A single bout of upper-body exercise has no effect on postprandial metabolism in persons with chronic paraplegia

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Abstract

Purpose: The acute effects of a single bout of upper-body exercise on postprandial metabolism in persons with spinal cord injury is currently not well understood. The primary aim of this study was to evaluate the effects of a single bout of upper-body high-intensity interval exercise (HIIE) and moderate-intensity continuous exercise (MICE), in comparison to a no-exercise control (REST) condition on postprandial metabolic responses in persons with chronic paraplegia.

Methods: 10 participants (eight males, two females, age: 49 ± 10 yrs, time since injury: 22 ± 13 yrs) with chronic paraplegia took part in a randomised cross-over study, consisting of three trials: HIIE (8 x 60 s at 70% peak power output (P_{PEAK})), MICE (25 min at 45% P_{PEAK}), and REST, at least 3 days apart. Exercise was performed in the fasted state, and participants consumed a mixed-macronutrient liquid meal 1-h post-exercise. Venous blood and expired gas samples were collected at regular intervals for 6-h post-meal consumption.

Results: There were no significant differences in postprandial iAUC for triglycerides (p=0.59) or glucose (p=0.56) between conditions. Insulin iAUC tended to be lower following MICE (135 ± 85 nmol/L· 360 min^{-1}) compared to REST (162 ± 93 nmol/L · 360 min^{-1}), but this did not reach statistical significance (P=0.06, *d*=0.30). Participants reported a greater fondness (P=0.04) and preference for HIIE over MICE.

Conclusions: Following an overnight fast, a single bout of upper-body exercise before eating, has no effect on postprandial metabolism in persons with chronic paraplegia, irrespective of exercise intensity. This suggests that alternative exercise strategies may be required to stimulate postprandial substrate oxidation for this population.

Key Words: EXERCISE INTENSITY, SPINAL CORD INJURY, INSULIN, GLUCOSE, TRIGLYCERIDES

Introduction

Individuals with a spinal cord injury (SCI) are at an increased risk of developing cardiovascular disease (CVD) in comparison to the non-disabled population (1). It is therefore unsurprising that this population present a high prevalence of risk factors associated with CVD, including central adiposity (2), dyslipidaemia (3), and impaired glucose tolerance (4). The role of regular exercise training in the prevention of these CVD risk factors is well-established in non-injured humans, and current SCI-specific exercise guidelines recommend that people with chronic SCI engage in at least 30 minutes of moderate-to-vigorous intensity aerobic exercise three times per week to improve cardiometabolic health (5). Specifically, there is consistent evidence that upper-body moderate-intensity continuous training improves fasting insulin sensitivity and reduces waist circumference in persons with chronic SCI (6). These chronic adaptations are a result of numerous individual bouts of exercise, but the metabolic responses to a single-bout of upper-body exercise in this population are not well understood.

In particular, the effect of a single-bout of upper-body exercise on postprandial metabolism is important to determine as humans spend most of the waking-day in a fed state, with elevated postprandial glucose and triglyceride responses, both independent risk factors for CVD (7, 8). In addition, persons with SCI may have exaggerated postprandial lipaemic and glycaemic responses compared to the non-disabled population, which may partially explain their increased risk of developing CVD (9, 10). A single-bout of moderate-intensity continuous exercise (MICE) (90 min at 50% maximal oxygen update) can decrease the postprandial triglyceride response to a high-fat meal consumed ~12-18 h post-exercise in healthy non-disabled individuals (11). In people with type-2 diabetes, a single bout of MICE performed in the postprandial state can reduce short-term glucose area under the curve and the prevalence of 24-h hyperglycaemia (12). However, it is unclear how a single-bout of upper-body MICE affects subsequent postprandial responses in persons with SCI.

There has been growing interest in high-intensity interval exercise (HIIE) as an alternative solution to MICE to improve cardiometabolic health outcomes in persons with SCI (13). HIIE can be generally characterised as repeated short intervals eliciting ≥80% (but often 85-95%) of maximum heart rate (14). This interest stems from a randomised controlled trial demonstrating that 180 min/week of MICE is sufficient to improve cardiorespiratory fitness and fasting insulin sensitivity, but not fasting glucose, peripheral insulin sensitivity, or the lipid profile, suggesting a higher exercise intensity is required (15). Training programmes involving HIIE and MICE elicit comparable improvements, in insulin sensitivity, blood pressure, and body composition, in non-disabled overweight and obese individuals (16). Pilot work in individuals with SCI also indicate similar improvements in insulin sensitivity following training programmes involving HIIE and MICE (17). HIIE is particularly appealing given the reduced time commitment, and is often cited as more enjoyable than MICE (18). This finding has recently been replicated during upper-body exercise in persons with chronic SCI (19). It also appears that a single-bout of HIIE can attenuate the postprandial glucose and triglyceride to meal, to a similar extent as MICE in non-injured humans (20, 21).

Bailey et al. (22) recently reported that postprandial glucose responses were attenuated by regularly breaking up sedentary time with short bouts of moderate-intensity arm crank ergometry in persons with chronic paraplegia. However, to our knowledge, there are no published studies assessing the effect of a single bout of upper-body exercise on subsequent metabolic responses to a mixed-macronutrient test in this population. Therefore, the aim of this study was to evaluate the effects of both an acute bout of upper-body HIIE and MICE, in comparison to a no-exercise control condition (REST) on postprandial metabolic responses to a mixed-macronutrient meal in persons with chronic paraplegia. We hypothesised that HIIE and MICE would be equally and more effective at reducing the total serum triglyceride response in comparison to the no-exercise condition.

Methods

This study was approved by South West (Bristol) National Research Ethics Committee (REC reference number 19/SW/0021). All participants provided written informed consent and the study conformed to the principles of the Declaration of Helsinki. The study was registered as a clinical trial at ClinicalTrials.gov (https://clinicaltrials.gov/) under the identifier NCT04011137.

Participants

We aimed to recruit 11 participants, based on an *a*-priori sample size calculation (Cohen's *d*=0.97, α=0.05, ß=0.80) to detect a significant difference in the total postprandial triglyceride response between HIIE and the no-exercise control condition (20). A total of 13 individuals with chronic paraplegia agreed to take part in this randomised cross-over study, two participants were withdrawn due to difficulties with venous cannulation, and one participant withdrew due to a lack of time, leaving a total of ten participants (eight males, two females) completing all components of the study. Participant descriptive characteristics are presented in Table 1.

Participants were eligible to participate if they met all the following criteria: aged between 18 and 65 years, chronic (>1 yr post-injury) spinal cord lesion at or below the second thoracic level, self-reported wheelchair use of >75% of waking day in individuals with motor-incomplete injuries, and body mass not changed by >3% over the previous three months. Individuals who self-reported the use of lipid lowering agents and/or anti-hyperglycaemic drugs, type 2 diabetes *mellitus* medication, active medial issues (including pressure sores, urinary tract infection, and upper-body musculoskeletal issues) or contraindications to exercise testing were excluded.

Study Design

Participants visited the laboratory on four separate occasions (one pre-experimental visit, three experimental trials). The pre-experimental procedures included basic anthropometric measurements, an assessment of resting metabolic rate (RMR) and peak aerobic capacity ($\dot{V}O_{2PEAK}$), and HIIE familiarisation session. A sub-maximal exercise test was also performed to allow the individual calibration of a physical activity monitor, which participants wore for a 7-day period commencing immediately following this initial visit. The three experimental trials (MICE, HIIE, and REST) were then performed in a randomised order, at least 3 days apart. Participants arrived in a fasted state and performed one of the three conditions, which was followed by a 6-h mixed meal tolerance test (MMTT) (Figure 1).

(INSERT FIGURE 1 HERE)

Pre-experimental visit

Participants arrived at the laboratory following an overnight fast (>10 h), having refrained from caffeine and alcohol (24-h prior) and strenuous physical activity (48-h prior). Body mass was measured using platform wheelchair scales (Decto ® BRW1000, Missouri, USA). Supine length, waist and hip circumferences were measured with participant's lying flat on a medical bed. Resting metabolic rate (RMR) was estimated via indirect calorimetry from four 5-minute expired gas samples collected into Douglas Bags (Hans Rudolph, MO, USA) through a mouthpiece. Ambient O_2 and CO_2 fractions, in addition to atmospheric pressure and temperature were measured at close proximity to the participants to account for changes in an enclosed laboratory environment (23). Fractions of expired O_2 and CO_2 were measured using a paramagnetic O_2 and infrared CO_2 analyser (miniMP 5200, Servomex, Crowborough, UK), calibrated with known concentrations of gas on the morning of testing. RMR was calculated using stoichiometric equations (24), and was recorded as the mean of three samples differing by $\leq$100 kcal $\cdot$ day^{-1}.

144 A sub-maximal incremental exercise test was then performed on an electronically
145 braked arm-crank ergometer (Lode Angio, Groningen, Netherlands), consisting of four 3-
146 minute stages, starting at 5 W, and increasing by either 10 or 15 W (depending on self-reported
147 fitness). Energy expenditure (using the Douglas Bag method) and heart rate for each stage were
148 used to perform an individual calibration of a chest-worn physical activity monitor
149 (Actiheart^{TM}, Cambridge Neurotechnology Ltd, Papworth, UK) (25). Participants were
150 instructed to wear the device for 7 days to monitor habitual physical activity patterns.
151 Subsequently, physical activity energy expenditure, and physical activity level (PAL) were
152 estimated (26).

153 Following an adequate rest, participants then performed a $\dot{V}O_{2PEAK}$ test on an
154 electronically braked arm-crank ergometer. The ramp-based protocol included a two-minute
155 warm-up at 10 W before increasing by 1 W every 6 seconds. Before the test, participants were
156 fitted with a rubber-face mask connected to two-way breathing valve, this was connected to a
157 computerised metabolic system (TrueOne® 2400, ParvoMedics, Salt Lake City, UT). The
158 system was calibrated with a known concentration of gas (20% O_2, 8% CO_2) and a 3-L
159 calibration syringe, on the morning of testing. Heart rate and single-breath data were recorded
160 simultaneously on the software throughout the entire test. A cadence of ~75 rpm was
161 encouraged throughout, and the test was terminated at volitional fatigue or when cadence
162 dropped below 50 rpm. $\dot{V}O_{2PEAK}$ was defined as the highest 15-breath rolling average for $\dot{V}O_2$.
163 Peak power output (P_{PEAK}) was defined as the highest power output achieved before
164 termination of the test. All participants achieved a valid $\dot{V}O_{2PEAK}$ according to the following
165 criteria: peak HR ≥ 95% age-predicted maximum for upper-body exercise (200 b · min^{-1} - Age),
166 rating of perceived exertion (RPE) ≥ 19, and a peak respiratory exchange ratio (RER) ≥ 1.10.
167 Participants then performed a shortened HIIE protocol on the electronically braked arm-crank
168 ergometer, consisting of a one-minute warm-up at 10% P_{PEAK}, followed by four 60-s intervals

at 70% P_{PEAK}, interspersed by 60-s recovery intervals at 10% P_{PEAK}. Participants were encouraged to reach a cadence of at least 75 rpm prior to the start of each high-intensity bout.

Experimental trials

Before all three conditions, participants refrained from strenuous physical activity in the 48-h prior, and consuming alcohol or caffeine in the 24 h prior. Participants arrived at the laboratory at the same time each morning (between 08:00 and 10:00) to minimise diurnal variation, following an overnight fast (>10 h) and having consumed ~1 pint of water on waking. In the two days before the first experimental trial, participants completed a non-weighed food diary, and asked to replicate this before each experimental trial. Trials were completed within the follicular phase of the menstrual cycle (3-10 days after onset of menses) for the eumenorrheic females taking part in the study.

Upon arrival, body mass was measured, a resting expired gas sample obtained, and a fasting blood sample taken via venepuncture ('PreEx') from the antecubital vein. One of three conditions was then performed in a randomised order (≥3 days apart): i) REST - a no-exercise control condition, ii) MICE - 25-min at 45% P_{PEAK}, and iii) HIIE - eight 60-s intervals at 70% P_{PEAK}, interspersed with 60-s recovery intervals at 10% P_{PEAK}. Both exercise protocols began with a 5-min warm-up at 10% P_{PEAK}, and the HIIE condition included a 5-min cool-down at the same intensity. Participants wore a rubber face mask connected to a computerised metabolic system as previously described. Heart rate, RPE (global, local, and central), and affective valence were recorded at the end of the warm-up (0), 25, 50, 75, and 100% through each exercise condition. Affective valence was measured using the Feeling Scale, whereby participants are asked how they feel at the current moment using an 11-point scale, ranging from, "Very Bad" (-5) to "Very Good" (+5) (27). Expired gases were averaged across 1-minute intervals and total exercise energy expenditure was calculated using published equations for

high-intensity exercise (28). When RER exceeded 1.0, energy expenditure was calculated assuming a relationship of 5 kcal utilised for each 1 L of O_2 consumed (29).

Within 30-min of exercise completion, participants completed a modified Physical Activity Enjoyment Scale (PACES) (30). Participants also completed a 5-item questionnaire relating to exercise self-efficacy (31). This measure asked participants to consider how confident they were to be able to perform the exercise protocol (once to five times per week) over the next 4 weeks, with responses ranging from "Not at all" (0%) to "Extremely confident" (100%), in increments of 10%. After completion of both exercise trials, participants were asked which type of exercise they preferred, and their fondness of each, on a 7-point Likert scale ranging from "Very much dislike" (1) to "Extremely like" (7).

At 30-min post-exercise, expired gas and blood samples were obtained ('PostEx'), after a cannula was inserted into an antecubital vein. At 60-min post-exercise, participants then consumed a mixed-macronutrient liquid meal that provided a total energy content of 65% RMR, chosen to meet resting energy requirements for the study hours in which no other food was consumed (i.e. ~17 hours). The macronutrient composition (45% calories from carbohydrate, 37% calories from fat, and 18% calories from protein) was designed to reflect that of a typical meal in persons with SCI (32). Participants were given 10-min to consume the meal. Expired gas samples were taken at 60, 120, 180, 240, 300, and 360-min post drink consumption. Blood samples were drawn at 0, 15, 30, 45, 60, 90, 120, 180, 240, and 360 min post meal consumption. All blood samples were taken with the participant's hand in a heated hand-box (55ºC) (33).

All arterialised blood samples collected (10 mL) were dispensed into treated serum collection tubes, and then centrifuged at 4000 g for 10 min at 4°C. The serum was then apportioned into aliquots, cooled immediately on dry-ice and then stored in a -80°C freezer for

long-term storage before analysis. Serum triglyceride, glucose, NEFA, and glycerol concentrations were determined using an automated analyser (Randox RX Daytona, Co., Antrim, UK). Serum insulin concentrations were determined by commercially available enzyme-linked immunosorbent assay (Mercodia AB, Uppsala, Sweden). Expired gas samples were used to estimate carbohydrate and fat oxidation rates, using previously published equations (24).

Statistical Analysis

Paired t-tests were performed to compare total exercise energy expenditure, exercise enjoyment, exercise self-efficacy, and fondness between MICE and HIIE. The normality of the paired differences was checked using a Shapiro-Wilk test, and if significant, Wilcoxon tests were performed instead. Mixed-model ANOVA's (condition x time) were performed to analyse serum blood analytes (glucose, insulin, triglycerides, non-esterified fatty acids (NEFA), and glycerol) and indirect calorimetry derivates (carbohydrate and fat oxidation rates, and RER) over time. Two-way ANOVA's were used to compare $\%HR_{PEAK}$, RPE, and affective valence over time between MICE and HIIE. One-way repeated ANOVA's were performed to compare the total (TAUC) and incremental area under the curve (iAUC) in the postprandial period (0 to 360 min) for glucose, insulin, and triglycerides, NEFA, and glycerol. Where significant interaction effects were found, Bonferroni comparisons were performed to identify the source of variation. Sphericity was determined with Greenhouse-Geisser epsilon; all values <0.75 were corrected with Greenhouse-Geisser corrections. Statistical significance was accepted at $P \leq 0.05$. All data are presented as mean (lower 95% CI, upper 95% CI) unless otherwise noted. In addition, effect sizes (Cohen's *d*) were calculated, and interpreted as: small effect = 0.20-0.49, medium effect = 0.50-0.79, and large effect ≥0.80.

241 **Results**

242 ***Participant Characteristics***

243 The mean (±SD) $\dot{V}O_{2PEAK}$ of the male (n=8) and female (n=2) participants was 21.4 ± 5.4
244 $ml \cdot min^{-1} \cdot kg^{-1}$ and 15.8 ± 0.6 $ml \cdot min^{-1} \cdot kg^{-1}$, respectively. Therefore, the fitness classifications
245 of the male participants were: poor (n=1), average (n=2), good (n=3), and excellent (n=2)
246 (34). Eight participants (80%) could be classified as a living a sedentary lifestyle (PAL ≤
247 1.60). Nine participants (90%) had a raised fasting glucose concentration (≥5.6 $mmol \cdot L^{-1}$),
248 and four participants (40%) could be classified as having hypertriglyceridemia (fasting
249 triglycerides ≥ 1.7 $mmol \cdot L^{-1}$) (35).

250 *(INSERT TABLE 1 HERE)*

251 Mean (±SD) RMR was 1595 ± 227 $kcal \cdot day^{-1}$, therefore participants consumed a total 1037 ±
252 148 kcal for the MMTT, consisting of 129 ± 18 g of carbohydrate, 41 ± 6 g of fat, and 42 ± 6
253 g of protein.

254 ***Exercise characteristics***

255 Mean (±SD) P_{PEAK} was 100 ± 28 W. Participants exercised at 45 ± 13 W for the MICE
256 condition which corresponded to an overall exercise intensity of 58 ± 7% $\dot{V}O_{2PEAK}$. During the
257 HIIE condition, participants exercised at 70 ± 20 W and 10 ± 3 W for the 'high' and 'recovery'
258 phases respectively. This corresponded to an overall exercise intensity of 58 ± 8% $\dot{V}O_{2PEAK}$ for
259 the HIIE condition; 57 ± 10% $\dot{V}O_{2PEAK}$ for the 'high' intervals and 59 ± 8% $\dot{V}O_{2PEAK}$ for the
260 'recovery' intervals.

261 The mean (±SD) total exercise energy expenditure was greater during MICE (128 ± 24 kcal)
262 compared to HIIE (98 ± 15 kcal, $P<0.01$). The $\%HR_{PEAK}$ was greater in HIIE compared to

MICE at 75% (P=0.02, *d*=0.42) of exercise completion, and tended to be greater at 50% (P=0.08, *d*=0.34) and 100% (P=0.09, *d*=0.35) of exercise completion (Figure 2).

(INSERT FIGURE 2 HERE)

There were no significant interaction effects between conditions at any time-point for global (P=0.75), local (P=0.94), and central (P=0.73) RPE, or affective valence (P=0.97). There was not a significant difference in enjoyment (mean ± SD) between HIIE (93 ± 14) and MICE (82 ± 23) (P=0.13). However, participants reported a greater fondness (mean ± SD) for HIIE (5.5 ± 1.0) compared to MICE (4.1 ± 1.5) (P=0.04; *d*=1.15). Participant's also reported a higher exercise self-efficacy at being able to perform four (P=0.03; *d*=0.54) and five (P=0.04; *d*=0.33) bouts per week of HIIE compared to MICE. Eight participants stated a preference for the HIIE, and two participants for MICE.

Serum blood analytes

There were no significant interaction effects between conditions at any time-point for serum insulin (P=0.77; Figure 3), glucose (P=0.98; Figure 4), or triglycerides (P>0.99; Figure 5). However, there was a significant effect of condition for glucose (P<0.01; Figure 4), with the mean blood glucose concentration lower for the HIIE condition, in comparison to the MICE and REST (both P<0.01). Serum insulin TAUC (data not shown, *d*=0.27) and iAUC (*d*=0.30) tended to be lower following MICE compared to REST (both P=0.06) (Figure 3). There were no significant differences between conditions for TAUC (data not shown) or iAUC for glucose (P=0.27 and P=0.56 respectively; Figure 4) and triglycerides (P=0.74 and P=0.59 respectively; Figure 5).

(INSERT FIGURES 3, 4 AND 5 HERE)

There were no significant interaction effects between trials at any time-point for serum NEFA or glycerol, although there was a significant effect of condition for glycerol

(P=0.01), with mean glycerol concentration higher in the HIIE condition compared to the resting control condition (P=0.02) (data not shown). Additionally, serum NEFA (P=0.20) and glycerol TAUC (P=0.37) did not differ between conditions (data not shown).

Indirect calorimetry

There were no significant interaction effects between trials at any time-point for fat (P=0.84) and carbohydrate (P=0.71) oxidation rates, or RER (P=0.85). However, there was a significant effect of condition for both fat and carbohydrate oxidation, and RER across the whole trial (all P<0.01). RER was significantly lower in the MICE condition compared to both the HIIE (P=0.02) and resting control condition (P<0.01).

Discussion

The purpose of this study was to determine the effect of prior upper-body exercise (MICE and HIIE) on postprandial responses to a mixed-macronutrient meal in individuals with chronic paraplegia. Contrary to our hypothesis, a single bout of upper-body exercise was insufficient to reduce the subsequent postprandial triglyceride responses in comparison to the no-exercise condition. Despite no differences in postprandial glucose responses, the insulin response tended to be lower following MICE in comparison to the no-exercise REST condition. Participants reported a preference, and a greater fondness and self-efficacy for HIIE compared to MICE.

Upper-body MICE and HIIE had no effect on the subsequent postprandial triglyceride response in comparison to the no-exercise REST condition. This contrasts findings from non-injured populations that a single acute bout of MICE or HIIE performed 12-18 h prior to a standardised meal attenuates the postprandial triglyceride response (11, 36). Although studied less extensively, prior research indicates that this effect appears to still hold true when exercise is performed immediately (≤1-h) prior to the tolerance test (37, 38). However, it appears that

311 the magnitude of this effect is partially dependent on the energy expended during exercise and
312 there may be an exercise energy expenditure threshold needed to elicit changes in postprandial
313 triglycerides (20, 39). Therefore, an insufficient exercise energy expenditure (~100-130 kcal),
314 which is a result of the limited active muscle mass involved in upper-body exercise, may
315 partially explain the lack of change observed in the postprandial triglyceride response in the
316 present study. It is also important to note that following consumption of the liquid meal,
317 participants were initially in a positive energy balance, which appears to diminish the beneficial
318 effect of exercise on postprandial triglycerides (20).

319 There was also no beneficial effect of either exercise condition on postprandial glucose
320 responses in comparison to the no-exercise condition. This is perhaps unsurprising, given that
321 studies have demonstrated that 60-min of treadmill walking in the fasted state has no effect on
322 glucose responses to a mixed-macronutrient meal in persons with obesity (37) and
323 hyperglycaemia (40). An increased rate of appearance of glucose from the liquid meal during
324 the initial 3-h post-exercise period is likely to be the reason for the lack of difference in
325 postprandial glucose, offsetting the increased clearance rate (41). However, it is interesting to
326 note that Short et al. (42) found that glucose clearance was increased following 35-min
327 moderate-to-vigorous handcycle exercise in adolescents with spina bifida or cerebral palsy.
328 The reasons for this discrepancy with the present study are not immediately clear, but may be
329 related to the basal glucose tolerance of participants, and/or differences in the quantity and
330 macronutrient content of the oral tolerance test.

331 Despite the lack of differences in postprandial glucose following either exercise
332 condition, the insulin iAUC tended (20%, P=0.06) to be lower following MICE compared to
333 the no-exercise REST condition, with eight participants displaying a reduction.
334 Comparatively, Farah & Gill (37) observed a 19% reduction in insulin AUC, but no change
335 in glucose response, when 60-min of walking at 50% maximal O_2 uptake was performed in

the fasted state, prior to an 8.5 h postprandial period, in overweight men. It is well-established that even in individuals with insulin-resistance, a single acute bout of aerobic exercise increases insulin sensitivity for up to 24-h (43). However, given the curvilinear relationship between exercise energy expenditure and ensuing improvements in insulin sensitivity, it is likely that the exercise conditions in the present study, that represent a realistic exercise stimulus for this population, were not sufficient to induce a change in insulin sensitivity (44).

Whilst there was no significant difference in exercise enjoyment between MICE and HIIE, participants did report a preference for HIIE, in addition to a greater fondness and exercise self-efficacy. Further, despite the higher $\%HR_{PEAK}$ achieved during the HIIE, levels of affective valence during exercise were similar compared to MICE. These findings largely support previous research in habitually active persons with chronic SCI who reported a greater preference and higher enjoyment for HIIE compared to MICE, and no differences in affective valence (19). Given that individuals are more likely to adhere to exercise that they enjoy and are confident they can perform (45), HIIE appears to be a viable training modality for persons with chronic SCI.

A significant strength of this study is that our sample of participants was representative of people with chronic paraplegia (i.e. physically inactive with poor metabolic health). It has been conservatively estimated that almost two thirds of individuals with chronic SCI have cardiometabolic syndrome (46), and in the current study, nine out of the ten participants would be classified as having this condition. Additionally, the macronutrient content of the MMTT reflected the habitual diet of persons with SCI (21), and allowed for triglyceride concentrations to peak at 4-5 h post-meal consumption without participant's being in a large energy deficit across the trial day. Finally, the exercise protocols were matched for total time commitment, and represented realistic and achievable exercise sessions for this population, that closely

match the SCI-exercise guidelines (5, 19). For example, in a free-living environment, persons with chronic paraplegia perform an average of just 17 min per day of moderate-to-vigorous physical activity (47), which is less than both MICE and HIIE conditions. Therefore, we believe our findings have considerable real-world relevance.

The main limitation of this study is that despite the exercise protocols matching those previously characterised is this population (19), there was no difference in $\%\dot{V}O_{2PEAK}$ between MICE and HIIE, and the $\%HR_{PEAK}$ achieved was only marginally higher for HIIE. It is possible that a more vigorous exercise intensity during the HIIE condition may have elicited changes in postprandial metabolism. Additionally, we did not match the MICE and HIIE conditions for energy expenditure, and therefore the total energy expenditure of MICE was ~30 kcal greater than HIIE. Thirdly, due to participant drop-out, we failed to reach our target sample size of 11, however based on the observed effect size (d=0.04) for our primary outcome (triglyceride TAUC) between HIIE and REST, one extra participant would not have meaningfully changed our findings regarding postprandial triglyceride responses. Finally, the MMTT contained a large bolus of calories (1037 ± 148 kcal), which isn't typically consumed in a habitual diet. Whilst a more ecologically valid approach would have been to study responses to a typical breakfast and lunch meal, the total energy consumed ensured participants resting energy requirements were met.

There remain large knowledge gaps with regards to the effect of a single-bout of upper-body exercise on postprandial metabolism in persons with chronic SCI. To address this, future studies should assess the effect of exercise performed the evening prior to a MMTT, as the activity of the enzyme (lipoprotein lipase) believed to be primarily responsible for exercise-induced reductions in postprandial triglycerides peaks at 8-h post-exercise in skeletal muscle (48). However, we speculate that any localised activation of lipoprotein lipase, is unlikely to result in a reduction in the postprandial triglyceride response, given the limited active muscle

mass involved in upper-body exercise. Additionally, both HIIE and MICE performed in the postprandial state appear to improve 24-h glucose profiles in a free-living environment in non-injured populations (49, 50), and it would be useful to understand if this effect is still present in persons with chronic SCI. Finally, we only recruited individuals with paraplegia, but this work should also be expanded to individuals with tetraplegia, who experience an early onset of exercise fatigue due to cardiovascular impairments.

Conclusions

Following an overnight fast, acute upper-body exercise is not sufficient to improve subsequent postprandial responses to a large mixed-macronutrient meal in persons with SCI, irrespective of exercise intensity. This is likely due to the substantially lower active muscle mass and consequently reduced energy expenditure that can be achieved during upper-body exercise compared to whole and/or lower-body exercise. These findings highlight the need to identify alternative strategies to stimulate postprandial substrate oxidation in this population, including maximising exercise energy expenditure (e.g. combining upper-body exercise with functional electrical stimulation cycling and/or resistance training), combining exercise with dietary restriction, or performing regular bouts of activity throughout the day.

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Conflicts of Interest

All authors have no conflicts of interest to declare and acknowledge that the results of the present study do not constitute endorsement by the American College of Sports Medicine, and are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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568 **Figure Legends**

569 **Figure 1.** Schematic of experimental trial days (laboratory visits 2-4).

570 **Figure 2.** Heart rate (expressed as a % of HR_{PEAK}) at 0, 25, 50, 75, and 100% of exercise
571 completion during MICE and HIIE. *indicates significant difference ($P \leq 0.05$) between
572 conditions.

573 **Figure 3.** Serum concentrations of insulin (a) across each condition and iAUC (individual
574 responses also denoted) for serum insulin (b) across the 6-h postprandial period following
575 consumption of the MMTT. The hashed box represents consumption of the meal.

576 **Figure 4.** Serum concentrations of glucose (a) across each condition and iAUC (individual
577 responses are also denoted) for serum glucose (b) across the 6-h postprandial period
578 following consumption of the MMTT. The hashed box represents consumption of the meal.

579 **Figure 5.** Serum concentrations of triglycerides (a) across each condition and iAUC
580 (individual responses are also denoted) for serum triglycerides (b) across the 6-h postprandial
581 period following consumption of the MMTT. The hashed box represents consumption of the
582 meal.