REGULAR PAPER

J. Physiol. Sci. Vol. 56, No. 5; Oct. 2006; pp. 347–353
Online Sep. 28, 2006; **doi:10.2170/physiolsci.RP005606**

Oxygen Uptake Kinetics Following 20 Days of Unilateral Lower Limb Suspension

Norio HOTTA[1], Kohei SATO[2], Keisho KATAYAMA[3], Shunsaku KOGA[4], Kazumi MASUDA[5], Motohiko MIYACHI[6], Hiroshi AKIMA[3], and Koji ISHIDA[3]

[1]Graduate School of Medicine, Nagoya University, Nagoya, Japan; [2]Research Institute of Physical Fitness, Japan Women's College of Physical Education, Tokyo, Japan; [3]Research Center of Health, Physical Fitness and Sports, Nagoya University, Nagoya, Japan; [4]Applied Physiology Laboratory, Kobe Design University, Kobe, Japan; [5]Faculty of Education, Kanazawa University, Kanazawa, Japan; and [6]Laboratory of Physical Activity and Health Evaluation, National Institute of Health and Nutrition, Tokyo, Japan

Abstract: The purpose of the present study was to examine the effect of unilateral lower limb suspension (ULLS) deconditioning on oxygen uptake kinetics. Eight healthy males underwent ULLS for 20 days and performed a series of 6-min square-wave transitions from rest to 60-W single-leg cycling exercises just before and after ULLS. To characterize the kinetics of the oxygen uptake response, a single exponential model was applied to the data until the end of the fast component omitted the first 15 s of the on-transit using a nonlinear least-squares fitting procedure. The following results were found: (i) the time constant of oxygen uptake was unchanged before and after ULLS; (ii) although there was no significant difference in the baseline and the asymptotic amplitude of the fast component, the asymptote, i.e., the absolute asymptotic amplitude of the fast component (the sum of the baseline and the asymptotic amplitude), and the end exercise oxygen uptake were decreased after ULLS; (iii) the contribution of the slow component to the total response of oxygen uptake was unchanged at pre- and post-ULLS. In conclusion, the asymptote in the fast component and the end exercise oxygen uptake were decreased after 20-d ULLS, though the response speed and the amplitude of the slow component of oxygen uptake were not changed. It is suggested that deconditioning as a result of limb disuse affects oxygen uptake response.

Key words: oxygen uptake fast component, oxygen uptake slow component, limb disuse.

In general, to analyze oxygen uptake ($\dot{V}O_2$) kinetics in exercising humans, $\dot{V}O_2$ is usually measured at the mouth by means of the breath-by-breath method. The response speed of $\dot{V}O_2$ to exercise, i.e., the time constant of $\dot{V}O_2$ kinetics of the fast component in which $\dot{V}O_2$ increases exponentially and reaches a steady state within 2–3 min after the onset of exercise, is affected by O_2 delivery systems consisted of central and peripheral circulation, and the function of O_2 utilization, such as the activity of oxidative enzymes in the muscle [1, 2]. In cases where the intensity of exercise is heavy, $\dot{V}O_2$ increases moderately after the end of the fast component, and this is known as the slow component. Although the mechanisms remain speculative, it is thought that the recruitment of fast twitch fibers or the added recruitment of muscle fibers, which have not yet participated in muscle contraction, is the primary cause [3].

It is known that the fast component of $\dot{V}O_2$ kinetics is faster in trained than in untrained individuals [4]. This would indicate that because the time to start producing lactic acid obstructing muscular contraction is shortened, burdens of exercise decrease. Further, Carter *et al.* [5] revealed that the $\dot{V}O_2$ slow component was attenuated by 6 weeks of endurance training. This would imply that the subjects were able to accomplish the same level of exercise without the mobilization of added muscular fibers or fast twitch fibers. The endurance tolerance of each muscle fiber would be increased. Therefore it is conceivable that endurance training would speed up $\dot{V}O_2$ kinetics and would lead to the elimination of the $\dot{V}O_2$ slow component so that humans could continue exercising without as much effort in comparison with before endurance training.

On the contrary, little is known about the effect of inactivity on $\dot{V}O_2$ kinetics. An investigation performed by Convertino *et al.* [6] revealed that $\dot{V}O_2$ kinetics in an upright position became slowed after bed rest deconditioning. To our knowledge, their research is the only one of its kind that has compared $\dot{V}O_2$ kinetics before and after inactivity, so their research is thought to be very beneficial. However, there are times in which humans are forced into not only whole body inactivity, such as bed rest, but also into limb disuse, such as when an arm or leg is set in a cast or in limb suspension. Until now there have been no studies that have compared $\dot{V}O_2$ kinetics before and after limb

Received on May 27, 2006; accepted on Sep 25, 2006; released online on Sep 28, 2006; doi:10.2170/physiolsci.RP005606
Correspondence should be addressed to: Norio Hotta, Research Center of Health, Physical Fitness and Sports, Nagoya University, Furo-cho, Chikusa-ku, Nagoya, 464-8601 Japan. Tel: +81-52-789-5927, Fax: +81-52-789-3957, E-mail: hotta-n@med.nagoya-u.ac.jp

disuse. Previous studies have reported that even limb disuse attenuates muscle oxidative capacity [7], function of peripheral circulation [8, 9], and muscle strength [10]. Thus even limb disuse might have an influence on $\dot{V}O_2$ kinetics.

We have therefore decided to investigate the effects of limb disuse on $\dot{V}O_2$ kinetics. Slightly more than a decade ago, unilateral lower limb suspension (ULLS) was developed by Berg *et al.* [10] to expose the lower limb to unloading, and in their research they clearly showed that muscle atrophy and a decrease in muscle strength occur in the suspended leg after ULLS, similar to the results of bed rest. We recognized that ULLS could be the equivalent of limb disuse and measured $\dot{V}O_2$ during cycling exercise, using only the ULLS leg before and after 20 d of ULLS.

METHODS

Subjects. Eight healthy men, whose average age, height, and body mass were 20.0 ± 0.2 (mean ± SD) years old, 169.6 ± 6.6 cm, and 62.8 ± 5.4 kg, respectively, volunteered to participate in this study. The subjects were informed of the experimental protocol and the possible risks involved in this study before writing their consent. Approval of this study was given by the ethics committee of the Research Center of Health, Physical Fitness and Sports at Nagoya University.

Experimental procedure. Initially, preliminary testing was carried out to familiarize all subjects with the experimental procedures and apparatuses. The actual experiments were performed, on a day different from the preliminary testing, just before (Pre) and after 20 days of ULLS (Post).

ULLS. Each subject's left lower limb was suspended using a harness in the same way as in a previous study [10]. All ambulatory activities were conducted for 20 days by means of crutches. The harness was made of tubular nylon strips and allowed for the suspension of the left leg by means of a strap secured around the waist and attached to the foot. The harness was fastened so that the toe of the subject was lifted approximately 15 cm above ground level, and the knee was fixed at an angle of 90–130° (180° = full knee extension).

To prevent deep venous thrombosis, we made sure that each subject wore a knee-length compression stocking, drank water frequently, and performed light exercise of the ankle joint, which has been recommended by some airlines to prevent economy-class syndrome, at least 3 times a day during ULLS. The subjects were allowed to move the hip, knee, and ankle joints. To reduce joint stiffness, they were required to move their leg musculature in the morning and evening. To monitor compliance, the subjects kept diaries and were interviewed about their activities 2–3 days a week during ULLS. We then measured the skin temperatures of the leg calves by using a data logger (HR3087, YOKOGAWA, Japan). The sensors were put on the calves of both legs for approximately 10 min. We also measured the circumferences of the thighs and calves at the same spots at Pre and Post.

Exercise test. The subjects performed a series of 6-min square-wave transitions from rest to 60-W single-leg cycling exercise using an electromechanically braked bicycle ergometer (Aerobike 800, COMBI, Japan) three times. Resting intervals were taken until HR returned to within 5 beats/min of the pre-exercise value according to the methods of a previous study [6]. The pedaling rate was kept constant at 60 rpm with the aid of a metronome. The position of the saddle for each subject before and after ULLS was kept the same.

Measurements. Respiratory parameters were determined by means of the breath-by-breath method. The gas fractions were analyzed by a mass spectrometer (ARCO-1000, Arco System, Japan) every 10 ms. Inspired and expired gas volumes were measured by a Fleisch pneumotachometer (WLCU-5201, Westron, Japan). Breath-by-breath data were analyzed continuously using customized software on a computer to calculate $\dot{V}O_2$, carbon dioxide output ($\dot{V}CO_2$), expiratory minute ventilation ($\dot{V}_E$), and respiratory exchange rate (RER). Heart rate (HR) was measured beat-to-beat from the R spike using an electrocardiogram through a bioamplifier (AB 621G, Nihon Kohden, Japan). Beat-to-beat arterial blood pressure (BP) waveforms were measured by means of a Portapres Model 2 noninvasive BP monitor (TNO-TPD BMI, The Netherlands). Systolic BP (SBP) and diastolic BP (DBP) were obtained at the instantaneous pressure outputs, and mean BP (MBP) was calculated from the formula: MBP = 1/3 (SBP-DBP) + DBP. They were converted from analog to digital data using an A/D converter (CBI-3133B, Interface, Japan) at a sampling frequency of 100 Hz and stored on a computer (PC-LM700, NEC, Japan).

Kinetic analysis. To remove nonphysiological datum points resulting from coughing and sneezing, any breaths more than four standard deviations away from the mean of the surrounding six breaths (3 before and 3 after) were deleted according to the methods presented in a previous study [11]. The breath-by-breath data were aligned with the onset of exercise and then linearly interpolated between each breath to yield a datum point at 1-s intervals. Ensemble averaging was carried out across three repetitions. Beat-to-beat HR and BP data were analyzed in the same way as the breath-by-breath data. Also, $\dot{V}O_2$ data were averaged every 15 s.

Many investigators observe $\dot{V}O_2$ response to both moderate (< anaerobic threshold, AT) exercise without the slow component and heavy (>AT) exercise with the slow component, and the analyzing procedures are different. However, we measured $\dot{V}O_2$ response to exercise only at 60 W. Therefore to confirm whether the slow component existed, the on-transit of $\dot{V}O_2$ response to the exercise at

Pre was modeled as mono-exponential, beginning after the first 15 s and continuing to the 3rd min, and beginning after the first 15 s and continuing to the end (6th min) for each subject. As a result, since time constants of the latter in all subjects were larger when compared with those of the former (Fig. 1), we determined that the intensity was >AT and that the slow component was contained in the $\dot{V}O_2$ response.

The resulting $\dot{V}O_2$ response was modeled with nonlinear least-squares fitting procedures to an exponential response by computer software (Origin 6.1). The on-transit of $\dot{V}O_2$ response to 60-W intensity exercise was modeled as a mono-exponential, beginning after the first 15 s (the end of phase I, the start of phase II) and continuing to a new steady state of the fast component (the end of phase II) [12].

$$\dot{V}O_2(t) = \dot{V}O_2,BL + \Delta\dot{V}O_2,fast\,(1 - e^{-(t-TD)/\tau})$$

where $\dot{V}O_2$,BL is the baseline, $\Delta\dot{V}O_2$,fast is the asymptotic amplitude to which $\dot{V}O_2$ projects (Fig. 2), τ is the time constant of the response, and TD is the delay time. To find the end of the fast component, i.e., the start of the slow component (the end of phase II and the start of phase III), two alternative indexes were used following the methods used in a previous study [13]: (i) the maintenance of the flat profile of the residual plot, as judged by visual inspection; (ii) the demonstration of a local threshold for increase in the chi-squared value (Fig. 2). The magnitude of the $\dot{V}O_2$ slow component ($\dot{V}O_2$,sc) (Fig. 2) was taken as the difference between the amplitude of the final measured value averaged for the last 30 s ($\dot{V}O_2$,end) and the asymptote, i.e., absolute amplitude, in the fast component, demonstrated as the sum of $\dot{V}O_2$,BL and $\Delta\dot{V}O_2$,fast ($\dot{V}O_2$,fast) (Fig. 2). The percentage of contribution of the slow component to the total response of $\dot{V}O_2$ (%$\dot{V}O_2$,sc) thus equals: (($\dot{V}O_2$,end – $\dot{V}O_2$,fast)/$\Delta\dot{V}O_2$,fast) × 100.

As for $\dot{V}_E$, RER, HR, and MBP, we averaged them for 1 min before the onset of exercise and for 15 s before the 3rd min and 6th min and defined them as BL, 3rd and 6th.

Statistical analysis. All values were expressed as means ± SD. We compared the variables using the Wilcoxon signed-ranks test. Statistical analyses were computed by software (StatView 5.0), and the level of significance was set at 5%.

RESULTS

Effect of ULLS on the muscle

As for the circumference of the thigh, the difference in the ULLS leg between Pre and Post (–1.49 ± 1.2 cm) was significantly ($P < 0.05$) larger than that of the control leg

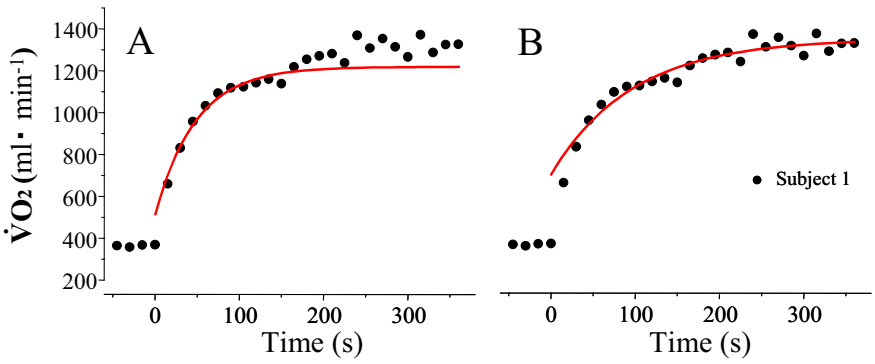

Fig. 1. $\dot{V}O_2$ response for a representative subject with model fits. The case with the mono-exponential fit limited to until 3 min after the start of exercise (**A**), and with the entire response modeled with a mono-exponential (**B**). Note that response speed is different between A and B (τ = 47.8 and 96.1 s).

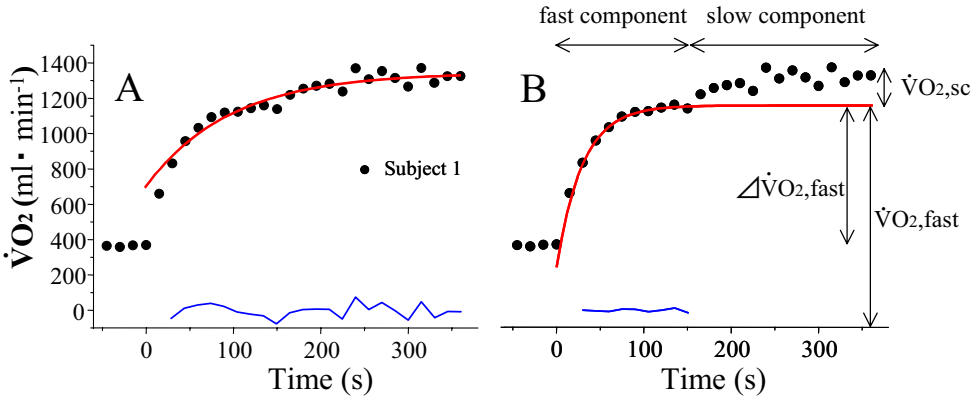

Fig. 2. $\dot{V}O_2$ response for a representative subject with model fits and residuals. The case with the entire response modeled with a mono-exponential omitted for the first 15 s (**A**) and with the mono-exponential fit limited to the fast component omitted for the first 15 s (**B**). Note that the residuals of B, shown below, are smaller than those of A. $\Delta\dot{V}O_2$,fast, asymptotic amplitude of the fast component (the increase in $\dot{V}O_2$ from the baseline to the asymptote of the fast component); $\dot{V}O_2$,fast, the asymptote, i.e., the absolute asymptotic amplitude of the fast component (the sum of the baseline and the asymptotic amplitude); $\dot{V}O_2$,sc, the amplitude of the slow component (the difference between $\dot{V}O_2$,fast and $\dot{V}O_2$ at the end of exercise).

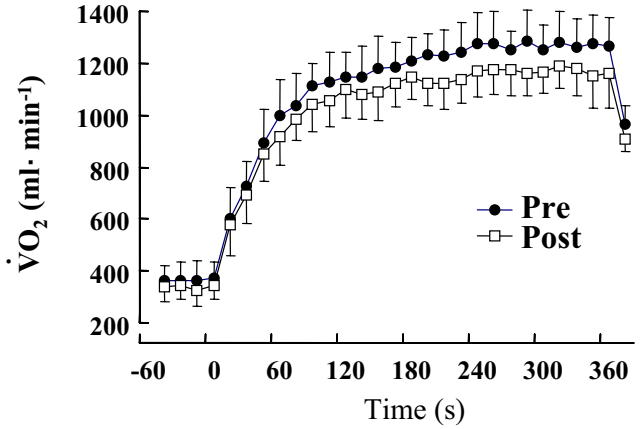

Fig. 3. Ensemble-averaged 15-s interval values of $\dot{V}O_2$ before and after ULLS. The filled circles indicate the averaged values of $\dot{V}O_2$ before ULLS, and the open squares show them after ULLS (n = 8 subjects). Values are means ± SD.

(–0.28 ± 0.6 cm). Similarly, the amount of change in the circumference of the calf was significantly ($P < 0.05$) different between the ULLS leg (–1.33 ± 0.9 cm) and the control leg (0.16 ± 0.6 cm). The skin temperature of the ULLS calf was found to be lower than that of the control leg, and the mean difference was 1.3 ± 0.9°C throughout the ULLS term.

$\dot{V}O_2$ kinetics

Figure 3 shows the ensemble-averaged 15-s interval values of $\dot{V}O_2$ before and after ULLS in the 8 subjects. The changes in parameters of $\dot{V}O_2$ kinetics are presented in Table 1. Although $\dot{V}O_2$,BL and $\Delta\dot{V}O_2$,fast were unchanged, $\dot{V}O_2$,fast and $\dot{V}O_2$,end were decreased significantly ($P < 0.05$) after ULLS. τ did not change between before and after ULLS, and no significant difference between Pre and Post was detected in $\dot{V}O_2$,sc and $\%\dot{V}O_2$,sc.

Respiratory and circulatory parameters other than $\dot{V}O_2$

We display respiratory and circulatory parameters other than $\dot{V}O_2$ in Table 2. Significant differences between Pre and Post were not detected in HR and MBP with regard to BL, 3rd and 6th. BL, 3rd and 6th of RER was also unchanged before and after ULLS. As for $\dot{V}_E$, although BL at Post was significantly ($P < 0.05$) lower than that of Pre, 3rd and 6th were unchanged.

DISCUSSION

The major results were as follows: (i) $\dot{V}O_2$,fast and $\dot{V}O_2$,end were declined after ULLS, though τ and $\%\dot{V}O_2$,sc were not changed; (ii) HR and MBP responses were not altered before and after ULLS.

Limb disuse

In this study, the circumferences of the thigh and calf were decreased. In fact, an accompanying study by Akima *et al.* (unpublished observation) revealed by means of magnetic resonance imaging (MRI) that muscle atrophy in the thigh occurred after ULLS in the same way as in previous studies [10, 14, 15] and that the degree of muscle atrophy as a result of ULLS was unchanged as compared to that of bed rest. In addition, calf skin temperature of the ULLS leg was lower than that of the control leg similar to a previous study [16]. Thus it is evident that the ULLS leg was exposed to disuse for 20 days.

Response speed of the fast component

It is known that the response speed of the fast component is controlled by O_2 delivery to and utilization by the exercising muscles [1, 2]. Previous studies have demonstrated that limb disuse by casting attenuated the muscle oxidative capacity in the immobilized limb [7], that ULLS reduced the femoral artery diameter in the side of the suspended leg [9], and that the number and luminal diameter of capillaries in the muscles of rats decreased after hind limb suspension [8]. Accordingly, there was a possibility that ULLS would slow response speed of the fast component. Contrary to our expectations, however, the response speed of $\dot{V}O_2$, i.e., τ, was unchanged after ULLS (Table 1), and this result does not agree with a previous study, which revealed that $\dot{V}O_2$ kinetics were slowed after bed rest [6]. These conflicting results could have been caused

Table 1. $\dot{V}O_2$ response parameters for 60-W exercise before and after ULLS.

		Pre	Post
$\dot{V}O_2$,BL	(ml·min^{-1})	365 ± 65	337 ± 53
τ	(s)	33.9 ± 11.3	35.3 ± 11.9
$\Delta\dot{V}O_2$,fast	(ml·min^{-1})	813 ± 65	772 ± 67
$\dot{V}O_2$,fast	(ml·min^{-1})	1,178 ± 106	1,110 ± 96*
$\dot{V}O_2$,end	(ml·min^{-1})	1,272 ± 107	1,156 ± 122*
$\dot{V}O_2$,sc	(ml·min^{-1})	93.2 ± 46.1	46.1 ± 61.4
$\%\dot{V}O_2$,sc	(%)	11.6 ± 5.7	5.9 ± 7.8

Values are means ± SD; n = 8 subjects. $\dot{V}O_2$,BL, baseline; τ, time constant; $\Delta\dot{V}O_2$,fast, asymptotic amplitude of the fast component; $\dot{V}O_2$,fast, the asymptote, i.e., the absolute asymptotic amplitude of the fast component (the sum of the baseline and the asymptotic amplitude); $\dot{V}O_2$,end, exercise end value; $\dot{V}O_2$,sc, the amplitude of the slow component; $\%\dot{V}O_2$,sc, the percentage of contribution of the slow component to the total response of $\dot{V}O_2$. * Significant difference between Pre and Post ($P < 0.05$).

Table 2. Respiratory and circulatory parameters for 60-W exercise before and after ULLS.

			Pre	Post
$\dot{V}_E$	($l \cdot min^{-1}$)	BL	13.7 ± 2.3	12.8 ± 2.2*
		3rd	41.9 ± 7.4	41.8 ± 8.2
		6th	45.1 ± 9.7	43.9 ± 6.3
RER		BL	0.83 ± 0.05	0.79 ± 0.05
		3rd	1.02 ± 0.04	1.01 ± 0.05
		6th	0.99 ± 0.03	0.98 ± 0.04
HR	(bpm)	BL	85 ± 11	82 ± 10
		3rd	127 ± 13	125 ± 13
		6th	135 ± 15	131 ± 15
MBP	(mmHg)	BL	79 ± 8	87 ± 10
		3rd	104 ± 8	100 ± 10
		6th	103 ± 9	99 ± 13

Values are means ± SD; n = 8 subjects. $\dot{V}_E$, expiratory minute ventilation; RER, respiratory exchange rate; HR, heart rate; MBP, mean blood pressure; BL, baseline; 3rd, third minute value; 6th, end exercise value. * Significant difference between Pre and Post ($P < 0.05$).

by the following. First, bed rest induces cardiac muscle atrophy and attenuates central circulation so that HR is up-regulated at rest and during exercise [6, 17, 18]. In fact, from the results that $\dot{V}O_2$ kinetics in a supine position were not altered after bed rest, Convertino et al. [6] concluded that the attenuation of the capability of central circulation could slow $\dot{V}O_2$ kinetics. On the contrary, it should be hard for limb disuse to reduce the capability of central circulation because the subjects went about their daily routines as usual, except for the fact that the ULLS leg was suspended in a harness. Actually, in this study HR and MBP at rest and their responses to exercise were unchanged after ULLS (Table 2). Therefore the cause of unchanged τ of $\dot{V}O_2$ in this study was possibly due to unaltered central circulation. Second, because a previous study [6] did not do an analysis using exponential fitting, whereas we did, the difference in how the data were analyzed might have produced this discrepancy.

The amplitude of the fast component

The subjects performed the same work (60 W and 60 rpm) at Pre and Post, and $\dot{V}_E$ during exercise was unchanged before and after ULLS in the same way as in a previous study [6] (Table 2). Moreover, the energy substrate that was utilized during exercise should be the same before and after ULLS because RER during exercise was not changed after ULLS (Table 2). Nevertheless, the asymptote in the fast component (the absolute amplitude of the fast component), i.e., $\dot{V}O_2$,fast, fell after ULLS (Table 1). Although a significant difference was not detected in the asymptotic amplitude of the fast component, i.e., $\Delta\dot{V}O_2$,fast (Table 1), the resting value of $\dot{V}O_2$ before the start of exercise, i.e., $\dot{V}O_2$,BL, was found to be unaltered at Pre and Post (Table 1). Therefore it is assumed that the amplitude of the fast component tended to be down-regulated after ULLS.

With regard to the reason for the declined asymptote of the fast component, the following possibilities might account for it. Many investigators have reported that increasing the percentage of the recruitment of the fast twitch fibers, i.e., type II fibers, decreases the amplitude of the fast component [3, 19, 20]. In this study, after ULLS, muscle strength was weakened (Dr. Akima's unpublished observation). Thus relative work intensity at Post should be increased as compared with that of Pre, and for that reason the recruitment of larger high-threshold fibers, which are mostly type II fibers, could be facilitated more after ULLS, taking into consideration the size principle [21]. Therefore the reason why the asymptote of the fast component was down-regulated after ULLS could be possibly due to the alteration of the recruitment of muscle fibers. Another possibility proposed by Koga *et al.* [22] was that under the circumstances in which O_2 delivery to and utilization by the working muscles were compromised, the amplitude of the fast component was more sensitive to a limitation in O_2 delivery than was the associated τ. Therefore it is possible that ULLS weakened the capability of O_2 delivery in peripheral circulation and utilization in the muscles and that the limited O_2 delivery might have down-regulated the asymptote of the fast component. In any case, further research is required because the recruitment of muscle fibers, the function of O_2 delivery in the peripheral circulation, and the O_2 utilization of the muscles were not evaluated.

The slow component

The hypothesis that the recruitment of type II fibers or the added recruitment of muscle fibers, which have not yet

participated in muscle contraction, as the mechanism of the slow component is convincing [3]. Previous studies have demonstrated that even when the amplitude of the fast component is declined because of a facilitated recruitment of type II fibers, the value of $\dot{V}O_2$ at the end of exercise is unchanged in >AT exercise [3, 20]. Koga *et al.* [22] also revealed that even when the amplitude of the fast component is down-regulated as a result of the restriction of O_2 delivery in circumstances in which O_2 extraction and delivery were compromised, the end exercise $\dot{V}O_2$ is the same as that of the control condition because of the compensation of the elevated amplitude of the slow component in >AT exercise. However, in this study in which exercise intensity was determined >AT, in spite of the fact that the asymptote of the fast component fell, the $\dot{V}O_2$,end after ULLS was lower than before ULLS, and $\%\dot{V}O_2$,sc was unchanged after ULLS. The reason for this would possibly be that the exercise intensity (60 W), which was utilized in this study, was just above AT, where the slow component was less likely to be observed. Many investigators employ 50% of the difference between AT and peak oxygen uptake ($\dot{V}O_{2\ peak}$) as the exercise intensity to observe the slow component. Accordingly, if we had also utilized the exercise intensity that many investigators employ, the amplitude of the slow component should have increased after ULLS. Alternatively, some human studies show the magnitude of atrophy of type II fibers to be larger than that of slow twitch fibers (type I fibers) in the vastus lateralis muscle after bed rest or unloading [14, 23, 24]. Additionally, in this study it was speculated that type II fibers were more actively recruited during muscle contractions in the fast component after ULLS in comparison with before ULLS. So after the fast component, it might be possible that type II fibers, which have a higher O_2 cost per tension development compared with type I fibers, might be more difficult to recruit in muscle contractions after ULLS as the additional recruitment of muscle fibers to replace the fatigued fibers. As a result, the amplitude of the slow component did not increase much, leaving $\dot{V}O_2$,end after ULLS lower than before ULLS.

What the declined asymptote in the fast component of $\dot{V}O_2$ implies

What does the declined asymptote in the fast component, i.e., $\dot{V}O_2$,fast, imply? If we simply take it to mean the subjects were performing the same exercise while utilizing less O_2, the exercise efficiency would be higher. However, if we take the decreased $\dot{V}O_2$,fast to mean a more facilitated recruitment of type II fibers or a delayed response in $\dot{V}O_2$, this would indicate that the energy-supplying system becomes dependent on glycolysis more than oxidation and that more lactate is produced. This possibility is supported by reports demonstrating that muscle oxidative capacity decreases after inactivity [7, 24]. Therefore after ULLS, the subjects might be harder pressed to carry out the exercise tasks. Further research will be needed, however, because no lactate data were taken.

In conclusion, the asymptote in the fast component and the end exercise $\dot{V}O_2$ were decreased after 20-d ULLS, though the response speed and the amplitude of the slow component of $\dot{V}O_2$ were not changed. It is suggested that muscle deconditioning as a result of limb disuse affects $\dot{V}O_2$ response.

We appreciate the cooperation of the subjects in the present study. We would also like to thank Drs. B.J. Whipp, Y. Ikegami and N. Kasuga for advising us, Dr. N. Kondo for lending us his apparatus, and Mr. J. Myerson for reviewing the English in this manuscript. This study was supported by a Grant-in-Aid for Scientific Research from the Japanese Ministry of Education, Culture, Sports, Science and Technology (grant no. 17650193).

REFERENCES

1. Grassi B. Limitation of sleletal muscle $\dot{V}O_2$ kinetics by inertia of cellar respiration. In: Jones AM , Poole DC, editors. Oxygen uptake kinetics in sport, exercise and medicine. London and New York: Routledge; 2005. p. 212-29.
2. Hughson RL. Regulation of $\dot{V}O_2$ on-kinetics by O_2 delivery. In: Jones AM, Poole DC, editors. Oxygen uptake kinetics in sport, exercise and medicine. Londn and New York: Routledge; 2005. p. 185-211.
3. Jones AM, Pringle JS, Carter H. Influence of muscle fiber type and moter unit recruitment on $\dot{V}O_2$ kinetics. In: Jones AM, Poole DC, editors. Oxygen uptake kinetics in sport, exercise and medicine. London and New York: Routledge; 2005. p. 261-93.
4. Cerretelli P, Pendergast D, Paganelli WC, Rennie DW. Effects of specific muscle training on $\dot{V}O_2$ on-response and early blood lactate. J Appl Physiol. 1979;47:761-9.
5. Carter H, Jones AM, Barstow TJ, Burnley M, Williams C, Doust JH. Effect of endurance training on oxygen uptake kinetics during treadmill running. J Appl Physiol. 2000;89:1744-52.
6. Convertino VA, Goldwater DJ, Sandler H. $\dot{V}O_2$ kinetics of constant-load exercise following bed-rest-induced deconditioning. J Appl Physiol. 1984;57:1545-50.
7. Kitahara A, Hamaoka T, Murase N, Homma T, Kurosawa Y, Ueda C, Nagasawa T, Ichimura S, Motobe M, Yashiro K, Nakano S, Katsumura T. Deterioration of muscle function after 21-day forearm immobilization. Med Sci Sports Exerc. 2003;35:1697-702.
8. Kano Y, Shimegi S, Takahashi H, Masuda K, Katsuta S. Changes in capillary luminal diameter in rat soleus muscle after hind-limb suspension. Acta Physiol Scand. 2000;169:271-6.
9. Bleeker MW, De Groot PC, Poelkens F, Rongen GA, Smits P, Hopman MT. Vascular adaptation to 4 wk of deconditioning by unilateral lower limb suspension. Am J Physiol Heart Circ Physiol. 2005;288:H1747-55.
10. Berg HE, Dudley GA, Häggmark T, Ohlsén H, Tesch PA. Effects of lower limb unloading on skeletal muscle mass and function in humans. J Appl Physiol. 1991;70:1882-5.
11. Bearden SE, Moffatt RJ. $\dot{V}O_2$ and heart rate kinetics in cycling: transitions from an elevated baseline. J Appl Physiol. 2001;90:2081-7.
12. Whipp BJ, Ward SA, Lamarra N, Davis JA, Wasserman K. Parameters of ventilatory and gas exchange dynamics during exercise. J Appl Physiol. 1982;52:1506-13.
13. Rossiter HB, Ward SA, Kowalchuk JM, Howe FA, Griffiths JR, Whipp BJ. Dynamic asymmetry of phosphocreatine concentration and O_2 uptake between the on- and off-transients of moderate- and high-intensity exercise in humans. J Physiol (Lond). 2002;541:991-1002.
14. Hather BM, Adams GR, Tesch PA, Dudley GA. Skeletal muscle responses to lower limb suspension in humans. J Appl Physiol. 1992;72:1493-8.
15. Adams GR, Caiozzo VJ, Baldwin KM. Skeletal muscle unweighting: spaceflight and ground-based models. J Appl Physiol. 2003;95:2185-201.
16. Adams GR, Hather BM, Dudley GA. Effect of short-term unweighting on human skeletal muscle strength and size. Aviat Space Environ Med. 1994;65:1116-21.
17. Katayama K, Sato K, Akima H, Ishida K, Takada H, Watanabe Y, Iwase M, Miyamura M, Iwase S. Acceleration with exercise during head-down bed rest preserves upright exercise responses. Aviat Space Environ Med. 2004;75:1029-

35.
18. Suzuki Y, Iwamoto S, Haruna Y, Kuriyama K, Kawakubo K, Gunji A. Effects of 20 days horizontal bed rest on mechanical efficiency during steady state exercise at mild-moderate work intensities in young subjects. J Gravit Physiol. 1997;4:S46-52.
19. Barstow TJ, Jones AM, Nguyen PH, Casaburi R. Influence of muscle fiber type and pedal frequency on oxygen uptake kinetics of heavy exercise. J Appl Physiol. 1996;81:1642-50.
20. Pringle JS, Doust JH, Carter H, Tolfrey K, Jones AM. Effect of pedal rate on primary and slow-component oxygen uptake responses during heavy-cycle exercise. J Appl Physiol. 2003;94:1501-7.
21. Henneman E, Somjen G , Carpenter DO. Excitability and inhibitability of motoneurons of different sizes. J Neurophysiol. 1965;28:599-620.
22. Koga S, Shiojiri T, Shibasaki M, Kondo N, Fukuba Y, Barstow TJ. Kinetics of oxygen uptake during supine and upright heavy exercise. J Appl Physiol. 1999;87:253-60.
23. Edgerton VR, Zhou MY, Ohira Y, Klitgaard H, Jiang B, Bell G, Harris B, Saltin B, Gollnick PD, Roy RR. Human fiber size and enzymatic properties after 5 and 11 days of spaceflight. J Appl Physiol. 1995;78:1733-9.
24. Hikida RS, Gollnick PD, Dudley GA, Convertino VA, Buchanan P. Structural and metabolic characteristics of human skeletal muscle following 30 days of simulated microgravity. Aviat Space Environ Med. 1989;60:664-70.