Original Article

Kinetics and steady-state of $\dot{V}O_2$ responses to arm exercise in trained spinal cord injury humans

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Study design: Cross-sectional study comparing trained spinal cord injured (SCI) subjects (lesion level: L1~T6) with healthy young subjects (CONT).

Objective: To investigate the kinetics of response in oxygen uptake ($\dot{V}O_2$) in human upper-body skeletal muscles, nine trained SCI subjects underwent submaximal supine arm exercises.

Method: The SCI subjects underwent an incremental arm exercise test until exhaustion. The days after this first round of testing, breath-by-breath $\dot{V}O_2$ and beat-by-beat heart rate (HR) on- and off-kinetics were determined during three repetitions of constant exercise at 50% of $\dot{V}O_{2peak}$. The overall time course of response was determined from the half time ($t_{1/2}$). Increased capillary blood lactate production ($\Delta[La]b$) at the onset of exercise was defined as the difference between at rest and at the end of exercise. Cardiac output ($\dot{Q}$) was measured using the acetylene rebreathing method during the steady state of exercise. In accordance with the Fick principle, the difference in arterial-venous O_2 content ($Ca-\bar{v}O_2$) was defined as $\dot{V}O_2/\dot{Q}$.

Results: During the steady state of the submaximal arm exercise, a more significant increase in the steady state of $\dot{Q}$ was obtained in the CONT subjects than in the trained SCI subjects: respectively, 14.9 ± 1.4 l/min versus $(12.7 \pm 0.8$ l/min). There was no difference in the steady state of $\dot{V}O_2$ between the two groups; as a result, SCI subjects had the greater $Ca-\bar{v}O_2$. Meanwhile, $\dot{V}O_2$ on- and off-kinetics became much faster in the trained SCI subjects than in the CONT subjects. In addition, $t_{1/2}$ HR on-kinetics was not significantly different between the SCI and CONT groups. Increased $\Delta[La]b$ was closely related to larger $t_{1/2}$ $\dot{V}O_2$ on-kinetics ($r = 0.624$, $P < 0.05$).

Conclusion: It is concluded that the acceleration of $\dot{V}O_2$ on- and off-kinetics in the trained SCI subjects was observed even though there was no difference in HR on- and off-kinetics between the SCI and CONT groups and a lower steady state of $\dot{Q}$ in the trained SCI subjects. $\dot{V}O_2$ kinetics would therefore be the limiting factor in oxidative phosphorylation in the upper skeletal muscles, thereby providing a lower lactic O_2 -deficit (ie $\Delta[La]b$).

Sponsorship: This study was partly supported by the grant from Frontier Science Promotion in Kumamoto, Japan (1997, 1998).

Spinal Cord (2002) 40, 631–638. doi:10.1038/sj.sc.3101383

Keywords: spinal cord injured subjects; oxygen uptake; kinetics; half time; supine position; arm exercise

Introduction

Spinal cord injured (SCI) subjects have disadvantage factors including lower-limb blood pooling secondary to an inactive leg muscle pump and impaired

autonomic control below the level of spinal lesion. Both of these factors contribute to an altered circulatory response to the upper body.^{1–3} For SCI subjects, the supine position has been suggested not only to remove peripheral blood pooling in the lower limbs but also to improve central and peripheral circulation (ie promote greater venous return) by reducing perfusion pressure, thereby creating lower-

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gravity conditions even when the upper limbs are being exercised.⁴ The supine position, therefore, makes it possible to accurately evaluate the energy metabolism potential of the arm skeletal muscles in SCI subjects during exercise, without having to worry about circulatory conditions, such as blood pooling, in the lower limbs.

From previous studies of the metabolic machinery in the skeletal muscles, it has been established that the time constant of oxygen uptake ($\dot{V}O_2$) kinetics during arm exercise tends to be much greater, ranging from 60 to 120 s, as compared to that during leg exercise.^{5–7} Barstow *et al*⁸ reported that in paraplegia, $\dot{V}O_2$ kinetics during arm exercise was normal, being similar with those previous studies.^{5–7} This is due to the greater recruitment of fast-twitch fibers, the lower activation of oxidative enzymes, and the lactate production at the onset of exercise.⁹ However, swimmers with well-trained upper arms have faster $\dot{V}O_2$ kinetics during arm exercise, with a half time ($t_{1/2}$) of $\dot{V}O_2$ on kinetics of 47 ± 7 ($\bar{x} \pm SD$) s at 80% of maximal oxygen uptake.¹⁰ We are interested in finding out how much we can shorten the $t_{1/2}$ of $\dot{V}O_2$ kinetics in trained SCI subjects, and whether the $t_{1/2}$ of $\dot{V}O_2$ kinetics in these subjects will be able to approach that in untrained healthy able-bodied subjects on the design for effective clinical rehabilitation. We provided the evidence that $\dot{V}O_2$ kinetics are more sensitive to exercise training states than other physiological variables determined at peak exercise,¹¹ thus, the clinical evaluation in trained SCI subjects will be better to evaluate $\dot{V}O_2$ kinetics during arm exercise.

From another aspect of the steady-state exercise, Hopman *et al*^{12,13} reported that lower stroke volume (SV) in SCI subjects was compensated for by increased heart rate (HR) and, consequently at the same $\dot{V}O_2$ cardiac output ($\dot{Q}$) was similar to that in the able-bodied subjects. However, the compensation factor is not only a higher HR but also greater oxygen availability in working muscles to obtain the same $\dot{V}O_2$, in the case of trained SCI subjects, the latter may

greatly contribute. We hypothesize that, after the effects of cardiovascular response in the lower limbs of the SCI subjects have been neutralized by the alteration of posture position, the greater metabolic machinery in the upper trained muscles of these subjects induce faster $\dot{V}O_2$ kinetics and greater O₂ availability than in healthy but untrained able-bodied individuals. Thus, the aim of the present study was to evaluate the $\dot{V}O_2$ kinetics during submaximal supine arm exercise in a group of trained spinal cord injured subjects compared with untrained but able-bodied subjects.

Methods

Subjects

Nine trained spinal cord injured subjects (SCI; age: 35.1 ± 3.1 year, $\bar{x} \pm SEM$, damage level: T6 to L1) volunteered to participate in this study. These SCI subjects underwent a continuous wheelchair-basketball training program (basic skill training and game training, ~ 2 h/day, 3 days/week) with an intensity of approximately 80%HR_{peak}. Although we could observe the inter-individual variability of wheelchair-basketball training period (Table 1), all subjects have experienced for at least 2 years. Our previous observation provides the proof that greater metabolic potentials will be retained, as long as exercise training is continued.¹¹ Reference data were obtained from 10 healthy untrained able-bodied subjects (CONT; age: 23.3 ± 1.6 year, height: 169 ± 1.5 cm, weight: 66 ± 2.3 kg) who did not undergo any specific training program during at least 2 months before. Written, informed consent was obtained after each subject received a detailed explanation of the purpose and protocols of the experiments, which were approved by the ethics committee of the Institutional Review Board of the Prefectural University of Kumamoto. The SCI group's individual characteristics are listed in Table 1.

Table 1 The characteristics and lung function in the trained SCI subjects

	Age (year)	Sex	Mass (kg)	VC (L)	FEV1.0 (L)	FEV1.0/VC (%)	TSI (months)	Exercise career (year)	Lesion level	Condition
1	29	male	62	4.01	3.32	82.8	74	5	L1	complete
2	42	male	52	4.10	3.05	74.4	241	19	T11-12	complete
3	23	male	56	3.67	3.15	85.8	75	4.5	T12-L1	incomplete
4	36	male	75	3.93	2.87	73.0	128	9	T7	complete
5	45	female	65	2.92	2.55	87.3	324	17	T6	complete
6	27	male	50	3.42	2.95	86.3	59	5	T6	complete
7	19	male	71	4.52	3.97	87.8	38	2	T11	incomplete
8	51	male	67	3.47	2.55	73.5	385	31	L1	complete
9	44	male	60	4.22	3.6	85.3	256	20	L1	complete
Mean	35.1		62	3.81	3.11	81.8	176	12.5		
SEM	± 3.1		± 2.2	± 0.13	± 0.12	± 1.8	± 37	± 2.7		

VC=vital capacity (L); FEV1.0=forced expiratory volume at one second; TSI=time since injury (months). See text for further details

Experimental design

Before the exercise test, each subject underwent a clinical examination, a resting electrocardiogram (ECG 9020, Nihon-Koden, Japan) and spirometry (AS-300, Minato Medical Sciences, Japan) to determine lung volume and bronchial flow. Bronchial flow was determined from forced expiratory volume during 1 s (FEV1.0) and normalized FEV1.0 was determined by vital capacity (VC).

In both the CONT and SCI groups, the subjects underwent an incremental supine arm exercise (*incremental exercise*: starting from rest, 20 W added every 3 min) on an electromagnetically braked arm cranking ergometer (75XL, Conbi, Japan) until voluntary exhaustion, which was defined as the inability to sustain the recommended cranking frequency of ~ 60 revolutions/min (rpm) despite vigorous encouragement by the operators (Figure 1). Pedaling frequency was digitally displayed to the subjects throughout the tests. The criteria of peak performance was applied that (1) the subject was unable to sustain a cranking frequency of ≥ 40 rpm for the assigned load; and (2) gas exchange ratio (R; calculated as $\dot{V}CO_2/\dot{V}O_2$) were reached >1.05 .

A few days after the incremental test, each subject performed three repetitions of a square-wave exercise (*constant exercise*), on the same arm cranking ergometer, at a workload corresponding to 50% of the 'peak' $\dot{V}O_2$ determined the days before. A constant load, corresponding to 50% of $\dot{V}O_{2peak}$, was utilized in order to avoid complexities associated with the so-called 'slow component' of $\dot{V}O_2$ on-kinetics,¹⁴ which should become manifest at higher percentages of $\dot{V}O_{2peak}$. Pedaling frequency was also kept at ~ 60 rpm during this constant exercise test. Each subject rested at least 10–15 min at a time between

repetitions. On-transitions were from rest (the subject lay on a bed with both hands tightly strapped to the pedals) to the imposed load, which was attained in ~ 3 s. Off-transitions were from the imposed load to rest. Orders to start and stop pedaling were given by voice to the subjects, without warning. Pulmonary ventilation ($\dot{V}_E$), $\dot{V}O_2$ and CO_2 output ($\dot{V}CO_2$) were determined breath-by-breath using a computerized metabolic cart (AE-280; Minato Medical Sciences, Japan). Expiratory flow and inspiratory flow measurements were performed by a mass flow sensor (hot-wire anemometer), and were calibrated before each experiment by a 3-liter syringe at three different flow rates. Tidal volume (V_T) and $\dot{V}_E$ were calculated by integrating the flow tracings recorded at the subject's mouth. $\dot{V}O_2$ and $\dot{V}CO_2$ were determined by continuously monitoring PO_2 and PCO_2 at the mouth of the subject throughout the respiratory cycle and from established mass balance equations, after alignment of the expiratory volume and expiratory-gas tracings and A/D conversion. Expiratory PO_2 and PCO_2 were determined by mass spectrometry (WSMR-1400, Westorn, Japan) from a sample drawn continuously from the inside of the mouthpiece at 1 ml/s; the loss of volume was neglected in our calculations. The O_2 and CO_2 concentrations were calibrated before each experiment by utilizing gas mixture of known composition. Digital data were transmitted to a personal computer for storage. $\dot{V}O_2$ and $\dot{V}CO_2$ were expressed in STPD, and $\dot{V}_E$ was expressed in BTPS. Heart rate (HR) was determined beat-by-beat from the R-R intervals using a cardiometer coupler (AG901, Nihon-Koden, Japan). During the constant exercise test, 20 μ l of earlobe capillary blood was obtained for the determination of lactate concentration ([La]b) by an enzymatic method (Sports 1500,

Figure 1 Experimental scheme for supine arm exercise

YSI, USA) at resting and at the end of exercise in the first bout of constant exercise at 50% of $\dot{V}O_{2peak}$. We could not measure [La]b in one SCI subject because of transient trouble with the device. An increase in the capillary blood lactate concentration ($\Delta[La]b$) at the onset of exercise was defined as the difference between the concentration obtained at rest and that obtained at the end of exercise.

Measurement of cardiac output

After obtaining the steady state of arm exercise at 50% of $\dot{V}O_{2peak}$, we measured cardiac output ($\dot{Q}$) using the acetylene rebreathing method.¹⁵ For this measurement, each subject rebreathed a mixture of 8%Ar-25%O₂-0.6%C₂H₂-66.4%N₂ from a closed-system with 2.5-liter rubber anesthesia bag. The concentrations of C₂H₂, O₂, and Ar were continuously monitored by a mass spectrometer (WSMR-1400, Westorn, Japan) interfaced with an NEC computer for data storage and processing. Cardiac output was calculated from the exponential disappearance rate of C₂H₂ relative to Ar in several sequential inhalations and exhalations. In accordance with the Fick principle, stroke volume (SV) was defined as $\dot{Q}/HR$, and arterial-venous O₂ difference content (Ca- $\bar{v}O_2$) was also defined as $\dot{V}O_2/\dot{Q}$.

Data analysis

Resting values were obtained by calculating averages during the last 60 s of rest while undergoing the incremental exercise test. Values obtained during the last 30 s of the incremental exercise were considered 'peak' values of work rate (WR), $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$, and R.

As for the constant exercise, breath-by-breath $\dot{V}O_2$ data and beat-by-beat HR data obtained during the three repetitions were time-aligned and superimposed for each subject.¹¹ Steady-state values, defined as 'ss', and recovery resting were calculated over 60 s intervals, during the last minute of constant exercise, and between the fourth and fifth minutes of recovery. For on- (rest-to-exercise) and off- (exercise-to-rest) $\dot{V}O_2$ and HR kinetics analysis, data smoothing was obtained by calculating a five-point moving average,¹¹ which made it easy to visualize the $t_{1/2}$ point. These variables during the on- and off-transitions followed the standard kinetics, and were evaluated by fitting a polynomial function to $\dot{V}O_2$ and HR vs time data, and by solving the function for the time values at which the function reached 50% of the difference between the baseline and the new asymptotic value. $t_{1/2}$ has been reported to be an adequate indicator of metabolic activity in the skeletal muscles on the basis of the phase II response,^{9,10,16} which corresponds with our interest in gas exchange occurring at the muscle level; the time elapsed during phase I was also taken into consideration.^{9,10,16} Therefore, the overall time course of response was determined from $t_{1/2}$.

Statistical analysis

Data were analyzed using a two-way analysis of variance, between/within split-plot design, with repeated measures. Training status was the 'between' variable, and time was the 'within' variable. Whenever a significant difference was found, a Tukey's *post hoc* test was used for discrimination. Significance was set at 0.05. Data are presented as mean $\pm$ standard error ($\bar{x} \pm SEM$).

Results

VC, FEV1.0 and FEB1.0/VC in the SCI subjects exhibited normal range in standard criteria for pulmonary function tests (Table 1). At incremental arm exercise, $\dot{V}O_{2peak}$ was similar in both groups: 25.4 ± 1.7 ml/kg/min in the SCI group, and 26.2 ± 1.4 ml/kg/min in the CONT group, respectively (Table 2). Since R_{peak} was achieved over 1.05 in both groups (SCI, 1.14 ± 0.02 , CONT, 1.19 ± 0.02), they would undergo an incremental exercise until their exhaustion.

The steady-state 'ss' of cardiovascular and gas exchange variables at 50% of $\dot{V}O_{2peak}$ are shown in Table 3, in which $\dot{V}CO_{2ss}$, $\dot{V}_{Ess}$ and HR_{ss} in the SCI group were similar with those in the CONT group. $[La]b_{ss}$ in the SCI group was significantly lower than in the CONT group. Also, R_{ss} was 0.96 ± 0.03 in the SCI group and 1.03 ± 0.03 in the CONT group, reaching significance ($P < 0.05$). End-tidal PO_{2ss} and PCO_{2ss} were also the same in both groups. Interestingly, a significant increase in $\dot{Q}_{ss}$ was 14.9 ± 1.4 l/min in the CONT group compared with that in the SCI groups (12.7 ± 0.8 l/min), and the resultant increase of 16% in SV_{ss} was observed in the CONT group. Consequently, Ca- $\bar{v}O_{2ss}$ in the SCI group became significantly greater than in the CONT group.

Figure 2 shows breath-by-breath $\dot{V}O_2$ and beat-by-beat HR response at rest, during 5 min supine exercise at 50% of $\dot{V}O_{2peak}$ and during recovery, in a typical CONT and SCI subject. Significantly lower $t_{1/2}$ for $\dot{V}O_2$ on- and off-kinetics was shown in the SCI group during constant exercise (Figure 3). For $\dot{V}O_2$ kinetics, $t_{1/2}$ on-kinetics was not statistically significantly

Table 2 The value of ventilatory and gas exchange variables obtained at peak supine arm exercise

	CONT	SCI
WR (W)	76 ± 4	82 ± 5
$\dot{V}_E$ (l/min)	58.6 ± 4.2	58.1 ± 3.5
$\dot{V}O_2$ (ml/min)	1763 ± 118	$1550 \pm 100^*$
(ml/min/kg)	26.2 ± 1.4	25.4 ± 1.7
$\dot{V}CO_2$ (ml/min)	2101 ± 148	$1769 \pm 119^*$
HR (beats/min)	140 ± 5	$157 \pm 6^{**}$
R	1.19 ± 0.02	$1.14 \pm 0.02^{**}$

Values are mean $\pm$ SEM of two groups for work rate (WR), pulmonary ventilation ($\dot{V}_E$), O₂ uptake ($\dot{V}O_2$), CO₂ production ($\dot{V}CO_2$), heart rate (HR), and gas exchange ratio (R). *, ** $P < 0.05$, 0.01: significant difference vs CONT. See text for further details

different from that of off-kinetics. However, HR kinetics in the SCI group was very similar to the data obtained in the CONT group. $t_{1/2}$ on- for HR kinetics was significantly lower than $t_{1/2}$ off-, indicating a slower HR off-response during the recovery period.

Table 3 The steady-state values of cardiovascular and gas exchange variables obtained at 50% $\dot{V}O_{2peak}$ during supine arm exercise

	CONT	SCI
WR (W)	38 ± 2	41 ± 3
$\dot{V}_E$ (l/min)	26.6 ± 1.1	27.7 ± 1.9
$\dot{V}O_2$ (ml/min)	875 ± 44	863 ± 40.5
$\dot{V}CO_2$ (ml/min)	884 ± 45	833 ± 49
SV (ml)	138 ± 10	118 ± 9*
Q (l/min)	14.9 ± 1.4	12.7 ± 0.8*
HR (beat/min)	103 ± 4	105 ± 4
Ca- $\bar{v}O_2$ (ml/100ml)	5.9 ± 0.6	6.8 ± 0.7*
R	1.03 ± 0.03	0.96 ± 0.03*
PET O_2 (mmHg)	108 ± 1	108 ± 2
PET CO_2 (mmHg)	42 ± 2	38 ± 1
[La]b (mmol/l)	3.2 ± 0.4	1.5 ± 0.1*

Values are mean ± SEM of two groups for WR, $\dot{V}_E$, $\dot{V}O_2$, $\dot{V}CO_2$, HR, R and end-tidal O_2 and CO_2 pressures (PET O_2 , PET CO_2). Cardiac output (Q) was determined using acetylene rebreathing and arterial-venous O_2 difference content (Ca- $\bar{v}O_2$) was also defined as $\dot{V}O_2/Q$. * $P < 0.05$: significant difference vs CONT. See text for further details

Figure 2 Breath-by-breath $\dot{V}O_2$ and beat-by-beat HR responses at rest, during 5 min supine exercise at the onset of 50% of $\dot{V}O_{2peak}$ and during recovery in a typical CONT and SCI subjects. The half times ($t_{1/2}$) of the on- and off-responses are indicated by the symbol. $\dot{V}O_2$ on- in the trained SCI subject was much faster than in the CONT subject

Changes in blood lactate ($\Delta[La]b$) as a function of $t_{1/2}$ of $\dot{V}O_2$ on-kinetics were observed in both groups during supine arm cranking exercise at 50% of $\dot{V}O_{2peak}$ (Figure 4). Note especially that both groups had a shift of the points toward a shorter $t_{1/2}$ $\dot{V}O_2$ on-kinetics and a corresponding decrease in $\Delta[La]b$ ($r = 0.624$, $P < 0.05$; x intercept, 22.3 s) in all subjects. In addition, as a result of processing statistically in each group, the significant correlation was observed in the CONT group ($r = 0.71$, $P < 0.01$), otherwise, no correlation was found in the SCI group ($r = -0.25$, ns).

Discussion

For submaximal constant exercise, this is the first description of pulmonary $\dot{V}O_2$ and HR kinetics following the onset of exercise and after recovery when

Figure 3 Half time ($t_{1/2}$) for HR and $\dot{V}O_2$ on- and off-kinetics in the SCI group was compared with the CONT group. ** $P < 0.01$ Significantly different from the value in the CONT group. † $P < 0.05$ Significantly different from the value in off-. See text for further details

Figure 4 Changes in blood lactate concentration ($\Delta[La]b$) as function of $t_{1/2}$ of $\dot{V}O_2$ on-kinetics for the SCI group (open circle) and the CONT group (closed circle) performing supine arm cranking at 50% of $\dot{V}O_{2peak}$. $\dot{V}O_2$ on- and corresponding decrease in $\Delta[La]b$ in all subjects ($r=0.624$, $P<0.05$; x intercept, 22.3 s). See test for further details

the trained SCI subjects performed an arm exercise. It has been observed that $\dot{V}O_2$ kinetics in the trained SCI subjects was accelerated compared to healthy able-bodied subjects. This has been attributed, in part, to a small accumulation of the lactate in arm exercise. Meanwhile, the HR kinetics were very similar between the two groups. This is because of the noteworthy observation that O_2 ability to diffuse to mitochondria apparently increased in the trained SCI subjects during the steady-state of the arm exercise (Table 3), hence O_2 delivery to muscle would not be a limiting factor for $\dot{V}O_2$ kinetics. Thus, the dynamic rates of gas exchange adjustments are more accelerated in the trained muscles of the trained SCI subjects than in the untrained muscles of health subjects. These accelerated rates positively affect exercise tolerance, with important implications for the rehabilitation of spinal cord injuries.

Steady-state values in response to cardiovascular and gas exchange variables at 50% $\dot{V}O_{2peak}$ of constant exercise $[La]b_{ss}$ at 50% $\dot{V}O_{2peak}$ of constant exercise was significantly higher in the CONT group than in the SCI group, and the $\Delta[La]b$ was an increase of <3 mmol/l in the CONT group but <2 mmol/l in the SCI group without acting in a lactate buffering capacity. Consequently, R_{ss} and $\dot{V}CO_{2ss}$ were lower in the SCI group than in the CONT group. The $[La]b_{ss}$ increase by >3 mmol/l provides a greater contribution to the lactic O_2 metabolism in exercising muscles, since

it is related to the results of slower dynamic response of $\dot{V}O_2$ in the CONT group ($r=0.71$, $P<0.01$). Concomitantly, $\Delta[La]b$ is one of the important factors in regulating the $\dot{V}O_2$ kinetics at the onset of exercise⁹ as well as the muscle blood flow into working muscles.¹⁷ From another aspect of steady-state exercise, it seems likely that relatively less $\Delta[La]b$ would not influence $\dot{V}O_{2ss}$ in either the SCI group or the CONT group, because the slow component of $\dot{V}O_2$ was not observed after the exponential $\dot{V}O_2$ response.¹⁴

Using the C_2H_2 rebreathing method, it is a very interesting finding that, during arm exercise, the measured $\dot{Q}_{ss}$ in the CONT group could be much higher (a 17% increase) than in the SCI group. Meanwhile, $Ca\text{-}\bar{v}O_{2ss}$ was apparently increased in the SCI group with no difference in $\dot{V}O_{2ss}$ between the groups. Similarly, Davies and Shephard¹⁸ and Hjeltne¹⁹ also observed a hypokinetic circulation (lower $\dot{Q}$) in nine paraplegics. By contrast, Hopman *et al*^{12,13} observed a similar $\dot{Q}_{ss}$ with lower SV_{ss} , which was compensated for by increased HR_{ss} during submaximal exercise. From these observations, although blood pooling of the lower limbs would be considerably reduced in the supine position, the observed lower SV_{ss} and $\dot{Q}_{ss}$ during submaximal exercise in the SCI group may be attributed to venous blood pooling below the lesion. Secondly, exercise training could elicit a compensatory improvement in oxygen extraction in the upper muscles of the SCI group.

Does $\dot{V}O_2$ kinetics depend on muscle blood flow during exercise?

Interestingly, Hughson *et al*¹⁷ found that forearm exercise with the arm above the heart elicits the $\dot{V}O_2$ response that was attenuated early and augmented later in the exercise, compared with an exercise that was identical except that the arm was below the heart. In addition, Hughson *et al*²⁰ also confirmed the hypothesis that, if limited blood flow did indeed slow $\dot{V}O_2$ kinetics at the onset of supine exercise, then a lower-body negative pressure maneuver might be expected to increase perfusion pressure and then facilitate O_2 transport to the exercising leg, which would accelerate the $\dot{V}O_2$ kinetics even during supine exercise. From some observations, perfusion pressure in active muscle plays a key role in limiting $\dot{V}O_2$ kinetics, and the resultant reduction in perfusion pressure leads to reduced exercise tolerance and slower $\dot{V}O_2$ kinetics.^{17,20–22}

It is possible that blood flow into the upper muscles might form a blunted rise in O_2 delivery during supine arm exercise above the heart. Actually, however, $\dot{V}O_2$ kinetics in the present study became much faster as compared with that during arm cranking exercises in an upright posture in some previous studies.^{5,7,8,10}

Our observation of similar $t_{1/2}$ HR on- and off-kinetics in both groups suggests that the $\dot{V}O_2$ kinetics was not matched to the HR kinetics, at least during

the transient phases of exercise. Although we did not measure the cardiac output in the transient phases, if $\dot{Q}$ kinetics have the same tendency as HR kinetics, the remarkable difference in $t_{1/2} \dot{V}O_2$, in comparison between the SCI and CONT groups, is not attributed to, at least for the transition to exercise, O_2 delivery to muscle. But, this speculation is not in agreement with the recent work of slower kinetics for femoral arterial blood flow in a comparison between exercises taking place above the heart and below the heart,¹⁷ and a lower-body negative pressure maneuver.²⁰

$\dot{V}O_2$ on- and off-kinetics during constant exercise in lesion leg of SCI

In the trained-muscle group, greater metabolic potentials appears, ie faster $\dot{V}O_2$ kinetics. $t_{1/2} \dot{V}O_2$ on-kinetics in the SCI group was 35.6 ± 2.9 s, which is equal to that reported by Cerretelli *et al.*⁹ Interestingly, Barstow *et al.*²³ provided data showing that the mean response times of $\dot{V}O_2$ kinetics during lesion leg exercises with a functional electro stimulation (FES) maneuver were 165 ± 62 s ($\bar{x} \pm SD$) on-kinetics and 103 ± 28 s off-kinetics. However, the much slower recovery kinetics for phosphocreatine (PCr) was observed with $t_{1/2}$ of 5.8 min by ^{31}NMR in persons with paraplegia following 3 min of tetanic isometric contraction of the quadriceps.²⁴ Fundamentally, as we utilized functionally normal muscle groups in both the SCI and CONT groups, the physiologically higher metabolic potentials in the upper limbs of the SCI group can be observed, owing to the wheelchair exercise training.

Exercise training accelerates $\dot{V}O_2$ kinetics during constant exercise

The much faster $\dot{V}O_2$ kinetics in the SCI group must be the result of the increased aerobic capacity of the trained muscles as a result of the wheelchair exercise training. Changes in aerobic capacity are associated with parallel changes in mitochondrial density and capillarity of skeletal muscles.²⁵ Also, Taylor *et al.*^{26,27} observed a significant increase in slow twitch areas after endurance arm exercise training in SCI subjects, and it supported in faster $\dot{V}O_2$ kinetics in the trained SCI subjects. Interestingly, exercise training could bring about accelerated metabolic adjustment, ie, faster gas exchange kinetics, even in lesion muscles.²⁸ As well, inactivity, such as from bed-rest, in normal healthy subjects resulted in reduced exercise capacity and slower $\dot{V}O_2$ kinetics.²⁹

Aerobic exercise, such as wheelchair-basketball training, increases the total volume of mitochondria and the total volume of myofibrils in a given tissue due to muscle hypertrophy in the upper limbs.³⁰ The increased volume of mitochondria in arm muscles leads to enhanced aerobic capacity and to faster $\dot{V}O_2$ kinetics. There is a high possibility that our trained SCI subjects had greater upper-muscle mitochondria

volume due to their upper muscle hypertrophy, even though their lower limbs are atrophied. Thus, the endurance training of a specific muscle might be characterized by a faster rise in $\dot{V}O_2$ during submaximal exercise.⁹

$\Delta[La]b$ was related to slower $\dot{V}O_2$ on-kinetics during arm crank exercise

We found a close relationship between $t_{1/2}$ on $\dot{V}O_2$ kinetics and the lactate accumulation. This provided a greater lactic O_2 -deficit in the CONT group, and therefore a sluggish muscle $\dot{V}O_2$ adjustment. As previously reported, the $t_{1/2}$ of $\dot{V}O_2$ kinetics is accompanied by a smaller O_2 -deficit with lower $\Delta[La]b$.^{9,31,32} The x intercept of the regression line of 22.3 s (Figure 3) means less production of early lactate after the onset of exercise, which is in agreement with the values for contracting skeletal muscles *in situ* gastrocnemius in dogs.³³ Less lactate production may lead not only to the acceleration of $\dot{V}O_2$ kinetics, but may also contribute to the similar time constant $\dot{V}O_2$, independent on the exercise modes. Coincidentally, another noteworthy observation of the present study appears to be that, whereas the hastening of $\dot{V}O_2$ on-kinetics due to exercise training was completely independent of muscle atrophy in the lower limbs (unpublished data), the effects of $t_{1/2}$ HR on-kinetics were unaffected by the exercise training.

Conclusions

In studying a group of trained spinal cord injured subjects, we reached the following conclusions: (1) during the steady-state of constant exercise, greater $Ca\text{-}\bar{V}O_{2ss}$ in the trained SCI subjects would be effectively adapted, which compensated for the resultant reduction in $\dot{Q}_{ss}$ response, and led to the same $\dot{V}O_{2ss}$ at 50% and $\dot{V}O_{2peak}$; (2) faster $\dot{V}O_2$ both on- and off-kinetics would be attributed to peripheral (muscular) factors including less lactate production, and was not associated with HR on- and off-kinetics; and (3) a strong relationship between $\Delta[La]b$ and $t_{1/2}$ of $\dot{V}O_2$ on-kinetics during arm exercise was observed, suggesting a less lactic O_2 -deficit in the SCI subjects and therefore a faster muscle $\dot{V}O_2$ adjustment.

Acknowledgements

We appreciate the critical comments of Dr Shynsaku Koga, Kobe Design University, Japan. We gratefully acknowledge the expert technical assistance of Miss Y Nakamura, Miss C Murakami and Miss M Iwamizu.

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