



ORIGINAL ARTICLE

WILEY

Acute effects of breaking up prolonged sedentary time on cardiovascular disease risk markers in adults with paraplegia

Daniel P. Bailey¹  | Thomas M. Withers¹ | Vicky L. Goosey-Tolfrey²  |
David W. Dunstan^{3,4} | Christof A. Leicht² | Rachael B. Champion¹ |
Opie P. Charlett¹ | Louise Ferrandino¹

¹Institute for Sport and Physical Activity Research, School of Sport Science and Physical Activity, University of Bedfordshire, Bedford, UK

²School of Sport, Exercise and Health Sciences, The Peter Harrison Centre for Disability Sport, Loughborough University, Loughborough, UK

³Baker Heart and Diabetes Institute, Melbourne, Vic., Australia

⁴Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Vic., Australia

Correspondence

Daniel P. Bailey, Department of Life Sciences, Brunel University London, Uxbridge UB8 3PH, UK.
Email: daniel.bailey@brunel.ac.uk

Present address

Daniel P. Bailey, Division of Sport, Health and Exercise Sciences, Department of Life Sciences, Brunel University London, Uxbridge, UB8 3PH, UK
Thomas M. Withers, School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, B15 2TT, UK

Funding information

Heart Research UK, Grant/Award Number: RG2655/17/18

Elevated levels of cardiovascular disease (CVD) risk markers are highly prevalent in people with a spinal cord injury (SCI). Breaking up prolonged sedentary time with short, regular bouts of physical activity can reduce postprandial glucose and lipid levels in able-bodied individuals. The effects in people with paraplegia are unknown. The study aims were to examine the acute postprandial glucose (primary aim), lipid, blood pressure, and psychological responses (secondary aims) to breaking up prolonged sedentary time in individuals with paraplegia. This was a randomized crossover design trial. Fourteen participants with paraplegia (age 51 ± 9 years, trunk fat mass $44.3 \pm 7.7\%$) took part in the following two, 5.5-hour conditions: (1) uninterrupted sedentary time (SED), and (2) sedentary time interrupted with 2 minutes of moderate-intensity arm crank ergometer physical activity every 20 minutes (SED-ACT). Standardized breakfast and lunch test meals were consumed during each condition. The outcomes were compared between conditions using linear mixed models. Glucose area under the curve (AUC) was significantly lower during the lunch postprandial period in SED-ACT vs SED (incremental AUC 1.9 [95% CI 1.0, 2.7] and 3.0 [2.1, 3.9] mmol/L•2.5 hour, respectively, $P = .015$, $f = 0.34$). There were no differences between conditions for the breakfast or total 5.5 hours postprandial periods ($P > .05$). Positive affect was higher in SED-ACT than SED ($P = .001$). Breaking up prolonged sedentary time acutely attenuates lunch postprandial glucose and improves positive affect in people with paraplegia. This may have clinical relevance for reducing CVD risk and improving psychological well-being in this population.

KEYWORDS

activity breaks, cardiometabolic health, exercise, physical activity, sedentary behavior, spinal cord injury, wellbeing

1 | INTRODUCTION

Spinal cord injury (SCI) causes a loss of motor and sensory function across and below the level of the injury. It is estimated that 180 000 traumatic SCI cases occur each year globally¹ with an annual incidence rate of between 8.0 and 49.1 per million.² Although there is less research regarding the prevalence of non-traumatic SCI, incidence has been reported as 26.3 cases per million people per year.³

There are significant metabolic disturbances that occur following SCI that are associated with reduced muscle mass, increased fat mass, and reduced levels of anabolic hormones.⁴ Metabolic dysfunction in this population is characterized by dyslipidemia, impaired glucose tolerance, and insulin resistance.^{4,5} One study found that 50% of individuals with paraplegia had impaired postprandial glucose metabolism compared to 18% of able-bodied individuals.⁵ There may also be an exaggerated postprandial lipid response.⁶ Low levels of physical activity could be a major contributor to adverse metabolic health in people with SCI. Exercise interventions have led to beneficial acute and chronic metabolic responses in this population, and engagement in regular moderate-to-vigorous physical activity is thus recommended.⁷ There is also evidence that engaging in physical activity is associated with improved mental health in this population,⁸ which is important as mental well-being is often poor in people with SCI.⁹ However, physical activity levels are low in individuals with paraplegia¹⁰ and other interventions for metabolic health improvement should be explored.

Physical activity guidelines for the general population include recommendations for reducing and breaking up sedentary behavior¹¹ based on evidence that high levels of daily sedentary time are associated with adverse health outcomes, such as cardiovascular disease (CVD) and diabetes.¹² The adverse health consequences in the general population have been proposed to predominantly occur due to prolonged muscular contractile inactivity and reduced blood flow that causes disruption to metabolic processes that regulate glucose and lipid levels.¹³ This may be particularly relevant for individuals with paraplegia who may spend high amounts of time being sedentary,¹⁴ although this requires investigation in larger samples. Reductions in postprandial glucose, insulin, and triglycerides have been observed in response to breaking up sitting time with 2-5 minutes of light- or moderate-intensity walking every 20-30 minutes in able-bodied participants.^{15,16} There are also improvements in blood pressure, vascular function, and haemostatic markers.¹⁷ However, no previous study has evaluated the effects of breaking up sedentary time in individuals with paraplegia. The capability of people with SCI to interrupt sedentary time and its impact on health should be explored to appropriately inform physical activity guidelines for this population.

The aims of this study were therefore to compare postprandial glucose (primary aim), lipid, blood pressure, and psychological responses (secondary aims) to breaking up prolonged sedentary time vs uninterrupted sedentary time in individuals with paraplegia over a single day. It was hypothesized that breaking up sedentary time would lower the primary outcome (postprandial glucose) compared with uninterrupted sedentary time. It was also hypothesized that breaking up sedentary time would lower postprandial lipid and blood pressure levels and improve subjective well-being, affect, and self-efficacy for avoiding prolonged sedentary time (secondary outcomes).

2 | MATERIALS AND METHODS

2.1 | Study design and overview

The study protocol has been described previously in detail.¹⁸ This was a two-condition randomized crossover design trial and is reported in accordance with CONSORT guidelines. The trial was registered with the ISRCTN registry (ISRCTN51868437) and was approved by the Cambridge South NHS Research Ethics Committee (reference 17/EE/0076). Participants provided written informed consent prior to being accepted into the study and before randomization and test procedures.

Following a preliminary testing visit, participants took part in two experimental conditions in a random order. The two, 5.5-hour experimental conditions were as follows: (a) uninterrupted sedentary time and (b) sedentary time interrupted with 2 minutes of moderate-intensity arm ergometer exercise every 20 minutes. Two standardized mixed meals were provided during each condition. Participants took part in the conditions in a randomized order using a block approach with balanced block sizes. Randomization was completed by a researcher independent from the study using computer-generated numbers. Participants were blinded to the condition they were taking part in until arrival on the first experimental testing day. There was a washout period of ≥ 6 days between conditions. All data collection took place at the University of Bedfordshire Sport and Exercise Science Laboratories.

2.2 | Participants

Participants eligible to take part in this study were community-dwelling 18- to 60-year-olds with a self-reported chronic (>1 year) motor complete or incomplete traumatic SCI below T6 or a non-traumatic SCI (and presenting with mid to low-level paraplegia) defined according to the International Spinal Cord Injury Data Sets for non-traumatic SCI.¹⁹ Individuals with mid- to low-level paraplegia were the target population

for this study as these individuals often have a full or large level of functionality in their upper limbs, thus permitting the use of controlled amounts of physical activity in the protocols. Participants with injuries below the T5-T6 level of sympathetic innervation were selected as their metabolic response to exercise is interrupted less compared to higher level injuries and they are unlikely to suffer from autonomic dysreflexia. Individuals were excluded if they had hypotension, a history of autonomic dysreflexia, were pregnant, smoked, used glucose lowering medication, or had diabetes, renal failure, liver disease, a history of severe cardiovascular complications or other health issues that could affect their ability to complete the study protocols. All eligibility checks were via participant self-report.

2.3 | Preliminary testing visit

All participants attended a preliminary testing session where body mass (kg) was measured using wheelchair double beam scales (300 series; Marsden) followed by a dual-energy X-ray absorptiometry (DXA) scan (GE Medical Systems) to determine % fat mass of the trunk. The protocol for the DXA measures in this study has been described previously.¹⁸ Briefly, a trained individual conducted the scans and participants were positioned in line with standard protocols as closely as possible. Velcro restraints were used to maintain position of the legs. Trunk fat mass was used to describe adiposity as this is considered a valid measure of central obesity and is associated with poor metabolic health in individuals with SCI.²⁰ Whole body fat is not reported due to several participants not fitting within the scan area. Participants had their resting blood pressure measured, and waist circumference was measured three times (average recorded) using an adjustable tape measure after gentle expiration while supine or while standing for participants able to maintain that posture.

Participants were familiarized with the Borg 6-20 Rating of Perceived Exertion (RPE) scale using standardized verbal instructions from the researchers.²¹ They were asked to focus on the degree of how hard, heavy, and strenuous the physical task was. Participants were required to give their ratings verbally when instructed by the researcher. They were then given instructions on how to perform arm ergometry exercise and practiced doing this for up to two minutes. Following this, participants completed a short (~5-10 minutes) exercise test using the Lode Angio arm ergometer (Lode) to determine a moderate-intensity power output. A moderate-intensity was considered to be an RPE of 13 (somewhat hard). Just prior to the test, the RPE scale was reiterated with reference to the anchors of wording "somewhat hard" as opposed to "light" or "hard." The test started at 20 W, and participants were asked to cycle at ~70 rpm throughout the test. RPE was recorded at the end of each minute, and the resistance (power output) was

then increased by 5-20 W (based on fitness level and RPE change) until an RPE of 13 was achieved. This test was used in line with previous sedentary behavior studies in able-bodied individuals as it provides a more practical approach than a test of maximal oxygen uptake.^{15,16} The Borg 6-20 RPE scale can also be used as a valid and reliable tool to determine physical activity intensity in individuals with SCI.²²

2.4 | Experimental procedures

For each experimental condition, participants attended the laboratory at the same time in the morning following an overnight fast. They were asked not to consume caffeine or alcohol and not to exercise for the preceding 48 hours. A food diary and weighing scales were also provided prior to the first condition so that participants could record their dietary intake for 24 hours beforehand. This intake was then replicated the 24 hours prior to the second condition.

When participants arrived at the laboratory they rested for 5 minutes prior to resting blood pressure being measured. A fasting blood sample was then taken followed by consumption of a standardized breakfast meal. Once the breakfast had been consumed, the 5.5-hour experimental period commenced. Figure 1 shows the protocol for the experimental conditions. The two, 5.5-hour conditions were as follows:

1. Uninterrupted sedentary time (SED): participants remained seated and sedentary throughout this condition in a wheelchair.
2. Sedentary time interrupted with physical activity breaks (SED-ACT): participants performed physical activity for 2 minutes every 20 minutes at ~70 rpm using the Lode Angio arm ergometer. The activity was at the intensity (Watts) that yielded an RPE of 13 during the preliminary testing visit. The ergometer automatically adjusted the resistance to maintain a constant wattage during the activity breaks. Fifteen activity breaks were completed providing a total of 30-minutes of physical activity.

In both conditions, participants undertook sedentary behaviors, such as reading, writing, and using a laptop computer or a tablet, during periods when no activity was required. At 3 hours, participants consumed a standardized lunch meal. In order to minimize activity during each condition, participants were pushed in a wheelchair to the research kitchen to consume the standardized meals and to the lavatory when necessary.

2.5 | Food and water intake

The breakfast and lunch meals were standardized between conditions. Each meal provided 30% of the estimated daily

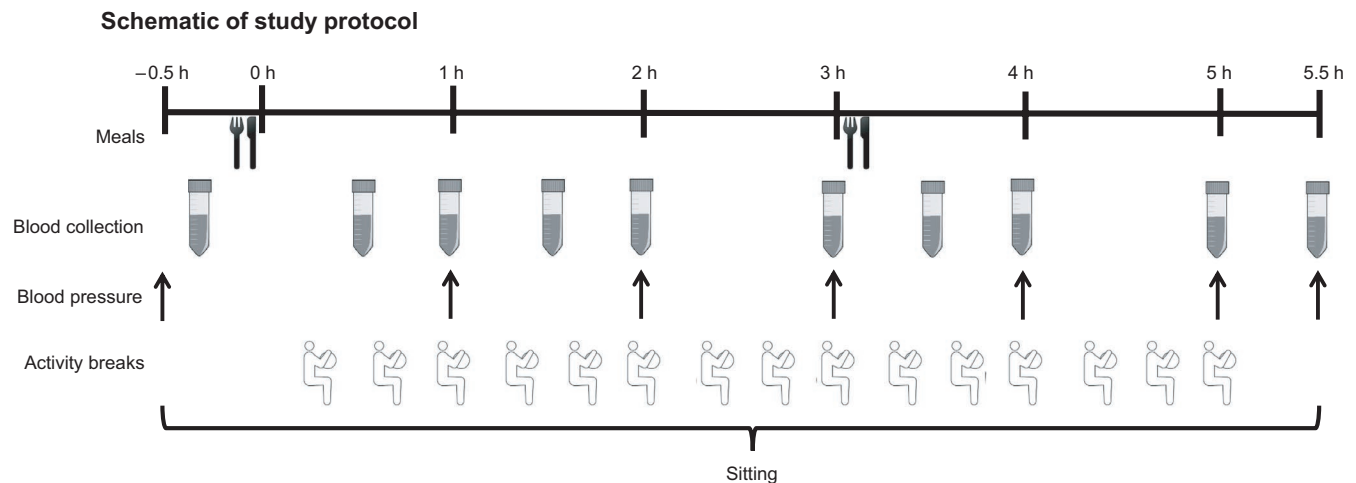


FIGURE 1 Schematic of experimental protocol

energy needs for each individual participant calculated using the Schofield equation²³ The macronutrient composition of the meals is in general agreement with guidelines recommended for a balanced diet.²⁴ The breakfast meal contained 54% carbohydrate (76 ± 11 g), 34% fat (20 ± 3 g), and 12% protein (17 ± 2 g). The lunch meal contained 54% carbohydrate (76 ± 11 g), 31% fat (18 ± 2 g), and 15% protein (21 ± 3 g). Both meals provided 564 ± 78 kcal. The breakfast and lunch meals had a glycaemic index of 43 and 72, respectively. Water intake was ad libitum during the first condition, and the same volume was provided in the second condition.

2.6 | Data collection

2.6.1 | Biochemical analysis

Capillary blood samples were collected via finger prick at baseline and 30, 60, 90, 120, 180, 210, 240, 300, and 330 minutes during the experimental conditions. Samples were taken immediately prior to the last activity bout of each hour in SED-ACT. The YSI 2300 STAT plus glucose and lactate analyzer (YSI) was used to analyze blood glucose concentrations immediately after blood collection. The YSI analyzer is a valid and reliable method with between-batch coefficient of variations ranging from 1.7% to 5.1% and a bias of -1.7% compared with a reference wet chemistry method.²⁵ Triglyceride concentrations were measured from plasma using the Reflotron Plus system (Roche Diagnostics). This system has a day-to-day coefficient of variation of 8.3% and a coefficient of correlation of .97 for triglycerides compared with wet chemistry analyses.²⁶ Remaining plasma was frozen at -80°C , from which insulin concentrations were later measured using an enzyme-linked immunosorbent assay (Mercodia).

2.6.2 | Blood pressure

Blood pressure was measured with an Omron M5-I (Omron Matsusaka) automated device in a seated position. Readings were taken at baseline and then at 60, 120, 180, 240, 300, and 330 minutes. Measurements were performed immediately prior to the last activity bout of each hour in SED-ACT.

2.6.3 | Psychological outcomes

Questionnaires were completed before and after each experimental condition to measure mood, affect, well-being, and social cognitions regarding the participant's ability to avoid prolonged sedentary time. The National Well-being Measurement²⁷ and Warwick Edinburgh Mental Well-Being Scale²⁸ were used to assess psychological well-being. The short Positive and Negative Affect Scale²⁹ measured current mood, and self-efficacy for avoiding prolonged sedentary time was measured using an adapted version of the Schwarzer and Renner Physical Exercise Self-Efficacy Scale.³⁰ Perceived fatigue was assessed at the beginning and end of each experimental condition using a Visual Analogue Scale (VAS) ranging from "0—not fatigued at all" to "10—extremely fatigued." A VAS was also used to evaluate the degree of difficulty in completing each experimental condition ranging from "0—not difficult at all" to "10—extremely difficult." Perceived intensity of the activity breaks in the SED-ACT condition was measured 15 seconds from the end of each activity bout using the Borg RPE scale.

2.7 | Sample size

The sample size was determined using GPower with incremental area under the glucose curve as the primary outcome.

Calculations were based on a previous study in which total area under the glucose curve was attenuated by 16% (effect size, $F = 0.61$) in response to breaking up sitting with walking for 2 minutes every 20 minutes compared with uninterrupted sitting in able-bodied adults.¹⁵ It was anticipated that a smaller effect might be observed in this study due to localized muscle contractions (ie, arm ergometer exercise) vs walking. Therefore, using a more conservative approach, sample size calculations were based on a smaller effect size ($F = 0.40$). Allowing for a within-person correlation of .6, 80% power, and an Alpha level of .05, it was estimated that at least 12 participants would be required. We aimed to recruit 18 participants to allow for dropout.

2.8 | Data analysis

For blood biomarkers, total area under the curve (tAUC) was calculated for the experimental condition period using the trapezoidal method.³¹ The area under the baseline concentration was then subtracted from the tAUC value to provide net incremental area under the curve (iAUC). Due to the breakfast and lunch meals differing in glycaemic index, AUC outcomes were calculated for the total 5.5-hour condition period and separately for the 3-hour breakfast and 2.5-hour lunch postprandial periods. Mean arterial pressure (MAP) was calculated as follows:

$$\text{MAP} \cong P_{\text{Dias}} + \frac{1}{3} (P_{\text{Systolic blood pressure}} - P_{\text{Diastolic blood pressure}}).$$

Each participant's respective net difference for glucose, insulin, triglycerides, and MAP response to breaking up sedentary time with physical activity breaks was calculated by subtracting the iAUC in SED-ACT from SED.

Statistical analysis was conducted using SPSS version 22.0 (SPSS INC.). Q-Q plots were used to assess normality of the data. Baseline insulin values and insulin tAUC for the whole condition were non-normally distributed and log-transformed prior to analysis. These were back transformed to present meaningful descriptive data. Differences between conditions for the primary and secondary outcome variables were determined using linear mixed models with condition and covariates as fixed factors and participants as random factors. It is recommended that 10-15 cases are required per covariate. Based on our sample size of 14, a maximum of one covariate was thus entered into the models. For cardiometabolic and psychological variables, the baseline outcome values were entered as covariates in these models. Data are reported as mean (95% CI) unless stated otherwise. Statistical significance was accepted as $P \leq .05$ and Cohen's f effect sizes of 0.1, 0.25, and 0.4 indicate small, medium, and large effects, respectively.

3 | RESULTS

Recruitment took place on a rolling basis over 17 months between May 2017 and October 2018. Eighteen participants provided consent and were randomized into the study. Four participants withdrew during the study (Figure 2). Analysis was conducted for the 14 participants (see Table 1 for characteristics) who completed all experimental conditions. Of the participants that had a non-traumatic SCI, one had post-polio syndrome and two had vertebral column degenerative disorders.

3.1 | Biochemical and blood pressure outcomes

Postprandial glucose iAUC responses for the 5.5-hour experimental period did not differ between conditions. There were also no differences between conditions for glucose, insulin, and triglycerides AUC or blood pressure variables for the 5.5-hour experimental period (see Table 2) or the breakfast postprandial period (Table S1). However, postprandial glucose iAUC and tAUC for the lunch postprandial period was significantly lower by 37% in SED-ACT compared with SED with a large effect size for this difference (Table 3). Insulin and triglyceride responses did not differ between conditions for the lunch postprandial period. Triglyceride data were not available for one participant during SED-ACT due to insufficient plasma being collected. The glucose, insulin, triglyceride, and MAP responses over time during each condition can be seen in Figure S1.

Figure 3 shows each participant's net glucose, insulin, and triglyceride response for the 5.5-hour experimental period during SED-ACT (difference between SED-ACT and SED) and shows a wide range of responses for each biochemical outcome. Of the 14 participants, 57% ($n = 8$) of participants had attenuated glucose, 64% ($n = 9$) had attenuated insulin, 62% ($n = 8$) had attenuated triglycerides, and 57% ($n = 8$) had attenuated MAP responses during SED-ACT. The net individual biochemical and blood pressure responses for the lunch postprandial period can be seen in Figure S2 and similarly shows a wide range of responses. During this period, 79% ($n = 11$) demonstrated attenuated glucose responses during SED-ACT, while 86% ($n = 12$) and 62% ($n = 8$) demonstrated attenuated insulin and triglyceride responses, respectively, during SED-ACT.

3.2 | Psychological outcomes

Positive affect was significantly higher in SED-ACT than SED (35.8; 95% CI 33.2, 38.4 and 31.0; 28.4, 33.6, respectively; $P = .001$; $F = 0.49$), whereas there was a trend for

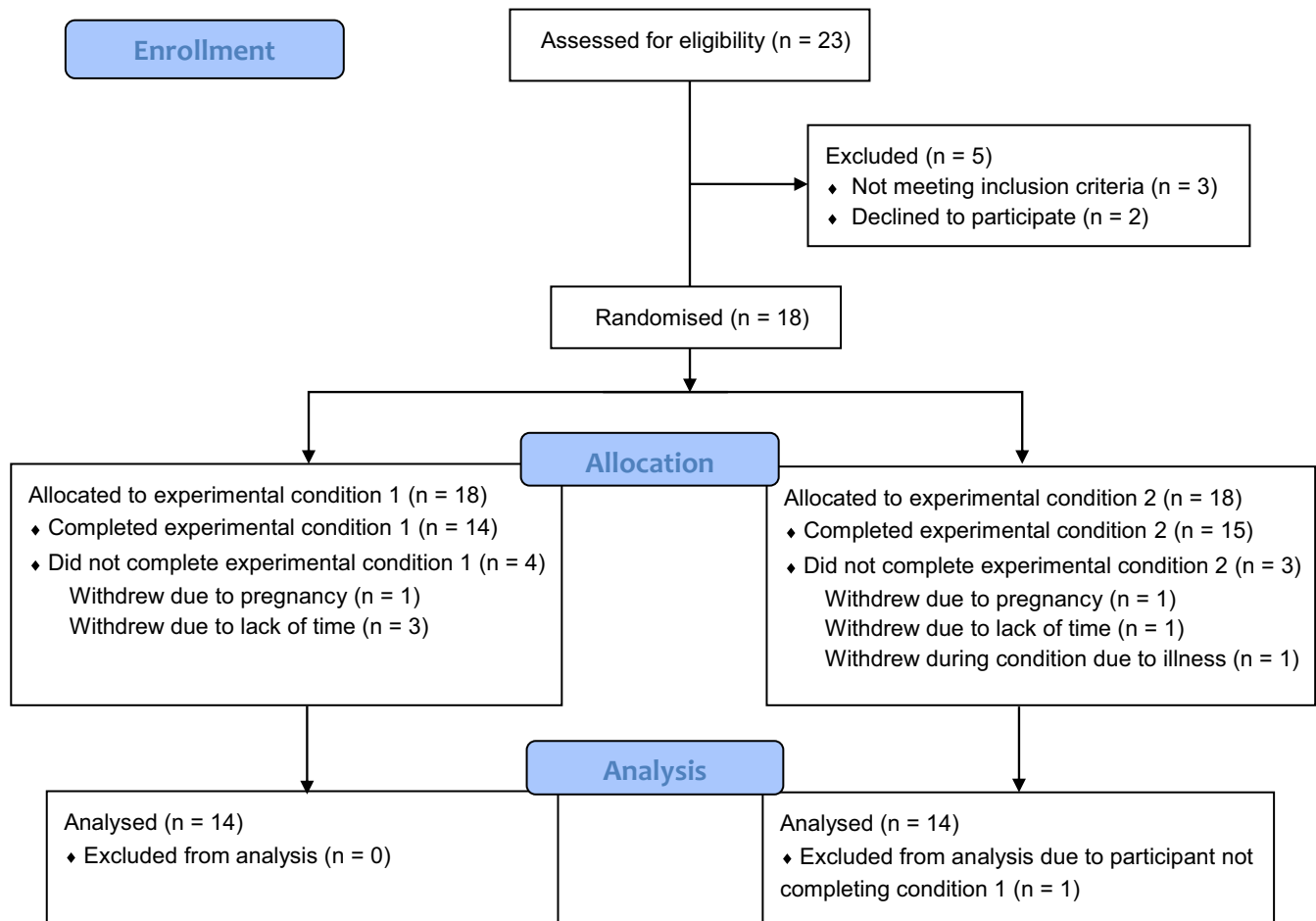


FIGURE 2 CONSORT diagram of participant progression through the study

negative affect being lower in SED-ACT than SED (10.9; 9.6, 12.2, and 12.0; 10.8, 13.3, respectively; $P = .079$; $F = 0.99$). There were no significant differences between conditions for any other psychological outcome ($P > .05$; data not shown). The RPE of the activity breaks in SED-ACT was 13.9 ± 0.5 , which is equivalent to “somewhat hard.”

4 | DISCUSSION

The main findings of this study were that breaking up prolonged sedentary time attenuated postprandial glucose after a lunch meal and may acutely improve psychological well-being in individuals with paraplegia. This is a novel finding as no previous study has investigated CVD risk markers or psychological responses to breaking up sedentary time in individuals with paraplegia.

Acute reductions in postprandial glucose in response to breaks in sedentary time have been consistently reported in able-bodied adults including protocols where sedentary time has been interrupted every 20 minutes with 2 minutes of physical activity, like in the present study, but with light- or moderate-intensity walking.^{15,16,32} The current findings

demonstrated that breaking up sedentary time did not affect glucose levels over a 5.5-hour condition, but there was a 37% attenuation in glucose after lunch. The implications of improved postprandial glucose following a lunch meal, but not breakfast, are not clear. Nevertheless, these findings could be clinically relevant as reductions in postprandial glucose are associated with a significantly lower risk of CVD.³³ It could be postulated that the activity breaks were only effective in attenuating glucose levels after consumption of the high glycaemic index lunch meal relevant to the lower glycaemic index breakfast. However, previous research found that breaking up sitting with 2 minutes of moderate-intensity walking every 20 minutes attenuated postprandial glucose regardless of the glycaemic index of the test meals provided.³² It is also possible that in adults with paraplegia, a higher energy expenditure or longer duration of activity breaks are required to account for the muscular contractions being localized to the arms. Further studies should attempt to determine the factors that may explain the responses seen.

The analysis of individual responses to breaks in sedentary time demonstrated that lunch postprandial glucose and insulin concentrations were attenuated in the majority of participants relative to uninterrupted sedentary time. Although

TABLE 1 Participant characteristics (n = 6 males and n = 8 females)

| | |
|---|-----------------|
| Age (y) | 51 ± 9 |
| Lesion level (n) | |
| T6 | 2 |
| T10 | 2 |
| T11 | 2 |
| T12 | 2 |
| L1 | 1 |
| L2 | 1 |
| L3 | 1 |
| L4 | 1 |
| L5 | 1 |
| Post-polio syndrome | 1 |
| Completeness (n) | |
| Complete injury | 4 |
| Incomplete injury | 10 |
| Nature of injury (n) | |
| Traumatic injury | 11 |
| Non-traumatic injury | 3 |
| Wheelchair user (n) | 9 |
| Ambulatory (n) | 5 |
| Body mass (kg) | 87.9 ± 22.7 |
| Waist circumference (cm) | 100.9 ± 18.2 |
| Trunk fat (%) | 43.5 ± 8.0 |
| Visceral adipose tissue volume (cm ³) | 1592.9 ± 1089.4 |
| Systolic blood pressure (mm Hg) | 128 ± 21 |
| Diastolic blood pressure (mm Hg) | 82 ± 15 |
| Resting heart rate (beats/min) | 75 ± 10 |
| Mean power during physical activity (W) | 53.9 ± 14.8 |

a large proportion of participants had lower insulin levels post-lunch in the SED-ACT condition, there was no difference at the sample level in mean insulin iAUC between the conditions. This could be because the study was not powered to detect changes in insulin. Although the minimum clinically meaningful change in postprandial glucose or insulin to a mixed meal is unknown, breaking up sedentary time could be recommended to individuals with paraplegia to reduce their glucose levels following a high glycaemic index lunch. In terms of practical application of these findings in real-life settings, individuals could break up their sedentary time using arm ergometry (if they have access to this equipment), wheelchair propulsion, or with activities of daily living (eg, cleaning, doing the laundry). However, adequately powered studies testing different protocols (eg, different volumes, intensities, and durations of activity) are needed to conclusively determine the potential cardiometabolic health benefits in this population and the feasibility and practical application of this type of intervention in real-life settings. It would also

be of interest to evaluate the feasibility and effectiveness of breaking up sedentary time relevant to longer duration exercise bouts. This could provide an alternative or complementary intervention strategy for individuals with paraplegia who find it difficult to adhere to structured exercise.

The mechanisms that underpin the attenuation in postprandial glucose that occur in response to breaking up sedentary time are not well understood. This study was unable to explore such mechanisms. Nonetheless, stimulation of the contraction-mediated glucose uptake pathway and increased expression of genes involved in carbohydrate metabolism (eg, dynein light chain, which may regulate GLUT-4 translocation) have been reported in response to breaking up sitting with 2-minute bouts of light- or moderate-intensity walking every 20 minutes in able-bodied individuals.³⁴ Individuals with SCI have decreased muscle fiber area and altered muscle fiber type (predominance of type IIx fibers) below the lesion level.⁴ This may impair insulin-mediated muscle glucose uptake that could occur in response to breaking up sedentary time. Studies are thus required to explore whether attenuated glucose responses are due to muscle and/or insulin-mediated pathways in this population.

There was no difference in triglyceride concentrations or blood pressure in response to breaking up sedentary time vs uninterrupted sedentary time. This is in agreement with studies in healthy able-bodied individuals.^{15,35} However, reductions in triglyceride and blood pressure levels have been observed in other studies with healthy^{36,37} and overweight/obese adults.¹⁷ One study in which triglycerides were attenuated over a single day used larger volumes of physical activity compared to the present study (ie, 20 minutes of light-intensity walking every hour).³⁷ It is thus possible that the lower energy expenditure and localized muscular contractions were insufficient to yield a change in the present study. Other studies that have demonstrated attenuation in postprandial triglycerides were in response to a test meal provided the day after breaking up sitting.³⁶ The activity of lipoprotein lipase, which is a key enzyme responsible for hydrolysis of triglycerides, peaks 8–22 hours following moderate-intensity exercise³⁸ and may explain why single-day protocols, such as in the present study, do not observe changes. Further studies utilizing protocols that expend more energy and are of long enough duration to examine the potential effects of changes in lipoprotein lipase activity are thus required.

In the present study, positive affect was higher in the activity breaks condition and there was also a trend for lower negative affect. Higher levels of physical activity are associated with improved subjective well-being in people with SCI.⁸ The present study suggests that it may also be appropriate to recommend breaks in sedentary time to improve psychological well-being acutely in community-dwelling individuals with paraplegia. This could be a promising finding as previous research has reported that nearly half of people with

TABLE 2 Cardiovascular disease risk marker values for the 5.5-h experimental conditions (n = 14)

| Variable | SED-ACT | SED | P for main effect of condition | Cohen's <i>f</i> effect size |
|---|----------------------|----------------------|--------------------------------|------------------------------|
| Baseline blood glucose (mmol/L) | 5.0 (4.4, 5.6) | 5.0 (4.4, 5.5) | .895 | — |
| Baseline plasma insulin (μ U/mL) | 11.0 (5.8, 16.3) | 11.2 (6.0, 16.4) | .374 | — |
| Baseline triglycerides (mmol/L) | 2.0 (1.5, 2.5) | 2.3 (1.8, 2.8) | .201 | — |
| Baseline mean arterial pressure (mm Hg) | 96.6 (88.2, 105.0) | 97.7 (89.3, 106.1) | .313 | — |
| Baseline systolic blood pressure (mm Hg) | 128.4 (116.9, 139.8) | 129.5 (118.0, 141.0) | .598 | — |
| Baseline diastolic blood pressure (mm Hg) | 80.6 (73.5, 87.8) | 81.9 (74.7, 89.0) | .361 | — |
| Blood glucose iAUC (mmol/L•5.5 h) | 5.1 (2.8, 7.4) | 6.5 (4.2, 8.8) | .275 | 0.16 |
| Blood glucose tAUC (mmol/L•5.5 h) | 33.7 (31.4, 36.0) | 35.1 (32.8, 37.4) | .276 | 0.16 |
| Plasma insulin iAUC (μ U/mL•5.5 h) | 217.1 (165.5, 268.8) | 202.9 (121.3, 284.5) | .753 | 0.08 |
| Plasma insulin tAUC (μ U/mL•5.5 h) | 285.4 (232.6, 338.1) | 262.7 (175.7, 349.8) | .980 | 0.08 |
| Triglyceride iAUC (mmol/L•5.5 h) | 3.5 (1.6, 5.4) | 2.1 (0.3, 4.0) | .194 | 0.26 |
| Triglyceride tAUC (mmol/L•5.5 h) | 16.2 (14.3, 18.1) | 14.8 (13.0, 16.6) | .194 | 0.19 |
| Mean arterial pressure (mm Hg) | 97.1 (96.7, 97.6) | 96.8 (96.4, 97.3) | .310 | 0.18 |
| Systolic blood pressure (mm Hg) | 125.9 (121.5, 130.3) | 123.9 (119.4, 128.3) | .366 | 0.12 |
| Diastolic blood pressure (mm Hg) | 76.6 (74.4, 78.9) | 76.8 (74.5, 79.0) | .934 | 0.03 |

Note: Data are mean (95% CI).

Abbreviations: iAUC, incremental area under the curve; SED, uninterrupted sedentary time; SED-ACT, sedentary time interrupted with physical activity breaks; tAUC, total area under the curve.

SCI sampled reported mental health problems.⁹ The effects of breaking up sedentary time in individuals with paraplegia should thus be evaluated in chronic interventions to explore the potential for long-term improvements in psychological well-being and postprandial metabolic responses.

The strengths of this study include the randomized cross-over design and inclusion of a range of CVD risk markers and psychological outcomes to assess the potential benefits of breaking up prolonged sedentary time. Further strengths include the controlled laboratory environment in which the meals consumed throughout the day were standardized and the standardization of diet and exercise prior to the experimental conditions. Future studies are required to establish whether breaking up sedentary time can be achieved in

free-living settings in the long-term and the chronic effects of such interventions. These interventions could evaluate the use of wheelchair propulsion as the activity mode as opposed to arm cranking, which was used in the present study in order to standardize the exercise intensity of each bout. Furthermore, the generalizability of the findings may be limited due to more females than males being included, which does not reflect the higher male to female ratio reported in the SCI population literature.² Another limitation of this study is the lack of information on the participants' physical activity levels, which could be important in determining the health benefits of reducing sedentary behavior.³⁹ Although this study included only individuals with injuries below T6 and employed a randomized crossover design, the sample

| Variable | SED-ACT | SED | <i>P</i> for main effect of condition | Cohen's <i>f</i> effect size |
|-----------------------------------|----------------------|----------------------|---------------------------------------|------------------------------|
| Blood glucose iAUC (mmol/L•2.5 h) | 1.9 (1.0, 2.7) | 3.0 (2.1, 3.9) | .015 | 0.34 |
| Blood glucose tAUC (mmol/L•2.5 h) | 15.3 (14.4, 16.1) | 16.4 (15.5, 17.2) | .015 | 0.34 |
| Plasma insulin iAUC (μU/mL•2.5 h) | 38.0 (−8.9, 84.8) | 57.7 (10.8, 104.5) | .122 | 0.11 |
| Plasma insulin tAUC (μU/mL•2.5 h) | 128.5 (101.4, 155.5) | 127.7 (100.7, 154.7) | .949 | 0.05 |
| Triglyceride iAUC (mmol/L•2.5 h) | 1.1 (0.23, 2.0) | 1.4 (0.6, 2.3) | .482 | 0.09 |
| Triglyceride tAUC (mmol/L•2.5 h) | 8.3 (7.4, 9.2) | 8.6 (7.8, 9.5) | .482 | 0.09 |

Note: Data are mean (95% CI). Bold *P* values indicate significant difference between SED-ACT and SED.

Abbreviations: iAUC, incremental area under the curve; SED, uninterrupted sedentary time; SED-ACT, sedentary time interrupted with physical activity breaks; tAUC, total area under the curve.

TABLE 3 Cardiovascular disease risk marker values for the lunch postprandial period (n = 14)

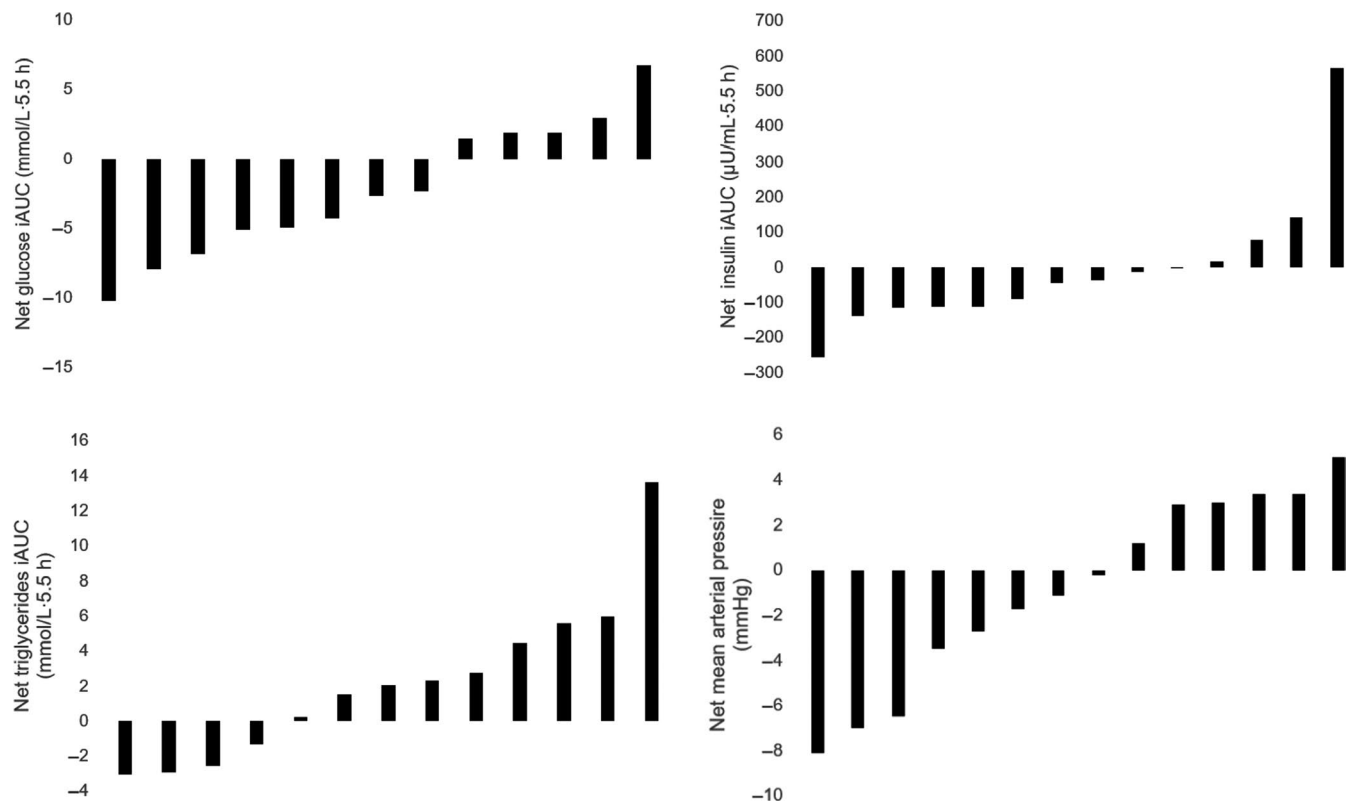


FIGURE 3 Net individual glucose, insulin, triglyceride, and mean arterial pressure responses during sedentary time interrupted with physical activity breaks (difference between breaks in sedentary time and uninterrupted sedentary time conditions). Each individual data point represents the response for a single study participant. Values above zero indicate increased concentrations in response to sedentary time interrupted with physical activity breaks; values less than zero indicate decreased concentrations in response to sedentary time interrupted with physical activity breaks. iAUC, incremental area under the curve

comprised of participants with complete and incomplete as well as traumatic and non-traumatic injuries, males and females, wheelchair, and non-wheelchair users. Furthermore, individuals who can walk are unable to constrict movement to only the arms/upper body when performing arm-cranking

exercise. This may have affected the standardization of the arm ergometer exercise between participants. This heterogeneity could influence the findings. However, this could also enhance external validity of the general SCI population, which is largely heterogeneous. It is difficult to ascertain

whether the single preliminary exercise test and short familiarization of the RPE scales was sufficient to anchor an RPE of 13. This may be a desirable line of enquiry for future work extending upon previous research reporting promising use of RPE during submaximal exercise in persons with an SCI.⁴⁰ Lastly, the effects of breaking up sitting time with walking in some previous studies with able-bodied individuals have yielded smaller effect sizes than that used to estimate the sample size for this study.¹⁶ This study may have thus been underpowered for the primary outcome.

In conclusion, this study suggests that breaking up sedentary time may attenuate postprandial glucose levels following lunch and improve psychological well-being acutely in individuals with chronic paraplegia. As engagement in regular exercise is poor, breaking up sedentary time should be further investigated as a potential intervention strategy for reducing CVD risk in this population. This would help to further inform physical activity and clinical care guidelines for individuals with chronic paraplegia.

5 | PERSPECTIVES

Breaking up prolonged sedentary time with short, regular bouts of moderate-intensity arm ergometer physical activity improved postprandial glucose responses following a lunch meal and acutely improved psychological well-being in individuals with paraplegia. This supports previous findings in able-bodied individuals in which breaking up sitting time with light or moderate-intensity walking reduced postprandial glucose levels over a single day. The results here suggest that breaking up prolonged sedentary time should be further explored as a potential intervention to improve cardiovascular health and psychological well-being in people with paraplegia.

ACKNOWLEDGEMENT

This work was supported by Heart Research UK under Grant [number RG2655/17/18].

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ORCID

Daniel P. Bailey  <https://orcid.org/0000-0003-3772-630X>
Vicky L. Goosey-Tolfrey  <https://orcid.org/0000-0001-7203-4144>

REFERENCES

- Lee BB, Cripps RA, Fitzharris M, Wing PC. The global map for traumatic spinal cord injury epidemiology: update 2011, global incidence rate. *Spinal Cord*. 2014;52(2):110-116.
- Singh A, Tetreault L, Kalsi-Ryan S, Nouri A, Fehlings MG. Global prevalence and incidence of traumatic spinal cord injury. *Clin Epidemiol*. 2014;6:309-331.
- New PW, Sundararajan V. Incidence of non-traumatic spinal cord injury in Victoria, Australia: a population-based study and literature review. *Spinal Cord*. 2008;46(6):406-411.
- Gorgey AS, Dolbow DR, Dolbow JD, Khalil RK, Castillo C, Gater DR. Effects of spinal cord injury on body composition and metabolic profile – part I. *J Spinal Cord Med*. 2014;37(6):693-702.
- Bauman WA, Spungen AM. Disorders of carbohydrate and lipid metabolism in veterans with paraplegia or quadriplegia: a model of premature aging. *Metabolism*. 1994;43(6):749-756.
- Nash MS, DeGroot J, Martinez-Arizala A, Mendez AJ. Evidence for an exaggerated postprandial lipemia in chronic paraplegia. *J Spinal Cord Med*. 2005;28(4):320-325.
- Martin Ginis KA, van der Scheer JW, Latimer-Cheung AE, et al. Evidence-based scientific exercise guidelines for adults with spinal cord injury: an update and a new guideline. *Spinal Cord*. 2018;56(4):308-321.
- Martin Ginis KA, Jetha A, Mack DE, Hetz S. Physical activity and subjective well-being among people with spinal cord injury: a meta-analysis. *Spinal Cord*. 2010;48(1):65-72.
- Migliorini C, Tonge B, Taleporos G. Spinal cord injury and mental health. *Aust N Z J Psychiatry*. 2008;42(4):309-314.
- Flank P, Fahlstrom M, Bostrom C, Lewis JE, Levi R, Wahman K. Self-reported physical activity and risk markers for cardiovascular disease after spinal cord injury. *J Rehabil Med*. 2014;46(9):886-890.
- Department of Health & Social Care. UK Chief Medical Officers' Physical Activity Guidelines; 2019. <https://www.gov.uk/government/publications/physical-activity-guidelines-uk-chief-medical-officers-report>. Accessed 9 September 2019.
- Bailey DP, Hewson DJ, Champion RB, Sayegh SM. Sitting time and risk of cardiovascular disease and diabetes: a systematic review and meta-analysis. *Am J Prev Med*. 2019;57(3):408-416.
- Hamilton MT, Healy GN, Dunstan DW, Zderic TW, Owen N. Too little exercise and too much sitting: inactivity physiology and the need for new recommendations on sedentary behavior. *Curr Cardiovasc Risk Rep*. 2008;2(4):292-298.
- Nightingale TE, Williams S, Thompson D, Bilzon JJJ. Energy balance components in persons with paraplegia: daily variation and appropriate measurement duration. *Int J Behav Nutr Phys Act*. 2017;14(1):132.
- Bailey DP, Locke CD. Breaking up prolonged sitting with light-intensity walking improves postprandial glycemia, but breaking up sitting with standing does not. *J Sci Med Sport*. 2015;18(3):294-298.
- Dunstan DW, Kingwell BA, Larsen R, et al. Breaking up prolonged sitting reduces postprandial glucose and insulin responses. *Diabetes Care*. 2012;35(5):976-983.
- Larsen RN, Kingwell BA, Sethi P, Cerin E, Owen N, Dunstan DW. Breaking up prolonged sitting reduces resting blood pressure in overweight/obese adults. *Nutr Metab Cardiovasc Dis*. 2014;24(9):976-982.
- Withers TM, Croft L, Goosey-Tolfrey VL, Dunstan DW, Leicht CA, Bailey DP. Cardiovascular disease risk marker responses to breaking up prolonged sedentary time in individuals with paraplegia: the Spinal Cord Injury Move More (SCIMM) randomised crossover laboratory trial protocol. *BMJ Open*. 2018;8(6):e021936.
- New PW, Marshall R. International spinal cord injury data sets for non-traumatic spinal cord injury. *Spinal Cord*. 2014;52(2):123-132.

20. Gorgey AS, Gater DR. Regional and relative adiposity patterns in relation to carbohydrate and lipid metabolism in men with spinal cord injury. *Appl Physiol Nutr Metab*. 2011;36(1):107-114.
21. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982;14(5):377-381.
22. van der Scheer JW, Hutchinson MJ, Paulson T, Martin Ginis KA, Goosey-Tolfrey VL. Reliability and validity of subjective measures of aerobic intensity in adults with spinal cord injury: a systematic review. *PM R*. 2018;10(2):194-207.
23. Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr*. 1985;39(Suppl 1):5-41.
24. Public Health England. Government Dietary Recommendations: Government recommendations for food energy and nutrients for males and females aged 1 – 18 years and 19+ years. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/547050/government_dietary_recommendations.pdf. Accessed 9 November 2016.
25. Johnson RN, Baker JR. Error detection and measurement in glucose monitors. *Clin Chim Acta*. 2001;307(1-2):61-67.
26. Rohac M, Gabl F. Comparison of two solid phase chemistry systems: Reflotron and Ektachem DT 60. *Clin Chem Lab Med*. 1987;25:811.
27. Tinkler L. Measuring National Well-being: Personal Well-being in the UK, 2014 to 2015. <https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing/bulletins/measuringnationalwellbeing/2015-09-23>. Accessed 10 October 2016.
28. Tennant R, Hiller L, Fishwick R, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes*. 2007;5(1):63.
29. Thompson ER. Development and validation of an internationally reliable short-form of the Positive and Negative Affect Schedule (PANAS). *J Cross Cult Psychol*. 2016;38(2):227-242.
30. Schwarzer R, Renner B. Social-cognitive predictors of health behavior: action self-efficacy and coping self-efficacy. *Health Psychol*. 2000;19(5):487-495.
31. Matthews JN, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. *BMJ*. 1990;300(6719):230-235.
32. Bailey DP, Maylor BD, Orton CJ, Zakrzewski-Fruer JK. Effects of breaking up prolonged sitting following low and high glycaemic index breakfast consumption on glucose and insulin concentrations. *Eur J Appl Physiol*. 2017;117(7):1299-1307.
33. O'Keefe JH, Bell DS. Postprandial hyperglycemia/hyperlipidemia (postprandial dysmetabolism) is a cardiovascular risk factor. *Am J Cardiol*. 2007;100(5):899-904.
34. Latouche C, Jowett JBM, Carey AL, et al. Effects of breaking up prolonged sitting on skeletal muscle gene expression. *J Appl Physiol*. 2013;114(4):453-460.
35. Peddie MC, Bone JL, Rehner NJ, Skeaff CM, Gray AR, Perry TL. Breaking prolonged sitting reduces postprandial glycemia in healthy, normal-weight adults: a randomized crossover trial. *Am J Clin Nutr*. 2013;98(2):358-366.
36. Miyashita M, Burns SF, Stensel DJ. Accumulating short bouts of brisk walking reduces postprandial plasma triacylglycerol concentrations and resting blood pressure in healthy young men. *Am J Clin Nutr*. 2008;88(5):1225-1231.
37. Champion RB, Smith LR, Smith J, et al. Reducing prolonged sedentary time using a treadmill desk acutely improves cardiometabolic risk markers in male and female adults. *J Sports Sci*. 2018;36(21):2484-2491.
38. Greiwe JS, Holloszy JO, Semenkovich CF. Exercise induces lipoprotein lipase and GLUT-4 protein in muscle independent of adrenergic-receptor signaling. *J Appl Physiol*. 2000;89(1):176-181.
39. Zhao R, Bu W, Chen Y, Chen X. The dose-response associations of sedentary time with chronic diseases and the risk for all-cause mortality affected by different health status: a systematic review and meta-analysis. *J Nutr Health Aging*. 2020;24(1):63-70.
40. Goosey-Tolfrey V, Lenton J, Goddard J, Oldfield V, Tolfrey K, Eston R. Regulating intensity using perceived exertion in spinal cord-injured participants. *Med Sci Sports Exerc*. 2010;42(3):608-613.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Bailey DP, Withers TM, Goosey-Tolfrey VL, et al. Acute effects of breaking up prolonged sedentary time on cardiovascular disease risk markers in adults with paraplegia. *Scand J Med Sci Sports*. 2020;30:1398–1408. <https://doi.org/10.1111/sms.13671>