Recovery Off-Kinetics Following Exhaustive Upper Body Exercise in Spinal Cord Injury

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Background: People with spinal cord injury (SCI) present with impaired autonomic control when the lesion is above T6. This could lead to delayed cardiorespiratory recovery following vigorous physical activity. **Objectives:** To characterize and compare gas exchange off-kinetics following exhaustive exercise in individuals with SCI and an apparently healthy control group. **Methods:** Participants were 19 individuals with SCI who presented with the inability to voluntarily lift their legs against gravity (age, 44.6 ± 14.2 years; AIS A, $n = 5$; AIS B, $n = 7$; AIS C, $n = 7$; paraplegia, $n = 14$; tetraplegia, $n = 5$) and 10 healthy comparisons (COM; age, 30.5 ± 5.3 years). All participants performed an arm ergometer cardiopulmonary exercise test (aCPET) to volitional exhaustion followed by a 10-minute passive recovery. O_2 uptake ($\dot{V}\text{O}_2$) and CO_2 output ($\dot{V}\text{CO}_2$) off-kinetics was examined using a mono-exponential model in which τ_{off} (τ_{off}) and mean response time (MRT) were determined. The off-kinetics transition constant (Kt_{off}) was calculated as $\Delta\dot{V}\text{O}_2/\text{MRT}$. Student t tests were used to compare SCI versus COM group means. **Results:** COM had a significantly higher relative peak $\dot{V}\text{O}_2$ compared to SCI (1.70 ± 0.55 L/min vs 1.19 ± 0.51 L/min, $p = .019$). No difference was observed for τ_{off} between the groups, however Kt_{off} for both $\dot{V}\text{O}_2$ and $\dot{V}\text{CO}_2$ was significantly lower in the SCI compared to the COM group. **Conclusion:** A reduced Kt_{off} during recovery may suggest inefficiencies in replenishing muscle ATP stores and lactate clearance in these participants with SCI. These findings may contribute to the observed lower cardiorespiratory fitness and greater fatigability typically reported in individuals with SCI. **Key words:** off-kinetics, recovery kinetics, spinal cord injury

Spinal cord injury (SCI) can result in impaired autonomic and somatic nervous system function, the severity of which is dependent on the location and completeness of the injury.¹⁻³ Physical and physiological impairments associated with SCI include muscle weakness and paralysis, altered skeletal innervation,⁴ cardiovascular and pulmonary dysregulation,⁵ as well as possible deficits in muscle oxygenation.^{6,7} A reduction in muscle mass and altered sympathetic drive have also been associated with lower exercise capacity in those with SCI compared to a healthy non-injured comparison group,⁸ which may increase the perception of fatigue during activities of daily living. Indeed, individuals with SCI have been reported to display greater levels of fatigue and fatigability during everyday tasks,^{9,10} which highlights the importance of understanding the role of recovery from physical activity in this population.

Recovery following physical activity is a determinant of the ability to participate in subsequent bouts of intermittent physical activity¹¹

and is an important component of cardiorespiratory fitness.¹² Faster oxidative recovery is proposed to lessen the oxygen deficit following strenuous activity, lowering the reliance on substrate level metabolism as an energy supplement,¹¹ thus providing for faster ATP repletion and decreased accumulation of metabolic acids. Reduction of the oxygen deficit could lead to lower levels of accumulated fatigue, resulting in a greater ability to perform subsequent bouts of physical activity. The process of recovery from physical activity is not well understood in people who have SCI as few studies have examined this outcome.

Recovery from strenuous exercise has been studied primarily in healthy uninjured individuals with a neurologically intact spinal cord, utilizing lower limb exercise.¹³⁻¹⁶ Further, these studies were conducted in participants with high cardiorespiratory fitness (average peak $\dot{V}\text{O}_2 \geq 60$ mL/kg/min),^{13,14} and none had used an arm ergometer to elicit a maximal effort. To our knowledge, only three studies have examined cardiorespiratory

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Figure 1. Differences in τ_{off} and mean response time (MRT) for spinal cord injury (SCI), paraplegia (PP), tetraplegia (TP), and control (COM) groups. *Significant difference between COM and SCI, $p < .05$. †Significant difference between COM and TP.

Figure 2. $\dot{V}O_2-Kt_{off}$ (mL/min/s) and $\dot{V}CO_2-Kt_{off}$ (mL/min/s). *Significant difference between control (COM) and spinal cord injury (SCI), $p < .05$. †Significant difference between COM and tetraplegia (TP). ‡Significant difference between COM and paraplegia (PP). §Significant difference between PP and TP.

recovery kinetics following a constant work rate test in participants with SCI.^{3,17,18} Barstow et al.¹⁷ observed the rate of oxidative recovery was slower following leg exercises using electrical stimulation as compared to volitional arm exercise, despite no significant difference in percent of peak $\dot{V}O_2$ achieved during exercise. Fukuoka et al.³ highlighted the possible beneficial impact of training status on $\dot{V}O_2$ off-kinetics, where well-trained participants with SCI had faster $\dot{V}O_2$ off-kinetics compared to an untrained healthy reference group during arm exercise. Improved cardiorespiratory fitness and faster $\dot{V}O_2$ off-kinetics was demonstrated by Fukuoka et al.,¹⁸ whereby 60 days of specific

wheelchair training resulted in faster $\dot{V}O_2$ off-kinetics during constant work rate tests. Recovery kinetics for these studies were examined following moderate-intensity exercise, however recovery from fatiguing volitional exercise has not been explored in those with SCI. The manner of oxidative recovery following exhaustive exercise may give insight into the system's ability to return to a state of oxidative homeostasis, which may be important in the performance of subsequent bouts of physical activity and highlights the need for examination of recovery following volitional exercise to fatigue in the SCI population.

The current study aimed to characterize $\dot{V}O_2$ and $\dot{V}CO_2$ off-kinetics following exhaustive arm exercise in individuals with SCI. Measures of $\dot{V}O_2$ and $\dot{V}CO_2$ off-kinetics were compared between groups of individuals with and without SCI following an arm ergometer cardiopulmonary exercise test (aCPET) to volitional exhaustion. It was hypothesized that $\dot{V}O_2$ and $\dot{V}CO_2$ off-kinetics would be prolonged in persons with SCI.

Methods

Participants with SCI (including paraplegia [PP] and tetraplegia [TP]) and comparison group (COM) of participants who did not have SCI were included in this study. Approval for this study was granted by the local institutional review boards of the participating institutions prior to recruitment, enrollment, and the outset of data collection.

Figure 3. Pearson correlation between physical fitness [$\dot{V}O_2$ (L/min)] and recovery [$\dot{V}O_2-Kt_{off}$ (mL/min/s)]. $r = -0.94$, $p > .001$ (• spinal cord injury [SCI] and ◊ control [COM]).

Table 1. Inclusion and exclusion criteria for the spinal cord injury (SCI) and control (COM) groups

SCI	COM
Inclusion	Inclusion
<ol style="list-style-type: none"> 1. Age 18 years or older. 2. Nonprogressive SCI 3. C5 function in both arms (i.e., bilateral elbow flexion manual muscle test ≥ 3) (3 = full ROM against gravity) 4. All AIS lower extremity muscles ≤ 2 (2 = full ROM gravity eliminated) 5. Answer no to all PARQ+ questions; infarction or medical clearance from primary physician if answer yes to any question 	<ol style="list-style-type: none"> 1. Age 18 years or older. 2. Answer “no” to all PARQ+ questions; infarction or medical clearance from primary physician if answered yes to any question
Exclusion	Exclusion
<ol style="list-style-type: none"> 1. ≤ 6 months (180 days) post SCI onset 2. Currently hospitalized 3. Current pressure sore/wound on a support surface 4. Significant shoulder pain during daily activities (Wheelchair Users Shoulder Pain Index >60) 5. Resting heart rate ≥ 120 bpm 6. Systolic blood pressure >180 mm Hg and/or diastolic blood pressure >100 mm Hg 7. Self-reported history of unstable angina or myocardial infarction within the previous month 	<ol style="list-style-type: none"> 1. Currently hospitalized 2. Resting heart rate ≥ 120 bpm 3. Systolic blood pressure >180 mm Hg and/or diastolic blood pressure >100 mm Hg 4. Self-reported history of unstable angina or myocardial infarction within the previous month 5. Answered “yes” to one or more questions on PARQ+ and not cleared by physician

Note: AIS = American Spinal Injury Association Impairment Scale; PARQ+ = Physical Activity Readiness Questionnaire; ROM = range of motion.

Participants were recruited as a convenience sample from the greater Washington, DC, and Northern Virginia areas of the United States. All participants were screened for the presence of inclusion and exclusion criteria (**Table 1**). Participants meeting all the inclusion criteria and lacking an exclusion criterion provided written informed consent and were enrolled in the study. The Physical Activity Readiness Questionnaire (PARQ+)¹⁹ was completed by the COM group during the informed consent process to ensure safe participation in exercise. SCI participants completed a sacral sparing self-report questionnaire²⁰ in order to calculate the American Spinal Injury Association Impairment Scale (AIS). Participants' height, weight, and resting vitals were recorded prior to the exercise test. Height for the

SCI group was measured while participants lay supine, while the height for COM participants were made using a stadiometer. Weight was taken on a digital floor scale, as the SCI group could be wheeled directly onto the scale.

Participants then performed an arm ergometer (Monark Rehab Trainer 881E, Sweden) cardiopulmonary exercise test (aCPET) to volitional exhaustion in one laboratory session. The starting resistance (between 5 and 35 Watts) and increment (5-10 Watts each minute) was based on the SCI participants' level of function and injury level, whereas the COM group was classified based on activity level alone. The activity level of the COM participants was based on self-reported weekly physical activity. The aCPET work-rate increment

was designed to ensure volitional exhaustion was achieved between 8 and 12 minutes. Participants were instructed to begin arm cranking at a rate of 50 rpm and to sustain this pedaling rate throughout the test. When participants could no longer maintain the designated cadence despite strong verbal encouragement from research staff (volitional exhaustion), the test was ended, and participants were asked to remain seated and quiet for another 10 minutes for continued collection of post-exercise pulmonary gas exchange and heart rate.

Breath-by-breath pulmonary gas exchange was measured in the COM group using a breath-by-breath gas exchange analysis system (Cardio2 Ultima; Medical Graphics Corp, St. Paul, MN) and in the individuals with SCI using a dynamic mixing chamber metabolic system (TrueOne 2400; Parvo Medics, East Sandy, UT). Participants were fit with either a nose clip and mouthpiece or a face mask and were instructed to breathe normally throughout the test. The mouthpiece and face mask were connected to the cardiopulmonary testing system by a pneumotach and umbilical cord. Prior to the testing session, calibration of the metabolic measurement system was performed according to standardized procedures using known concentration of gases and flow volumes. Heart rate (HR) was recorded beat-by-beat using a standard 12-lead electrocardiograph (Mortara Instruments Inc., Milwaukee, WI, or Quinton Q-Stress Test System, Vista, CA) with the electrodes placed in the Mason-Likar modification. Cardiopulmonary and HR responses were measured continuously and recorded during 5 minutes of quiet baseline rest, exercise to volitional exhaustion, and 10 minutes of seated passive recovery immediately following the aCPET.

Peak oxygen consumption ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), and respiratory exchange ratio (RER) were determined as an average of the last eight breaths of the highest work rate achieved. Raw $\dot{V}O_2$ and $\dot{V}CO_2$ data were time aligned to the start of recovery and fit with a 99% prediction band. Based on visual inspection, any data point falling outside the prediction band was excluded from future analysis as these were believed to be unrelated to the postexercise recovery response (e.g., the participant coughing or talking during data collection). Data

were then linearly interpolated to produce a data point for each second and averaged into 5-second time bins. $\dot{V}O_2$ off-kinetics was determined using a curvilinear least-squares fitting procedure (Origin Lab, 2017, Northampton, MA) according to the following function^{9,18}:

$$\dot{V}O_2(t) = \dot{V}O_2(EndEx) + \Delta \dot{V}O_2 (1 - \exp^{-(t-TD)/\tau_{off}})$$

Where $\dot{V}O_2(t)$ is the $\dot{V}O_2$ at any point during the recovery period, $\dot{V}O_2(EndEx)$ is the average $\dot{V}O_2$ from the last 30 seconds of exercise, $\Delta \dot{V}O_2$ is the amplitude of decay in $\dot{V}O_2$ from end of exercise to end of recovery, TD is the time delay, and τ_{off} is the time constant (time taken to reach 63% of the recovery response). Mean response time (MRT) was calculated by summing the TD and τ_{off} , which represented the overall magnitude of decay in the $\dot{V}O_2$ recovery response. The off-kinetics transition constant (Kt_{off}) was calculated as $\Delta \dot{V}O_2 / MRT$ (mL/min/s). As an off-kinetics index, Kt_{off} is a deceleration analog that normalizes the transition as a ratio of the amplitude of the transition decline in $\dot{V}O_2$ to the time constant of the transition. The higher the Kt_{off} the more rapid the recovery toward preexercise baseline levels of $\dot{V}O_2$ after subtracting a phase delay from the mean response time.¹³ The model was then fit from the beginning of Phase II to the end of the 10-minute recovery period. Phase I of the response was identified based on visual identification of the first downward deflection of the $\dot{V}O_2$ curve, and a Phase II fit was confirmed by minimization of the residuals. $\dot{V}CO_2$ off-kinetics were determined using a method identical to the one used for determination of $\dot{V}O_2$ off-kinetics by replacing $\dot{V}O_2$ with $\dot{V}CO_2$ in the equation.

HR values were recorded at rest, during exercise, and at the recovery period. Maximal HR was taken as the last HR obtained at the cessation of exercise, and recovery HR was represented each minute by the HR recorded at the end of each minute. The HR decrease during the recovery period was determined by subtracting the HR at minute 10 of recovery from the maximal HR achieved at the end of exercise.

Group differences at peak exercise ($\dot{V}O_{2peak}$, $\dot{V}CO_{2peak}$, RER, total exercise time, work rate [WR], HR), as well as $\dot{V}O_2$ and $\dot{V}CO_2$ off-kinetic parameters were statistically analyzed for significance using Student *t* tests. The SCI group was further divided

into subgroups of paraplegia (PP) and tetraplegia (TP). A one-way analysis of variance (ANOVA) was used to analyze differences in the $\dot{V}O_2$ and $\dot{V}CO_2$ off-kinetic parameters between the three groups, with a Tukey post hoc test to examine where differences occurred. Analysis of covariance (ANCOVA) was used to determine significant group differences in HR during recovery using maximal HR as the covariate and peak exercise variables ($\dot{V}O_{2peak}$, $\dot{V}CO_{2peak}$, RER, total exercise time, work rate) using age as a covariate. Pearson's product correlation was used to identify correlative relationships

Table 2. Variables during maximal exercise and recovery for spinal cord injury (SCI) and control (COM) groups

	SCI	COM
Maximal exercise		
$\dot{V}O_{2peak}$ (L/min)	1.19 (0.51)*	1.70 (0.55)
$\dot{V}CO_{2peak}$ (L/min)	1.40 (0.68)*	2.18 (0.62)
Peak work rate (Watts)	50.5 (28.7)	61.0 (26.3)
Total exercise time (seconds)	363 (123)*	477 (113)
RER	1.11 (0.13)*	1.3 (0.14)
Maximal HR (bpm)	131 (30)*	162 (15)
Recovery variables		
ΔHR (bpm)	58 (13)*	47 (21)
$\dot{V}O_2-Kt_{off}$ (mL/min/s)	-11.67 (7.8)*	-22.4 (8.03)
MRT (seconds)	84.69 (28.38)*	59.80 (9.63)
$\Delta \dot{V}O_2$ (L/min)	-0.85 (0.431)*	-1.32 (0.472)
$\dot{V}O_2$ TD (seconds)	18 (17.25)	11.02 (8.43)
τ_{off} (seconds)	66.7 (31.55)	48.78 (10.58)
$\dot{V}CO_2-Kt_{off}$ (mL/min/s)	-9.88 (6.79)*	-18.47 (6)
MRT- $\dot{V}CO_2$ (seconds)	128.53 (52.69)	98.64 (21.82)
$\Delta \dot{V}CO_2$ (L/min)	-1.0643*	-1.7585
$\dot{V}CO_2$ TD (seconds)	16.19 (33.7)	11.61 (15.54)
$\tau_{off}-\dot{V}CO_2$ (seconds)	112.34 (42.04)	87.03 (13.95)

Note: HR = heart rate; MRT = mean response time; RER = respiratory exchange ratio; TD = time delay.

*Significantly different from COM, $p < .05$.

between $\dot{V}O_{2peak}$ and $\dot{V}O_2$ off-kinetic parameters. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, NY). All data are presented as mean $\pm$ SD. Significance was accepted at $p \leq .05$ for two-tailed hypotheses.

Results

The group with SCI was comprised of 19 participants (PP, $n = 14$; TP, $n = 5$) with nonprogressive SCI or spinal cord disease who were at least 6 months postinjury and unable to voluntarily lift their legs against gravity. Of the five participants in the TP subset, three had incomplete cervical injuries and all used power wheelchairs. The TP subset on average had a 52% lower WR than the PP group. The COM was comprised of 10 apparently healthy individuals. There was no significant difference between the groups for weight, height, or body mass index (BMI), although participants with SCI were significantly older ($p = .006$) than the participants in COM.

Due to difficulty in obtaining accurate HR during maximal exercise on the arm ergometer, two of the participants in the SCI group (1 PP, 1 TP) were excluded from the HR data analysis, leaving 17 participants with SCI with complete HR data. There was no significant difference in preexercise HR between COM and SCI (81 ± 8 vs 77 ± 12 bpm). Peak HR was 23% higher ($p = .001$) in the participants with COM than SCI (Table 2). After controlling for peak HR, the decrease in HR after exercise was significantly greater in COM than SCI (58 ± 13 vs 47 ± 21 bpm) at 10 minutes of recovery (Table 2).

Peak $\dot{V}O_2$, $\dot{V}CO_2$, total exercise time, and RER were significantly higher for COM compared to the SCI group (Table 2). Figures 1 and 2 depict the off-kinetic outcomes for COM and SCI, including the PP ($n = 14$) and TP ($n = 5$) phenotypes in the SCI group. One SCI participant was excluded from the $\dot{V}CO_2-Kt_{off}$ analysis as a curve could not be fit to the data. Significant differences in the $\dot{V}O_2$ off-kinetic parameters for $\Delta \dot{V}O_2$, MRT, and Kt_{off} and $\dot{V}CO_2$ off-kinetic parameters for $\Delta \dot{V}CO_2$ and Kt_{off} were observed between SCI and COM (Table 2). There was no difference in τ_{off} for $\dot{V}O_2$ or $\dot{V}CO_2$ in either group. The SCI group was older compared to

COM, yet the difference in $\dot{V}_{O_2}\text{-}K_{t\text{off}}$ and $\dot{V}_{CO_2}\text{-}K_{t\text{off}}$ remained when age was used as a covariate. When examined based on SCI subset (PP and TP), only the MRT for $\dot{V}_{O_2}$ was different between COM and TP (**Figure 1**), while $K_{t\text{off}}$ for both $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ was lower in PP and TP compared to COM (**Figure 2**).

Discussion

Examination of gas exchange during recovery following exhaustive exercise provides information regarding the ability to return to a state of oxidative homeostasis and to perform subsequent bouts of physical activity.^{11,15} This study aimed to characterize the $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ off-kinetics following exhaustive exercise in individuals with SCI. Recovery kinetics reported using τ_{off} was not different between COM and SCI, however normalization of the recovery amplitude difference using $K_{t\text{off}}$ suggests less efficient recovery in participants with SCI in contrast to a non-injured comparison group. Within SCI, oxidative recovery appeared to be similar between the PP and TP phenotypes whereas $\dot{V}_{CO_2}$ kinetics was less efficient in TP than in PP.

Recovery kinetics in persons with SCI has been examined in three previous studies. Barstow et al.¹⁷ reported longer MRTs in the less conditioned lower limb compared to the upper limb, whereas Fukuoka et al.¹⁸ demonstrated faster $\dot{V}_{O_2}$ off-kinetics in trained persons with SCI versus untrained able-bodied controls using moderate-intensity arm ergometry exercise and after 60 days of wheelchair training.¹⁸ These studies suggest that recovery kinetics in persons with SCI may be associated with aerobic conditioning. The results of the current study appear to support previous findings whereby the less conditioned SCI group had lower $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ off-kinetics transition constants (**Table 2**) compared to their counterparts. The SCI group in this study reached 78% of the $\dot{V}_{O_{2\text{peak}}}$ based on a healthy reference group performing arm ergometry exercise, whereas the COM were 126% of this reference group (relative $\dot{V}_{O_{2\text{peak}}}$, SCI = 14.17 mL/kg/min, COM = 22.82 mL/kg/min, and reference group 18.1 mL/kg/min).²¹ Further, there was a strong negative correlation in the present study between physical fitness and recovery, such that greater $K_{t\text{off}}$ of $\dot{V}_{O_2}$ was observed in those with higher peak $\dot{V}_{O_2}$ ($r = -0.94, p > .001$) (**Figure 3**). These results support the

findings from the aforementioned studies whereby higher cardiorespiratory fitness is intrinsically linked to $\dot{V}_{O_2}$ recovery kinetics.

Simões et al.²² compared the recovery rate of oxygen consumption and HR in older and younger adults, and they observed both oxygen and HR recovery were prolonged in the older individuals. It was speculated that prolonged HR recovery may have been attributed to lethargic or delayed reactivity of vagal modulation and slower withdrawal of the sympathetic system.¹ In the present study, oxidative metabolic insufficiency and early fatigue/exhaustion of the peripheral muscles could have limited cardiorespiratory capacity and prolonged recovery in this SCI group. The COM group not only achieved significantly higher $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ during exhaustive exercise, but $K_{t\text{off}}$ of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ was also significantly higher during recovery compared to SCI (**Figure 2**). These variables indicate that although COM began the recovery period at a higher amplitude for HR, $\dot{V}_{O_2}$, and $\dot{V}_{CO_2}$, the rate of recovery and the system's ability to return to oxidative homeostasis was also faster than in the participants with SCI.

The time constant during off-kinetics (τ_{off}) is often used as a surrogate for recovery capacity.^{11,13,16,23-26} However, the use of this variable may not allow full understanding of the mechanics of recovery as it does not include the amplitude of change, only a rate value. In the present study, the course of recovery was examined after exhaustive exercise, which is different from previous studies that used constant work rate at moderate intensity. In addition, the amplitude of recovery for $\dot{V}_{O_2}$ was 55% greater for COM than SCI. While a significant group difference in τ_{off} was not found, a significant difference was observed for $K_{t\text{off}}$ that normalizes the amplitude of decline in $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ to the temporal component of recovery. Therefore, $K_{t\text{off}}$ may be a more appropriate measure when the amplitude of the response differs significantly between comparison groups.

Excessive hydrogen (H^+) accumulation resulting from prolonged repetition of intense or frequent muscle contractions has a detrimental effect on muscle function, specifically cross-bridge formation. Excessive H^+ impedes oxidative metabolism and sarcolemmal function and affects

the ability to engage in and sustain subsequent physical activity.²⁷ Increased CO₂ expiration is one mechanism of buffering excess ions, and thus the ability to fully clear CO₂ at the lung is related to the buffering capacity.²⁸ Hug et al.¹⁵ reported a faster $\dot{V}_{CO_2}$ clearance rate in trained cyclists compared to a moderately active comparison group. The faster $\dot{V}_{CO_2}$ clearance was concurrent with enhanced muscle pH, phosphocreatine, and inorganic phosphate off-kinetics.¹⁵ The reduced $\dot{V}_{CO_2}$ - $K_{t_{off}}$ in the current study suggests that buffering capacity may have been diminished in these participants with SCI.

Fatigability refers to the decline in performance during prolonged physical activity,²⁹ and it can be an indicator of an individual's ability to sustain exercise and daily physical activity. Adequate cardiorespiratory recovery following physical exertion could impact one's ability to repeat or engage in physical activity, therefore recovery and fatigability are linked. Fatigability has been shown to be exacerbated in persons with SCI.^{9,30} Results of the current study were in agreement with these previous reports, using aCPET duration as an index of fatigability. While accounting for different ability levels by staggering starting WR, the exercise duration was 32% longer in the COM group; the observed prolongation of metabolic recovery in participants with SCI could indicate higher fatigability in the SCI group compared to their non-injured counterparts.

Aerobic exercise training is well-understood to be beneficial for improving cardiorespiratory function and fitness in those with SCI³¹⁻³³ and in the general population.^{34,35} Factors facilitating oxidative metabolic recovery after sustained exercise are thought to be increased mitochondrial density, oxidative enzyme activity and/or concentration, tissue capillary density, and muscle oxygen perfusion.³⁶ In addition to increases in peak cardiorespiratory capacity, Fukuoka et al.¹⁸ demonstrated an improvement in both $\dot{V}_{O_2}$ on- and off-kinetics in participants with SCI, following a 60-day wheelchair training regimen. These findings suggest that recovery was improved as an adaptation to aerobic exercise training in the participants with SCI. The current study further elucidates the potential importance of aerobic exercise participation for improving aerobic

capacity in those with SCI, as metabolic recovery was less efficient compared to apparently healthy participants who did not have SCI. The peak $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ values measured during exercise were 30% and 38% lower in the SCI group (**Table 2**), indicating the SCI group had a lower aerobic capacity. This twofold effect, reduced aerobic capacity and less efficient recovery, may be improved upon following exercise training participation.¹⁸

This study has limitations. Subject availability and recruitment necessitated the subjects with SCI to be tested on a dynamic mixing chamber type system while those in the control group were tested using breath-by-breath methodology. Recent studies have demonstrated that both systems are highly reliable and provide accurate and similar information particularly at more moderate exercise intensities.³⁷⁻⁴¹ Whereas breath-by-breath technology is typically used when measuring gas exchange kinetics, the dynamic mixing chamber technique has been used less frequently but successfully for gas kinetic measurements.^{25,42} However, breath-by-breath systems may consistently yield slightly reduced underestimates of $\dot{V}_{O_2}$ and be slightly more sensitive to subject and breath variability at more strenuous intensities.^{37,40,41} This could have resulted in a conservative interpretation bias with respect to group comparisons in which $\dot{V}_{O_2}$ is lower in the group measured by mixing chamber technology, in this case those with SCI.

In the current study, participants were not randomly selected from a larger pool and the small sample does not permit stratification based on time since injury, injury level, physical fitness levels, or gender. These limitations obscure generalization to the SCI population at large and render the findings directly applicable to this specific sample. While findings of this study indicate that overall cardiorespiratory fitness was diminished in the participants with SCI, the study design did not include a measure of daily activity levels. Therefore, we could not account for the influence of physical activity on the study findings in either of the groups. Nonetheless, results of the study do imply that increased fatigability and prolonged recovery are likely to be found in at least some individuals with SCI.

HR was recorded on a minute-by-minute basis rather than beat-by-beat over the 10-minute

recovery period. This lessened the precision with which the HR data could be interpreted and limits analysis to the mean 10-minute HR recovery rather than a rate of recovery for analysis of the halftime or mean response time. A key component of the study of kinetics is to perform repeated tests in order to reduce noise and increase the confidence of the model fit.⁴³ The current study used only one exercise bout for the analysis of off-kinetics, which may have reduced the accuracy of the fit.

Diminished cardiorespiratory function has been associated with increased fatigue and fatigability and prolonged recovery, which may limit individuals' ability to engage in physical activity. In those with SCI, these manifestations could increase the risk for overuse injuries and thus limit their mobility both anatomically as well as physiologically. Difficulty in participating in physical activity can increase the likelihood of a sedentary lifestyle and the risk of acquiring cardiovascular, renal, and metabolic diseases; obesity; and cancer. These conditions have been reported to be more prevalent in those with SCI

than in the general population.^{44,45} Aerobic exercise training of the muscles of the upper extremities may improve cardiorespiratory fitness, decreasing the risk of adverse medical conditions associated with a sedentary lifestyle.

Conclusion

The current study observed reduced efficiency of recovery in a group of participants with SCI compared to a group of individuals who were apparently healthy and without a history of SCI. The findings were based on observations of lower $\dot{V}O_2$ and $\dot{V}CO_2$ off-kinetics transition constants, which appeared to be the most robust measures of gas exchange off-kinetics in this study population.

Conflicts of Interest

Dr. Cowan reports grants from the US Department of Defense during the conduct of the study. The other authors report no conflicts of interest.

REFERENCES

1. Myers JN, Hsu L, Hadley D, Lee MY, Kiratli BJ. Post-exercise heart rate recovery in individuals with spinal cord injury. *Spinal Cord*. 2010;48(8):639-644. doi: 10.1038/sc.2009.196
2. Sedlock DA, Schneider DA, Gass E, Gass G. Excess post-exercise oxygen consumption in spinal cord-injured men. *Eur J Appl Physiol*. 2004;93(1-2):231-236.
3. Fukuoka Y, Endo M, Kagawa H, Itoh M, Nakanishi R. Kinetics and steady-state of $\dot{V}O_2$ responses to arm exercise in trained spinal cord injury humans. *Spinal Cord*. 2002;40(12):631-638. doi: 10.1038/sj.sc.3101383
4. Jayaraman A, Liu M, Ye F, Walter G, Vandenborne K. Regenerative responses in slow- and fast-twitch muscles following moderate contusion spinal cord injury and locomotor training. *Eur J Appl Physiol*. 2013;113(1):191-200.
5. Machac S, Radvanský J, Kolár P, Kríž J. Cardiovascular response to peak voluntary exercise in males with cervical spinal cord injury. *J Spinal Cord Med*. 2016;39(4):412-420. doi: 10.1080/10790268.2015.1126939
6. Wouda MF, Weijden L, Lundgaard E, Strøm V. Energetic and cardiovascular responses to treadmill walking and stationary cycling in subjects with incomplete spinal cord injury. *Spinal Cord*. 2016;54(1):51-56. doi: 10.1038/sc.2015.120
7. Pépin A, Norman KE, Barbeau H. Treadmill walking in incomplete spinal-cord-injured subjects: 1. Adaptation to changes in speed. *Spinal Cord*. 2003;41(5):257-270. doi: 10.1038/sj.sc.3101452
8. Price M. Energy expenditure and metabolism during exercise in persons with a spinal cord injury. *Sports Med Auckl*. 2010;40(8):681-696. <http://dx.doi.org/10.2165/11531960-000000000-00000>
9. Gollie JM, Herrick JE, Keyser RE, et al. Fatigability, oxygen uptake kinetics and muscle deoxygenation in incomplete spinal cord injury during treadmill walking. *Eur J Appl Physiol*. 2017;117(10):1989-2000. doi: 10.1007/s00421-017-3685-y
10. Papaioordanidou M, Varray A, Fattal C, Guiraud D. Neural and muscular mechanisms of electrically induced fatigue in patients with spinal cord injury. *Spinal Cord*. 2014;52(3):246-250. doi: 10.1038/sc.2013.172
11. Dupont G, McCall A, Prieur F, Millet GP, Berthoin S. Faster oxygen uptake kinetics during recovery is related to better repeated sprinting ability. *Eur J Appl Physiol*. 2010;110(3):627-634.
12. Tomlin DL, Wenger HA. The relationship between aerobic fitness and recovery from high intensity intermittent exercise. *Sports Med Auckl NZ*. 2001;31(1):1-11.
13. Perrey S, Candau R, Borrani F, Millet GY, Rouillon JD. Recovery kinetics of oxygen uptake following severe-intensity exercise in runners. *J Sports Med Phys Fit Turin*. 2002;42(4):381-388.

14. Cleuziou C, Perrey S, Borrani F, et al. Dynamic responses of oxygen uptake at the onset and end of moderate and heavy exercise in trained subjects. *Can J Appl Physiol*. 2004;29(1):32-44. doi: 10.1139/h04-003
15. Hug F, Grelot L, Le Fur Y, Cozzone PJ, Bendahan D. Recovery kinetics throughout successive bouts of various exercises in elite cyclists. *Med Sci Sports Exerc*. 2006;38(12):2151-2158.
16. Mann T, Webster C, Lamberts R, Lambert M. Effect of exercise intensity on post-exercise oxygen consumption and heart rate recovery. *Eur J Appl Physiol*. 2014;114(9):1809-1820.
17. Barstow TJ, Scremin AM, Mutton DL, Kunkel CF, Cagle TG, Whipp BJ. Peak and kinetic cardiorespiratory responses during arm and leg exercise in patients with spinal cord injury. *Spinal Cord*. 2000;38(6):340-345.
18. Fukuoka Y, Nakanishi R, Ueoka H, Kitano A, Takeshita K, Itoh M. Effects of wheelchair training on VO₂ kinetics in the participants with spinal-cord injury. *Disabil Rehabil Assist Technol*. 2006;1(3):167-174.
19. Warburton DER, Jamnik VK, Bredin SSD, et al. Evidence-based risk assessment and recommendations for physical activity clearance: an introduction. *Appl Physiol Nutr Metab Physiol Appl Nutr Metab*. 2011;36(suppl 1):S1-S2. doi: 10.1139/h11-060
20. Liu N, Xing H, Zhou M-W, Biering-Sørensen F. Development and validation of a bowel-routine-based self-report questionnaire for sacral sparing after spinal cord injury. *Spinal Cord*. 2017;55(11):1010-1015. doi: 10.1038/sc.2017.77
21. Balady GJ, Weiner DA, Rose L, Ryan TJ. Physiologic responses to arm ergometry exercise relative to age and gender. *J Am Coll Cardiol*. 1990;16(1):130-135.
22. Simões RP, Bonjorno Jr JC, Beltrame T, Catai AM, Arena R, Borghi-Silva A. Slower heart rate and oxygen consumption kinetic responses in the on- and off-transient during a discontinuous incremental exercise: Effects of aging. *Braz J Phys Ther Rev Bras Fisioter*. 2013;17(1):69-76. doi: 10.1590/S1413-35552012005000056
23. Cunningham DA, Croix CM, Paterson DH, Ozyener F, Whipp BJ. The off-transient pulmonary oxygen uptake (VO₂) kinetics following attainment of a particular VO₂ during heavy-intensity exercise in humans. *Exp Physiol*. 2000;85(3):339-347.
24. Özyener F, Rossiter HB, Ward SA, Whipp BJ. Influence of exercise intensity on the on- and off-transient kinetics of pulmonary oxygen uptake in humans. *J Physiol*. 2001;533(Pt 3):891-902. doi: 10.1111/j.1469-7793.2001.t01-1-00891.x
25. Padilla-Pérez J. The on- and off-transient phase two VO₂ kinetics during submaximal exercise in young men. *Rev Hosp Juárez Méx*. 2013;80(1):6-13.
26. Sousa A, Rodríguez FA, Machado L, Vilas-Boas JP, Fernandes RJ. Exercise modality effect on oxygen uptake off-transient kinetics at maximal oxygen uptake intensity. *Exp Physiol*. 2015;100(6):719-729. doi: 10.1113/EP085014
27. Keyser RE. Peripheral fatigue: High-energy phosphates and hydrogen ions. *PM R*. 2010;2(5):347-358. doi: 10.1016/j.pmrj.2010.04.009
28. Ozcelik O, Ward SA, Whipp BJ. Effect of altered body CO₂ Stores on pulmonary gas exchange dynamics during incremental exercise in humans. *Exp Physiol*. 1999;84(5):999-1011. doi: 10.1111/j.1469-445X.1999.01868.x
29. Jordan B, Mehl T, Schweden TLK, Menge U, Zierz S. Assessment of physical fatigability and fatigue perception in myasthenia gravis. *Muscle Nerve*. 2017;55(5):657-663. doi: 10.1002/mus.25386
30. Shields RK. Fatigability, relaxation properties, and electromyographic responses of the human paralyzed soleus muscle. *J Neurophysiol*. 1995;73(6):2195-2206.
31. Carty A, McCormack K, Coughlan GF, Crowe L, Caulfield B. Increased aerobic fitness after neuromuscular electrical stimulation training in adults with spinal cord injury. *Arch Phys Med Rehabil*. 2012;93(5):790-795. doi: 10.1016/j.apmr.2011.10.030
32. Tweedy SM, Beckman EM, Geraghty TJ, et al. Exercise and sports science Australia (ESSA) position statement on exercise and spinal cord injury. *J Sci Med Sport*. 2017;20(2):108-115. doi: 10.1016/j.jsams.2016.02.001
33. Gorla JL, Costa e Silva Ade A, Borges M, et al. Impact of wheelchair rugby on body composition of subjects with tetraplegia: A pilot study. *Arch Phys Med Rehabil*. 2016;97(1):92-96. doi: 10.1016/j.apmr.2015.09.007
34. Sloth M, Sloth D, Overgaard K, Dalgas U. Effects of sprint interval training on VO₂max and aerobic exercise performance: A systematic review and meta-analysis. *Scand J Med Sci Sports*. 2013;23(6):e341-e352.
35. Esfandiari S, Sasson Z, Goodman J. Short-term high-intensity interval and continuous moderate-intensity training improve maximal aerobic power and diastolic filling during exercise. *Eur J Appl Physiol*. 2014;114(2):331-343.
36. Koppo K, Bouckaert J, Jones AM. Effects of training status and exercise intensity on phase II VO₂ kinetics. *Med Sci Sports Exerc*. 2004;36(2):225-232. doi: 10.1249/01.MSS.0000113473.48220.20
37. Winkert K, Kirsten J, Dreyhaupt J, Steinacker JM, Treff G. The COSMED K5 in breath-by-breath and mixing chamber mode at low to high intensities [published online ahead of print December 31, 2019]. *Med Sci Sports Exerc*. doi: 10.1249/MSS.0000000000002241.
38. Crouter SE, LaMunion SR, Hibbing PR, Kaplan AS, Bassett DR Jr. Accuracy of the Cosmed K5 portable calorimeter. *PLoS One*. 2019;14(12):e0226290. doi: 10.1371/journal.pone.0226290. eCollection 2019.
39. Perez-Suarez I, Martin-Rincon M, Gonzalez-Henriquez JJ, et al. Accuracy and precision of the COSMED K5 portable analyser. *Front Physiol*. 2018;9:1764. doi: 10.3389/fphys.2018.01764. eCollection 2018.
40. Ward SA. Open-circuit respirometry: Real-time, laboratory-based systems. *J Appl Physiol*. 2018;118(5):875-898.

41. Beijst C, Schep G, Breda Ev, Wijn PF, Pul CV. Accuracy and precision of CPET equipment: A comparison of breath-by breath and mixing chamber systems. *J Med Eng Technol.* 2013;37(1):35-42.
42. Lai N, Nasca MM, Silva MA, Silva FT, Whipp BJ, Cabrera ME. Influence of exercise intensity on pulmonary oxygen uptake kinetics at the onset of exercise and recovery in male adolescents. *Appl Physiol Nutr Metab.* 2008;33(1):107-117.
43. Ozyener F, Rossiter HB, Ward SA, Whipp BJ. Influence of exercise intensity on the on- and off-transient kinetics of pulmonary oxygen uptake in humans. *J Physiol.* 2001;533(Pt 3):891-902.
44. Gater DR. Obesity after spinal cord injury. *Phys Med Rehabil Clin N Am.* 2007;18(2):333-351, vii. doi: 10.1016/j.pmr.2007.03.004
45. 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 Metabol.* 2010;36(1):107-114. doi: 10.1139/H10-091