Arm Cycling Combined with Passive Leg Cycling Enhances VO_{2peak} in Persons with Spinal Cord Injury Above the Sixth Thoracic Vertebra

Tom Tørhaug, MD,[1,2] Berit Brurok, PhD,[1,3] Jan Hoff, PhD,[1,4] Jan Helgerud, PhD,[4,5,6] and Gunnar Leivseth, MD, PhD [2,7]

[1]St. Olavs University Hospital, Clinic of Physical Medicine and Rehabilitation, Department of Spinal Cord Injuries, Trondheim, Norway; [2]Norwegian University of Science and Technology, Faculty of Medicine, Department of Neuromedicine and Movement Science, Trondheim, Norway; [3]K.G. Jebsen Center of Exercise in Medicine, Department of Circulation and Medical Imaging Norwegian University of Science and Technology, Trondheim, Norway; [4] Norwegian University of Science and Technology, Faculty of Medicine, Department of Circulation and Imaging, Trondheim, Norway; [5] Hokksund Medical Rehabilitation Centre, Hokksund, Norway; [6]Telemark University College, Department of Sports and Outdoor Life Studies, Bø, Norway; [7]Department of Clinical Medicine, Neuromuscular Diseases Research Group, University of Tromsø, Norway

Objective: To test whether passive leg cycling (PLC) during arm cycling ergometry (ACE) affects peak oxygen uptake (VO_{2peak}) differently in individuals with spinal cord injury (SCI) at/above the 6th thoracic vertebra (T6) and below T6. **Methods:** We conducted a cross-sectional study, analyzed by univariate and multivariate regression models. Between- and within-group differences were examined during (a) ACE only, (b) ACE combined with PLC (ACE-PLC), and (c) ACE combined with functional electrical stimulation cycling (FES hybrid). Fifteen SCI subjects were recruited and grouped according to injury level: at/above T6 (SCI-high, n = 8) or below T6 (SCI-low, n = 7). VO_{2peak} tests during ACE only, ACE-PLC, and FES hybrid were performed in random order on separate days. **Results**: In the SCI-high group, mean (SD) VO_{2peak} was 19% higher during ACE-PLC than during ACE only [21.0 (3.8) vs 17.7 (5.0) $mL \cdot kg^{-1} \cdot min^{-1}$; p = .002], while VO_{2peak} during FES hybrid cycling was 16% higher than during ACE-PLC [24.4 (4.1) $mL \cdot kg^{-1} \cdot min^{-1}$; p = .001]. No significant differences among exercise modalities were found for the SCI-low group. **Conclusion**: Additional training modalities (eg, PLC) during ACE facilitate exercise in SCI-high individuals, but not to the level of the FES hybrid method. Conversely, additional training modalities may not increase training load in SCI-low individuals.
Key words: *arm ergometry test, ergometry, exercise test, oxygen consumption, spinal cord injury, wheelchair*

Adults with spinal cord injury (SCI) have a 5-fold higher prevalence of cardiovascular disease (CVD) compared to able-bodied adults.[1] The increased prevalence of CVD is associated with an inactive lifestyle in addition to hemodynamic, neurogenic, and metabolic malfunctions of both peripheral and central origin in response to physical exercise. Exercise is undoubtedly beneficial for all humans; however, developing a program for individuals with SCI that is motivating and simultaneously increases endurance and cardiovascular fitness has proven elusive. Although SCI guidelines that improve cardiovascular aerobic fitness have been published,[2-7] supporting evidence for these guiding principles is imprecise in defining high aerobic intensity and determination criteria for peak oxygen uptake (VO_{2peak}) tests. VO_{2peak} has proven to be a reliable predictor of mortality in both able-bodied and SCI patients with CVD,[8] and VO_{2peak} tests are sensitive to change, reproducible, and valid[9] when performed in core facilities. Although recommendations exist on how to perform VO_{2peak} tests in individuals with SCI,[10,11] definitions of a true VO_{2peak} and determination criteria for tests are often lacking.

Additionally, there is a limited range of exercise equipment available to improve musculoskeletal care and cardiovascular fitness in individuals with SCI with lower leg paresis.[12] Stationary arm crank/

Corresponding author: Tom Tørhaug, MD, St. Olav's University Hospital, Clinic of Physical Medicine and Rehabilitation, Spinal Cord Injuries Unit, 4rd Floor, Nevro Øst, Edvard Griegs gate 8, 7006 Trondheim, Norway; e-mail: tom.torhaug@ntnu.no; institution e-mail: inb-post@medisin.ntnu.no

Top Spinal Cord Inj Rehabil 2018;24(1):86-95

www.thomasland.com
Published online ahead of print November 20, 2017

doi: 10.1310/sci17-00029

rowing ergometers and arm cycles are commonly used for upper body exercise. For exercises that involve lower extremities, however, few modalities are available. A 2014 community-based study by Pelletier et al[13] demonstrated that, regardless of level of injury, individuals with SCI preferred stationary arm crank ergometry (ACE) to hybrid passive arm cycling and leg cycle stepper/passive leg cycle ergometer combinations. Explanations included safety issues and perceived barriers to hybrid modes, however the study demonstrated a lack of difference in energy expenditure. They concluded that in order to gain any metabolic advantage to hybrid exercise, the equipment should involve functional electrical stimulation (FES). Nonetheless, hybrid exercise may have added benefit for SCI subjects, so further study is required to identify more feasible and less resource-demanding modalities to combine with ACE.

FES is a computerized feedback-controlled system that can stimulate pedalling motion of paralyzed legs. Although cycle FES ergometers are resource intensive and expensive, they may represent a major advance in exercise conditioning for individuals with SCI.[14] This is due to the fact that FES devices recruit larger muscle masses. To increase the activation of total body muscle mass and thereby workload of the heart,[14] upper body exercises are often combined with simultaneous lower leg training. Several studies of SCI subjects concluded that passive leg cycling (PLC) was effective for enhancing physiological metabolic demand (VO_2),[15] was accessible, and could be performed without assistance,[16] while others found no such benefit.[17-19] It has been shown that ACE in combination with FES, or hybrid training of the lower extremities, increases VO_2 to a greater extent than arm crank exercises alone.[14] However, hybrid training regimens like ACE in combination with FES are not suitable for all SCI subjects. Moreover, the equipment is relatively expensive and requires specially trained personnel. However, immediate equating of studies is difficult. Brurok et al[14] documented that $VO_{2\ peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) and O_2 pulse ($mL \cdot beat^{-1}$) during FES hybrid cycling increased by 24% and 25% compared to ACE only. However, Bakkum et al[20] found no additional benefits of FES hybrid exercise compared to arm cycling alone in an 16-week open randomized controlled trial. However, relevant to this study, the trial did not report proper VO_{2peak} criteria. Given the disagreements in the literature,[15-21] additional investigations comparing exercise responses among different training modalities are needed.

Dynamic regulation of the cardiovascular system requires balanced outputs from the parasympathetic and sympathetic nervous systems (PSNS and SNS, respectively). Autonomic signaling maintains blood pressure during postural changes and exercise to maintain regional circulation. In the intact noninjured central and autonomic nervous systems (CNS and ANS), this results in targeted outflow and redistribution of blood to various organs to preserve homeostasis.[22] In individuals with SCI, however, spinal ANS failure results in an inverse relationship between the level and completeness of SCI and the extent of autonomic failure,[23-26] as autonomic failure increases with more cephalic SCI. Therefore, the selection of exercise modality must consider the extent of autonomic failure.

To date, the only randomized controlled study on passive ankle motion in individuals with SCI[27] was supportive for the use of the passive mode. Results from a single subject study[28] in 2015 suggest combined active-arm passive-leg exercise to be advantageous over arms-only exercise, producing cardiovascular improvements similar to those achieved by the full-scale FES-hybrid modality. Clinical SCI studies that have investigated peripheral or central cardiovascular adjustments to PLC[15-17,29,30] have reported mixed findings. A 2016 animal studies review[31] found PLC to be modulating spinal reflexes, reducing spasticity, and eliciting cardio-protective effects. The same researchers found PLC to promote cortical neuroplastic reorganization in individuals with SCI.[32] Despite the uncertain efficacy and complex translational processing of PLC, it seems common in clinical settings and is considered essential for maintaining musculoskeletal function in individuals with SCI.[17,18]

Investigating exercise responses between different apparatus necessitates systematic comparisons. When individuals with SCI are stratified by spinal level, such as at or above the 6th thoracic vertebra (T6) versus below T6 (termed SCI-high and SCI-low, respectively), unique responses are expected. In many cases, additional training components to increase the training load on the heart are used irrespective of degree and level of injury. Compared to SCI-low individuals, SCI-high individuals have more impaired SNS outflow, which may result in blood pooling in the lower extremities and a concomitant reduction in stroke volume. Lower leg exercise has been proposed to facilitate venous return in SCI subjects, although this has been questioned and other mechanisms for venous return in SCI-high subjects have been demonstrated.[21,23,24,33-35] A method to improve cardiovascular fitness in individuals with SCI in the same manner as able-bodied subjects is not yet defined[24] even though this issue is particularly relevant to SCI-high groups.[19,23,24,35] Thus, the primary aim of this study was to determine whether subjects with SCI at/above or below T6 respond differently to test modalities by comparing VO_{2peak} during (a) ACE only, (b) ACE combined with PLC (ACE-PLC), and (c) ACE combined with functional electrical stimulation cycling (FES hybrid).

Methods

Fifteen moderately active individuals with SCI were recruited after informed consent. They were allocated into 2 groups according to level of injury: at or above T6 (SCI-high, $n = 8$) or below T6 (SCI-low, $n = 7$).[21] Inclusion criteria were stable neurological state with lower motor neurons intact, American Spinal Injury Association Impairment Scale (AIS) A, and ability to FES cycle for a minimum of 1 minute. Exclusion criteria were pacemakers, severe autonomic dysreflexia, and decubitus in any area. Neurological condition according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI-AIS)[36] and general medical condition were assessed before testing. Body mass was recorded on a SECA digital chair scale 950 (Hamburg, Germany). Individual characteristics are listed in **Table 1**.

Ventilatory and pulmonary gas exchange parameters were measured using a Metamax II Cortex system (Cortex Biophysik GmbH, Germany). Participants wore a facemask with a volume transducer and tube to collect the gas. The Metamax unit samples gas concentrations every 10 seconds from a mixing chamber. Prior to testing, calibration was performed with a 3-L calibration syringe (Hans Rudolph Jäger GmbH, Germany). For ACE, the ERGOMED 840L (Siemens, Germany) was modified by changing pedals for arm use (**Figure 1**). The ERGYS 2 Rehabilitation System (Therapeutic Alliances Inc., Ohio) was used for both PLC and FES hybrid cycling (**Figure 1**).

Table 1. Clinicodemographic characteristics of SCI-low and SCI-high groups

	SCI-high (*n* = 8)	SCI-low (*n* = 7)
TSI, years	12.9 (±10.8)	13.6 (±11.7)
Weight, kg	73.3 (±8.4)	74.9 (±14.9)
AIS	A	A
LOI, range	C4-T5	T8-T12
Men/women	8/0	5/2
Age, years	36.4 (±13.5)	43.4 (±12.7)

Note: Data are presented in mean (*SD*). AIS = American Spinal Injury Association Impairment Scale; LOI = sensory and motor neurological levels of injury; SCI = spinal cord injury; SCI-high = at or above T6; SCI-low = below T6; TSI = time since injury.

Hemolyzed blood lactate ($[La^-]_b$) was measured by a Lactate Pro LT-1710 Analyzer (Arkray Factory Inc, KDK Corp., Japan) after VO_{2peak} testing of a capillary blood sample taken from a finger.

Heart rate (HR) was measured with Polar monitors (Polar Electro, Oy, Finland). Peak HR was determined as the highest HR measured at VO_{2peak}. A rating of perceived exertion (RPE, Borg 6-20) was recorded after each test. Oxygen pulse (O_2 pulse in $mL \cdot beat^{-1}$) was calculated as the ratio of VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) to peak HR ($beat \cdot min^{-1}$).

VO_{2peak} determination criteria

The 3 exercise tests with separate VO_{2peak} measurements were performed in random order on separate days. Participants were familiar with ACE but none were competitive wheelchair athletes. For determination criteria, VO_{2peak} was considered achieved when respiratory exchange ratio (RER) ≥ 1.1, $[La^-]_b \geq 7$, and RPE ≥ 15 (Borg 6-20). In the upper body mode, a VO_2 plateau (stable VO_2

Figure 1. The based equipment configuration for arm crank ergometry (ACE), arm crank ergometry and passive leg cycling (ACE-PLC), and functional electrical stimulation (FES) hybrid modalities.

despite increased power output and pulmonary ventilation) is rarely reached, so VO_{2peak} is used to denote maximal effort. When the aforementioned RER, $[La^-]_b$, and RPE criteria were met, the average of the highest VO_2 values within 3 consecutive 10-second measurements was calculated as VO_{2peak}. All tests were performed with the intention to reach determination criteria for peak aerobic power.

Test protocol for ACE

During ACE, the shoulder joint was horizontally aligned with the ACE axis and the elbows slightly flexed at the point of furthest reach. Subjects used their personal rigid frame or electrical wheelchairs, which were placed on a stable platform when required. All participants performed warm-up at their own cadence with zero loading for approximately 5 minutes. Then, 4 minutes of 30 W output on the ACE was followed by progression to peak ACE, where ACE workload was increased by 5 W/min for SCI-high and by 10 W/min for SCI-low subjects.

Test protocol for ACE-PLC

Participants performed combined ACE-PLC while seated in the ERGYS 2 (**Figure 1**) to optimize comparison. With legs fixed to the pedals, the test technician manually turned the flywheel at 70 rpm with timing aided by audible cues from a digital metronome. Otherwise, the testing procedure was identical to the ACE protocol described above.

Test protocol for FES hybrid

FES hybrid tests began with 5 minutes of warm-up on the ACE, followed by 4 minutes at 30 W on the ACE combined with 2 minutes of FES manual warm-up and then FES hybrid peak testing (**Figure 1**). No resistance on the flywheel during FES cycling was provided, whereas ACE workload was increased in 1-minute increments by 5 or 10 W (as described) until VO_{2peak} determination criteria were met. Five participants demonstrated severe muscle fatigue during pretests on the FES (2 SCI-high and 3 SCI-low subjects). Thus, to reach fatigue at approximately the same time for both arms and legs, FES cycling had to be individually set for these 5 participants. Several days prior to the test, the ACE power output (W) performance at 5 minutes before ACE_{peak} (denoted $5min_{peak}$) and ACE_{peak} were measured. Then, in the actual FES hybrid test, electrostimulation was started at the predefined $5min_{peak}$. Self-adhesive electrodes were used for electrical stimulation. Impulse frequency was set at 40 Hz and amplitude at 140 mA.[21] The other participants performed 2 minutes of manually assisted FES cycling warm-up at an intensity of 50% of the individually set muscle fatigue thresholds. Where necessary, the test personnel provided manual assistance to ensure that pedaling cadence did not drop below a default preset stimulation cut-off speed of 35 rpm and to ensure stimulation current throughout the test.

We certify that all applicable institutional and governmental regulations concerning the ethical study of human volunteers were followed during the course of this research. The research was conducted in accordance with the Declaration of the World Medical Association, and informed consent was obtained from the participants as required.

Statistical analyses

Tests for multivariate normality and a constant covariance matrix were performed using STATA 2014 statistical software (StataCorp, LP, Texas). Multivariate regression analyses were then used to examine differences in response variables among exercise modalities and between SCI-high and SCI-low groups. Separate multivariate regression analyses were also used to examine within-group differences by level of injury (LOI) in SCI-high subjects. A p value < .05 was considered statistically significant.

Results

Differences in peak O_2 uptake during ACE, ACE-PLC, and FES hybrid exercise modalities between SCI-high and -low groups

Performance on ACE as measured by VO_{2peak} differed significantly between SCI-high and -low groups ($F = 7.03$; $p = .02$). In contrast, groups showed similar VO_{2peak} on ACE-PLC ($F = 2.56$; $p = .13$) and FES hybrid ($F = 0.34$; $p = .57$).

Variation in exercise load among modalities in the SCI-high group

In the SCI-high group, mean VO_{2peak} (SD) during ACE-PLC was 19% higher than during ACE alone [21.0 (3.8) vs 17.6 (5.0) mL·kg^{-1}·min^{-1}; $F = 38.10$; $p = .001$; 95% CI, 18.3-23.4 and 14.1-21.2, respectively]. FES hybrid cycling induced an additional VO_{2peak} increase of 3.5 mL·kg^{-1}·min^{-1} compared to ACE-PLC [24.4 (4.1) mL·kg^{-1}·min^{-1}; $F = 20.68$; $p = .001$; 95% CI, 21.2-27.5] (**Figure 2**, **Table 2**), although absolute VO_{2peak} values (L·min^{-1}) did not differ significantly between modalities (**Table 2**). The mean O_2 pulse was 2 mL·beat^{-1} higher (24%) during ACE-PLC compared to ACE alone ($p = .003$; 95% CI, 1.2-4.3) and 7.8% higher during FES hybrid compared to ACE-PLC [11.0 (2.0) vs 10.2 (1.3) mL·kg^{-1}·min^{-1}; $p = .01$; 95% CI, 0.9-6.0]. Mean PO_{peak} was 10.5 W higher in the FES hybrid modality compared to ACE alone

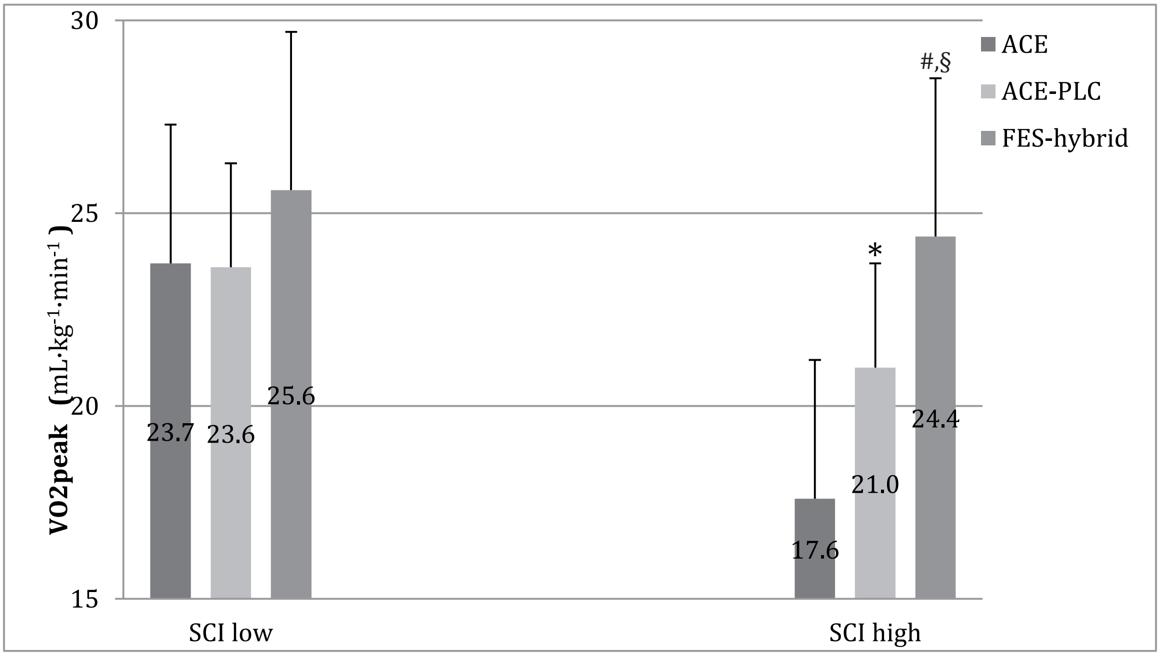

Figure 2. Peak oxygen uptake measured for the SCI-low and SCI-high groups during arm crank ergometry (ACE), arm crank ergometry and passive leg cycling (ACE-PLC), and functional electrical stimulation (FES) hybrid modalities. Data are presented in mean (±SD). VO_{2peak} = peak oxygen uptake. *Significant difference between ACE and ACE-PLC ($p \leq .05$). #Significant difference between ACE-PLC and FES hybrid cycling ($p \leq .05$). §Significant difference between ACE and FES hybrid cycling ($p \leq .05$).

Table 2. Peak physiological parameters for the SCI-high group

Variables	ACE (n = 8)	ACE-PLC (n = 8)	FES hybrid (n = 8)
VO_{2peak}			
($L \cdot min^{-1}$)	1.23 (±0.40)	1.56 (±0.43)[a]	1.80 (±0.40)[b,c]
($mL \cdot kg^{-1} \cdot min^{-1}$)	17.6 (±5.0)	21.0 (±3.8)[a]	24.4 (±4.1)[b,c]
V_E ($L \cdot min^{-1}$)	50.4 (±20.8)	56.7 (±22.6)	61.4 (±19.8)[c]
RER	1.14 (±0.07)	1.18 (±0.1)	1.18 (±0.07)
$[La^-]_b$ ($mmol \cdot L^{-1}$)	7.5 (±1.1)	7.4 (±1.2)	9.4 (±1.7)[b,c]
HR_{peak} ($beats \cdot min^{-1}$)	149 (±34)	154 (±30)	164 (±20)
Power output (W)	72.5 (±32)	80 (±28)	83 (±31)[c]
RPE	18 (±1)	18 (±1)	19 (±1)
O_2 pulse ($mL \cdot beat^{-1}$)	8.3 (±1.7)	10.2 (±1.3)[a]	11.0 (±2.0)[c]

Note: Data are presented in mean (±*SD*). ACE = arm crank ergometry; FES = functional electrical stimulation; HR = heart rate; $[La^-]_b$ = blood lactate; PLC = passive leg cycling; power output = peak power ACE output for each modality; RER = respiratory exchange ratio; RPE = rating of perceived exertion (Borg 6-20); V_E = ventilation; VO_{2peak} = peak oxygen uptake.

[a]Significant difference between ACE and ACE-PLC ($p \leq .05$).

[b]Significant difference between ACE-PLC and FES hybrid cycling ($p \leq .05$).

[c]Significant difference between ACE and FES hybrid cycling ($p \leq .05$).

[83 (31) vs 72.5 (32) W; p = .001; 95% CI, 6-15]. No differences in V_E, $[La^-]_b$, RER, HR_{peak}, RPE, and PO_{peak} were found between ACE-PLC and ACE alone (**Table 2**). Regression analysis showed that specific LOI (above T6) did not contribute to these differences among exercise modalities.

Variation in exercise load among modalities in the SCI-low group

In contrast to the SCI-high group, no significant differences in VO_{2peak} or other related parameters were observed among modalities in the SCI-low group (**Figure 2**, **Table 3**).

Autonomic dysreflexia

No signs of clinically relevant autonomic failure, dysreflexia, or related disturbances were observed during the course of this study.

Discussion

While ACE is a valuable modality to maintain fitness in individuals with SCI, training modalities involving the lower extremities can provide added benefit. This comparison of peak oxygen consumption (VO_{2peak}) and related metabolic responses during 3 different exercise testing conditions, ACE, ACE-PLC, and FES hybrid, in individuals classified as SCI-high or SCI-low revealed that ACE-PLC significantly increased VO_{2peak} compared to ACE alone in SCI-high but not SCI-low individuals. However, ACE-PLC did not reach the intensity level of FES hybrid as measured by VO_{2peak} and PO_{peak}. Our findings, therefore, indicate that for SCI-low adults, ACE alone is sufficient exercise for cardiovascular fitness as indicated by VO_{2peak}. The increased VO_{2peak} in the SCI-high group with additional lower extremity training modalities (ACE-PLC or FES hybrid) may result principally from compensation for neurophysiological regulation deficits, such as SNS dysfunction. Since PSNS pathways do not pass through the spinal cord, high-level SCI leads to unbalanced SNS:PSNS activity, [23,33] specifically reduced SNS efferent activity[23] and blunted circulatory responses[33] below the LOI. The SCI-high group may have a general decentralization of SNS control (sympathetic vessels + splanchnic vessels) compared to the SCI-low group. Consistent

Table 3. Peak physiological parameters for SCI-low group

Variables	ACE (n = 7)	ACE-PLC (n = 7)	FES hybrid (n = 7)
VO_{2peak}			
($L \cdot min^{-1}$)	1.74 (±0.24)	1.75 (±0.31)	1.90 (±0.38)
($mL \cdot kg^{-1} \cdot min^{-1}$)	23.7 (±3.6)	23.6 (±2.7)	25.6 (±4.1)
V_E ($L \cdot min^{-1}$)	76.6 (±13.4)	74.7 (±16.4)	80.2 (±21.1)
RER	1.25 (±0.11)	1.24 (±0.11)	1.23 (±0.07)
$[La^-]_b$ ($mmol \cdot L^{-1}$)	9.3 (±0.9)	9.0 (±1.8)	10.6 (±2.5)
HR_{peak} ($beats \cdot min^{-1}$)	185 (±11)	182 (±11)	182 (±9)
Power output (W)	96 (±23)	97 (±18)	98 (±19)
RPE	19 (±1)	18 (±1)	19 (±1)
O_2 pulse ($mL \cdot beat^{-1}$)	9.4 (±0.9)	9.6 (±1.4)	10.4 (±1.8)

Note: Data are presented in mean (±*SD*). ACE = arm crank ergometry; FES = functional electrical stimulation; HR = heart rate; $[La^-]_b$ = blood lactate; PLC = passive leg cycling; power output = peak power ACE output for each modality; RER = respiratory exchange ratio; RPE = rating of perceived exertion (Borg 6-20); V_E = ventilation; VO_{2peak} = peak oxygen uptake.

with this notion, exercise responses were enhanced and differently graded in the SCI-high group.

Theoretically, injury-related blunted HR and contractility responses of the heart may be present in the SCI-high but not the SCI-low group. Across training modalities, both HR_{peak} responses and work output were lower (20 $beats \cdot min^{-1}$ and 20 W lower) in the SCI-high compared to the SCI-low group. Nash et al[19] reported increased SNS activity leading to diffuse noradrenergic discharge affecting HR and withdrawal of vagal tone leading to cardio-acceleration selectively in the SCI-high group. However, the HR_{peak} responses (**Table 2**) in SCI-high subjects were moderate and do not suggest widespread SNS influence.

In exercising able-bodied individuals, spinal circuits are responsible for regulating cardiac activity and regional vascular tone to maintain systemic vascular homeostasis.[22] However, in individuals with SCI, spinal circuits comprising homeostatic control loops are disrupted. The SCI-high individuals exhibited a superior response to ACE-PLC and FES hybrid compared to the SCI-low group. These differences are unlikely due solely to increased lower leg venous return mediated by PLC or FES because similar responses were found when occlusive thigh cuffs were applied to promote circulatory adjustments.[21] Thus, a contribution from "venous pooling" is still unproven. Our findings are supported by those of Thijssen et al,[33] who assessed acute changes in blood flow in the brachial artery, portal vein (indirect splanchnic vessels flow), and femoral artery during ACE in SCI-high, SCI-low, and control subjects. A large decrease in splanchnic vessel blood flow was observed in SCI-low individuals and controls, whereas SCI-high individuals exhibited no change. The authors concluded that splanchnic vessels in the SCI-high group respond distinctly from local muscular vessels regarding blood redistribution during ACE testing. A recent study[37] found preserved vascular function during PLC in SCI-low individuals. Thus, the more functional SNS system in SCI-low appears to normalize responses among the 3 exercise modalities. A lower leg venous return effect during ACE-PLC appears unlikely as SCI-low subjects exhibited no changes in VO_{2peak} and related parameters. SCI-high individuals exhibited significantly increased pulmonary ventilation (VE). This probably reflects augmented abdominothoracic muscular work and a diaphragm pumping effect on the lungs. This mechanism alone does not increase VO_2, but may play an important role in promoting central blood redistribution and increasing systolic blood pressure.[19]

Individuals with SCI are less physically active and consequently certain diseases are more frequent with increasing age and time since injury.[38,39] In this study, the SCI-low individuals were approximately 10 years older than the SCI-high group. Ageing in individuals with SCI most likely contributes to deconditioning,[40] which implies reduced exercise tolerance that secondarily could have affected our VO_{2peak} data.

We also observed a trend towards an inverse relationship between LOI and VO_{2peak} within the SCI-high group. That is, the higher the LOI, the lower VO_{2peak}. Again, the lack of a significant correlation in regression analysis may be due to insufficient sample size, so this issue warrants further study.

Study limitations

The sample size is too small to draw general conclusions on the relationship between level of spinal injury and exercise response. However, small sample sizes are often the case in studies on individuals with SCI. The ISNCSCI-AIS score[36] does not correspond to the disruption of the autonomic pathways and the functional state of the autonomic nervous system was not evaluated. So contributions due to possible SNS:PNS imbalance or loss of central regulation are still uncertain.

Conclusions

In SCI-high individuals, training modalities in addition to ACE appear necessary to increase training load, while no additional training modality appears necessary to increase the training load in SCI-low individuals. In situations where the more advanced hybrid FES system is not available, PLC during ACE for SCI-high adults appears to facilitate exercise at a higher VO_2 and so may be sufficient to promote cardiovascular fitness.

Acknowledgments

The authors declare no conflicts of interest. The authors would like to thank all of the individuals with SCI participating in the study.

REFERENCES

1. Washburn RA, Figoni FS. Physical activity and chronic cardiovascular disease prevention in spinal cord injury: A comprehensive literature review. *Top Spinal Cord Inj Rehabil.* 1998;3:16-32.
2. Hoffman MD. Cardiorespiratory fitness and training in quadriplegics and paraplegics. *Sports Med.* 1986;3(5):312-330.
3. Jacobs PL, Nash MS. Exercise recommendations for individuals with spinal cord injury. *Sports Med.* 2004;34(11):727-751.
4. Anneken V, Hanssen-Doose A, Hirschfeld S, Scheuer T, Thietje R. Influence of physical exercise on quality of life in individuals with spinal cord injury. *Spinal Cord.* 2010;48(5):393-399.
5. Devillard X, Rimaud D, Roche F, Calmels P. Effects of training programs for spinal cord injury. *Ann Readapt Med Phys.* 2007;50(6):490-498, 480-489.
6. Giacobbi PR Jr, Stancil M, Hardin B, Bryant L. Physical activity and quality of life experienced by highly active individuals with physical disabilities. *Adapt Phys Activ Q.* 2008;25(3):189-207.
7. Nooijen CFJ, de Groot S, Postma K, et al. A more active lifestyle in persons with a recent spinal cord injury benefits physical fitness and health. *Spinal Cord.* 2012;50(4):320-323.
8. Keteyian SJ, Brawner CA, Savage PD, et al. Peak aerobic capacity predicts prognosis in patients with coronary heart disease. *Am Heart J.* 2008;156(2):292-300.
9. Keteyian SJ, Brawner CA, Ehrman JK, et al. Reproducibility of peak oxygen uptake and other cardiopulmonary exercise parameters: Implications for clinical trials and clinical practice. *Chest.* 2010;138(4):950-955.
10. Martel G, Noreau L, Jobin J. Physiological responses to maximal exercise on arm cranking and wheelchair ergometer with paraplegics. *Paraplegia.* 1991;29(7):447-456.
11. Walker R, Powers S, Stuart MK. Peak oxygen uptake in arm ergometry: Effects of testing protocol. *Br J Sports Med.* 1986;20(1):25-26.
12. Valent L, Dallmeijer A, Houdijk H, Talsma E, van der Woude L. The effects of upper body exercise on the physical capacity of people with a spinal cord injury: A systematic review. *Clin Rehabil.* 2007;21(4):315-330.
13. Pelletier CA, Ditor DS, Latimer-Cheung AE, Warburton DE, Hicks AL. Exercise equipment preferences among adults with spinal cord injury. *Spinal Cord.* 2014;52(12):874-879.
14. Brurok B, Helgerud J, Karlsen T, Leivseth G, Hoff J. Effect of aerobic high-intensity hybrid training on stroke volume and peak oxygen consumption in men with spinal cord injury. *Am J Phys Med Rehabil.* 2011;90(5):407-414.
15. Ballaz L, Fusco N, Cretual A, Langella B, Brissot R. Peripheral vascular changes after home-based passive leg cycle exercise training in people with

paraplegia: A pilot study. *Arch Phys Med Rehabil.* 2008;89(11):2162-2166.
16. Ballaz L, Fusco N, Cretual A, Langella B, Brissot R. Acute peripheral blood flow response induced by passive leg cycle exercise in people with spinal cord injury. *Arch Phys Med Rehabil.* 2007;88(4):471-476.
17. Ter Woerds W, De Groot PC, van Kuppevelt DH, Hopman MT. Passive leg movements and passive cycling do not alter arterial leg blood flow in subjects with spinal cord injury. *Phys Ther.* 2006;86(5):636-645.
18. Figoni SF, Rodgers MM, Glaser RM, et al. Physiologic responses of paraplegics and quadriplegics to passive and active leg cycle ergometry. *J Am Paraplegia Soc.* 1990;13(3):33-39.
19. Nash MS, Bilsker MS, Kearney HM, Ramirez JN, Applegate B, Green BA. Effects of electrically-stimulated exercise and passive motion on echocardiographically-derived wall motion and cardiodynamic function in tetraplegic persons. *Paraplegia.* 1995;33(2):80-89.
20. Bakkum AJ, Paulson TA, Bishop NC, et al. Effects of hybrid cycle and handcycle exercise on cardiovascular disease risk factors in people with spinal cord injury: A randomized controlled trial. *J Rehabil Med.* 2015;47(6):523-530.
21. Brurok B, Torhaug T, Leivseth G, Karlsen T, Helgerud J, Hoff J. Effect of leg vascular occlusion on arm cycling peak oxygen uptake in spinal cord-injured individuals. *Spinal Cord.* 2012;50(4):298-302.
22. Kaufman MP, Hayes SG. The exercise pressor reflex. *Clin Auton Res.* 2002;12(6):429-439.
23. Teasell RW, Arnold JM, Krassioukov A, Delaney GA. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. *Arch Phys Med Rehabil.* 2000;81(4):506-516.
24. West CR, Mills P, Krassioukov AV. Influence of the neurological level of spinal cord injury on cardiovascular outcomes in humans: A meta-analysis. *Spinal Cord.* 2012;50(7):484-492.
25. Krassioukov A, Claydon VE. The clinical problems in cardiovascular control following spinal cord injury: An overview. *Prog Brain Res.* 2006;152:223-229.
26. Gee CM, West CR, Krassioukov AV. Boosting in elite athletes with spinal cord injury: A critical review of physiology and testing procedures. *Sports Med.* 2015;45(8):1133-1142.
27. Chang YJ, Liang JN, Hsu MJ, Lien HY, Fang CY, Lin CH. Effects of continuous passive motion on reversing the adapted spinal circuit in humans with chronic spinal cord injury. *Arch Phys Med Rehabil.* 2013;94(5):822-828.
28. West CR, Currie KD, Gee C, Krassioukov AV, Borisoff J. Active-arm passive-leg exercise improves cardiovascular function in spinal cord injury: A case report. *Am J Phys Med Rehabil.* 2015;94(11):e102-106.
29. Muraki S, Ehara Y, Yamasaki M. Cardiovascular responses at the onset of passive leg cycle exercise in paraplegics with spinal cord injury. *Eur J Appl Physiol.* 2000;81(4):271-274.
30. Muraki S, Yamasaki M, Ehara Y, Kikuchi K, Seki K. Cardiovascular and respiratory responses to passive leg cycle exercise in people with spinal cord injuries. *Eur J Appl Physiol Occup Physiol.* 1996;74(1-2):23-28.
31. Nardone R, Orioli A, Golaszewski S, et al. Passive cycling in neurorehabilitation after spinal cord injury: A review. *J Spinal Cord Med.* 2016:1-9.
32. Nardone R, Langthaler PB, Bathke AC, et al. Effects of passive pedaling exercise on the intracortical inhibition in subjects with spinal cord injury. *Brain Res Bull.* 2016;124:144-149.
33. Thijssen DH, Steendijk S, Hopman MT. Blood redistribution during exercise in subjects with spinal cord injury and controls. *Med Sci Sports Exerc.* 2009;41(6):1249-1254.
34. Kooijman M, Rongen GA, Smits P, Hopman MT. Preserved alpha-adrenergic tone in the leg vascular bed of spinal cord-injured individuals. *Circulation.* 2003;108(19):2361-2367.
35. Schmid A, Huonker M, Barturen JM, et al. Catecholamines, heart rate, and oxygen uptake during exercise in persons with spinal cord injury. *J Appl Physiol.* 1998;85(2):635-641.
36. Waring WP, 3rd, Biering-Sorensen F, Burns S, et al. 2009 review and revisions of the international standards for the neurological classification of spinal cord injury. *J Spinal Cord Med.* 2010;33(4):346-352.
37. Venturelli M, Amann M, Layec G, et al. Passive leg movement-induced hyperaemia with a spinal cord lesion: Evidence of preserved vascular function [published online ahead of print November 5, 2013]. *Acta Physiol (Oxf).*
38. Martin Ginis KA, Latimer AE, Buchholz AC, et al. Establishing evidence-based physical activity guidelines: Methods for the Study of Health and Activity in People with Spinal Cord Injury (SHAPE SCI). *Spinal Cord.* 2008;46(3):216-221.
39. Rauch A, Hinrichs T, Oberhauser C, Cieza A, SwiSCI Study Group. Do people with spinal cord injury meet the WHO recommendations on physical activity? *Int J Public Health.* 2016;61(1):17-27.
40. Jensen MP, Truitt AR, Schomer KG, Yorkston KM, Baylor C, Molton IR. Frequency and age effects of secondary health conditions in individuals with spinal cord injury: A scoping review. *Spinal Cord.* 2013;51(12):882-892.

Appendix

Abbreviations

ACE = Arm crank ergometry is the quantitative measurement and evaluation of physical capacity and cardiopulmonary exercise tolerance (> stress and > strain) in both healthy and diseased subjects as well as trained athletes necessary during arm cranking.

AIS = ASIA Impairment Scale.

ASIA = American Spinal Cord Injury Association.

CVD = Cardiovascular disease includes disorders of the heart, blood vessels, and hemodynamic regulation.

HR = Heart rate is both a basic parameter of the exercise response during ergometry and a reference value for calculation of other parameters assessing cardiac response to stress.

ISNCSCI = International Standards for Neurological Classification after Spinal Cord Injury.

$(La^-)_b$ = Blood lactate concentration is indicative of lactate (lactic acid) produced within resting and working skeletal muscle.

PO = Power output is the amount of work performed per unit time in Watts (W, $J \cdot s^{-1}$).

PO_{peak} = Peak power output is the amount of work at peak performance.

V_E = Pulmonary ventilation is the rate at which gas enters or leaves the lungs. It is defined as tidal volume × respiratory rate ($L \cdot min^{-1}$).

RER = Respiratory exchange ratio is the ratio of carbon dioxide production to oxygen consumption ($\dot{V}CO_2/\dot{V}O_2$) measured across the mouth. In the steady state, when body CO_2 and O_2 stores are unchanging, this ratio serves as an indicator of gas exchange at the tissue level (ie, respiratory quotient, RQ) and reflects substrate utilization.

RPE = Rating of Perceived Exertion (Borg) reflects the subjective sensation of exertion and corresponds well to exercise capacity.

SCI = Spinal cord injury.

VO_{2peak} = Peak oxygen uptake is the highest oxygen uptake elicited during an exercise test to exhaustion in the absence of an oxygen uptake plateau. It is expressed either as an absolute rate in liters of oxygen per minute (L/min^{-1}) or as a relative rate in milliliters of oxygen per kilogram of bodyweight per minute ($mL \cdot kg^{-1} \cdot min^{-1}$).