent

294 on exercise intensity [34] which might be increased in HIIE in SCI. Thus energy cost, like $\dot{V}O_2$,

295 should be considered a useful but incomplete measurement of the physiological intensity of

296 exercise, and other metabolic parameters should be taken into account when considering HIIE

297 programming. Accordingly, our HIIE protocol was guided by knowledge of the heavy reliance

298 on carbohydrates during exercise in persons with SCI [23]. Due to this heavy reliance on

299 carbohydrates, we anticipated that a "long" [6] recovery phase would facilitate the clearance of

300 metabolic byproducts produced during the working phase; mitigating accumulation throughout

301 each successive interval. Examination of Figure 1C shows the coupling of RER with working

302 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

326 optimal HIIE protocol for a target physiological response. There are limitations to using indirect

327 calorimetry to calculate energy expenditure during exercise dominated by anaerobic metabolism

328 [39], and some of the assumptions of the stoichiometry equations [28] were violated during

329 certain parts of HIIE. Furthermore, matching the calorie cost of HIIE and MICE placed artificial

330 constraints on the potential benefits of MICE. It can be argued that MICE has a greater potential

331 capacity for energy expenditure because a greater exercise duration is possible due to the steady-

332 state nature whereas fatigue during HIIE likely limits the capacity for total calorie cost due to

333 exhaustion. However, it should be noted that the exercise intensity used in our study (53%

334 $\dot{V}O_{2peak}$) was similar to other HIIE publications in SCI [19] making our data comparable to

335 existing literature. Furthermore, long duration MICE could be considered undesirable due to the

336 time commitment and mundane nature of the task. With respect to our population, while the

337 participants in this study had a wide range of physical characteristics and fitness levels (Table 1),

338 50% of our sample had above-average cardiorespiratory fitness. Thus the results of our study

339 may be less applicable to persons with SCI who are at the lower end of the cardiorespiratory

340 fitness spectrum [27]. Finally, while autonomic function was not directly tested, our data (Table

341 1) showed that our participants had retained cardioacceleratory capacity and thus are not likely

342 experiencing the full extent of autonomic impairment that occurs with higher level SCI.

343 Therefore the results of this study cannot necessarily be applied to persons with higher level

344 injuries that result in paralysis of muscles involved in arm cycling along with stark autonomic

345 impairments that predispose an early onset of fatigue due to cardiovascular and neuroendocrine

346 limitations.

347

348 Our study is the first to demonstrate in SCI that, when appropriately adjusted, HIIE requires less

349 time to elicit a target calorie expenditure compared to MICE. Furthermore, fluctuations in RER

350 during HIIE, but not MICE, demonstrate differences in substrate partitioning between the two

351 exercise protocols. In order to deliver this sufficiently intense and time-efficient HIIE session in

352 SCI we used 2 min work and recovery phases prescribed at a workrate (70%:10% PO_{peak})

353 relatively lower than would be used in persons without disability completing leg cycling. Future

354 studies should determine if differences in the acute physiological response to MICE and HIIE

355 lead to differential adaptations to training interventions using these exercises to target health and

356 fitness.

357

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.

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Figure 1. Representative physiological responses to moderate intensity continuous exercise (MICE) and high intensity interval exercise HIIE)
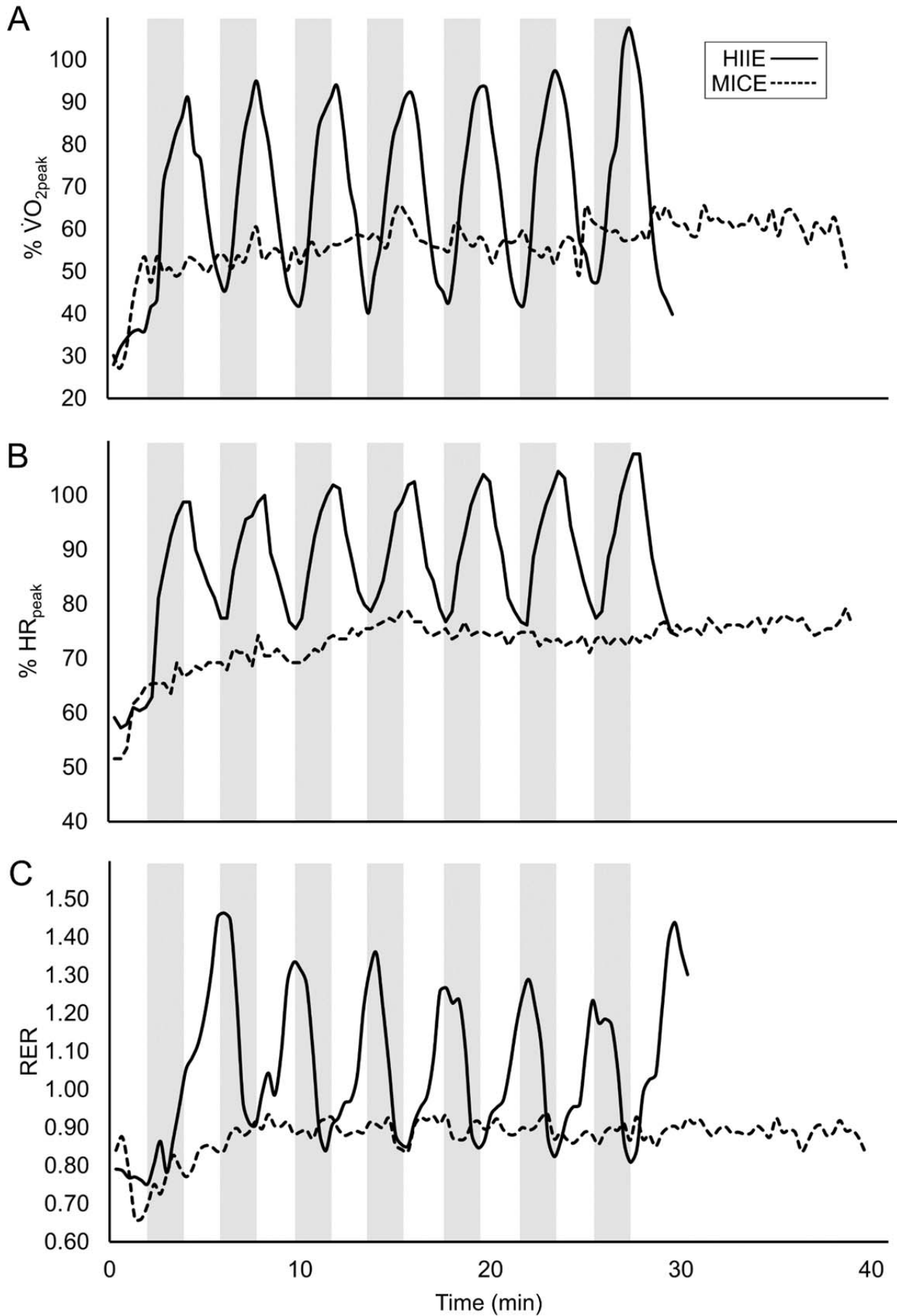
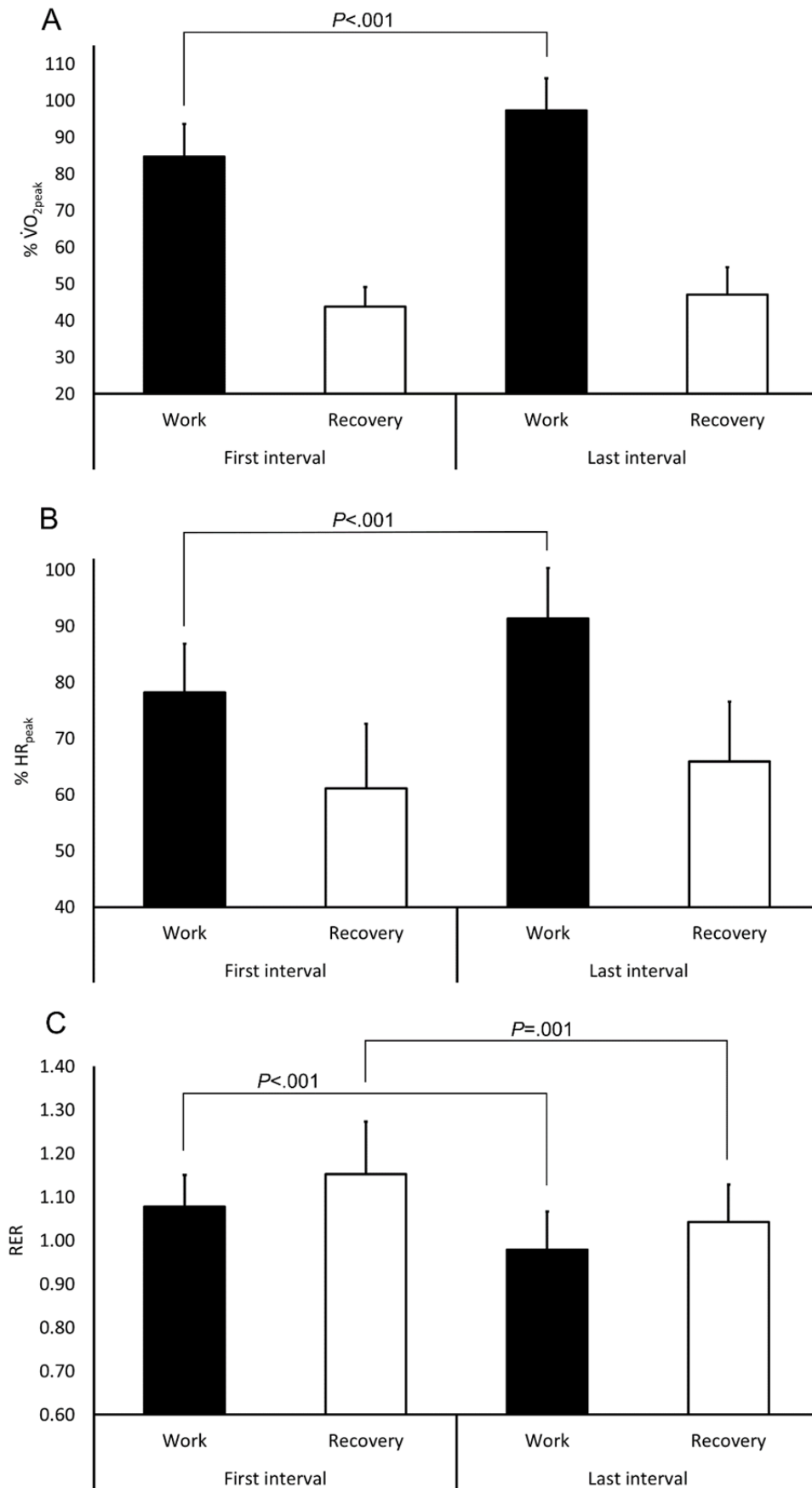Figure 2. Peak physiological responses to first and last intervals during high intensity interval exercise

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·kg^{-1}·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