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Synchronization between Tissue Oxygen Indexes in the Vastus Lateralis and Gastrocnemius after Impulse Exercise

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Key Words

synchronization, tissue oxygen index, impulse exercise, end tidal CO₂ pressure.

Abstract

The purpose of the present study was to examine whether there is synchronization between end tidal CO₂ pressure (PETCO₂) and tissue oxygen index (TOI) determined by spatially resolved spectroscopy (SRS) after impulse exercise. The impulse exercise was performed at 400 watts for 10 s. PETCO₂ was measured by the breath-by-breath method. The data obtained were interpolated into 1-s data using a three-dimensional spline. TOI was measured in the vastus lateralis and gastrocnemius muscles. The sampling frequency of TOI was 1 Hz. The 1-s data for TOI and PETCO₂ were analyzed by fast Fourier transform for a period from 5 to 20 min after impulse exercise. Power spectral density (PSD) was calculated. TOI oscillated before impulse exercise and then suddenly decreased and overshoot after the exercise. After about 5 min of recovery, TOI oscillated in the two muscles. For TOIs in the two muscles, there were two peaks in PSD. This indicated oscillations of TOIs in the two muscles. There was synchronization between TOIs in the two muscles. However, PETCO₂ did not clearly show oscillation. Cross power spectra (CPS) were obtained between TOIs in the two muscles. There were two peaks of CPS. The slow peak was 0.0034 ± 0.0022 Hz and fast peak was 0.0076 ± 0.0025 Hz. It was concluded that there was synchronization between TOIs in the vastus lateralis and gastrocnemius. However, this synchronization was not induced by PETCO₂ fluctuation.

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Introduction

It has been suggested that maximal oxygen uptake ($\dot{V}O_2$) is limited by maximal level of cardiac function or is regulated by skeletal muscle recruitment through a central neurally mediated mechanism [1-3]. In submaximal exercise, it has not been determined whether response of $\dot{V}O_2$ to a constant load is due to slow process of oxygen utilization in the active muscle or to slow blood delivery to the active muscle [4, 5], although muscle $\dot{V}O_2$ control has been reported to be more complex than previously suggested [6]. In these discussions, the basic concept is reductionism. In this concept, it is often assumed that a phenomenon is derived from a certain factor (cause). Searching causality is a typical example concerning reductionism in natural science. Accordingly, a study in which cause is investigated is still a mainstream in exercise physiology. In contrast to reductionism, a new concept of self-organization has arisen for the biological systems. In this theory, a certain direction is given by an upper system; for example, work load of exercise is given by the upper central nervous system and its direction produces interaction among lower systems such as the heart, lungs and working muscle. These organs are then adequately self-organized toward a given direction. Since there is no cause in this system, the object of study is interaction among organs. This interaction has actually been studied by synchronization or entrainment of rhythm among several organs.

It has been known that when an energy source e.g. glucose is given to glycolytic pathway, reduced nicotinamide adenine dinucleotide (NADH) oscillates in yeast [7]. In this pathway, adenosine triphosphate and adenosine diphosphate (ATP and ADP) play important roles as substances of feedback control for hexokinase, phosphofructokinase and pyruvatekinase [8]. This system is one example of a dissipative structure. It has also been known that the organization of mitochondrial metabolism is a complex dissipative structure in which substances oscillate in mitochondria [9]. Feedback control of respiratory chain complexes by inorganic phosphate has also been reported to be essential to explain the regulation of mitochondrial ATP synthesis flux in skeletal muscle [10]. This suggests oscillation in the respiratory system. Actually, Iotti et al. [9] reported an oscillatory recovery of phosphocreatine (PCr) in the muscle in humans from work. This recovery is thought to be related to ATP supply in the mitochondrial membrane, in which the respiratory system operates. Furthermore, since the oscillation of PCr was determined by a ^{31}P magnetic resonance spectroscopy (MRS) system that could not focus on one mitochondrion but gave the change in PCr on some mitochondria, this phenomenon in humans is thought to occur with the cooperation of some mitochondria.

Deoxygenation determined by near-infrared spectroscopy (NIRS) in the muscle in humans oscillates in an exercising state as well as in a resting state [11]. This deoxygenation oscillation is interpreted as follows [12-14]. First, a certain substance oscillates in mitochondria. This oscillating substance stimulates vascular endothelial cells and its oscillation is transmitted upward. When this transmission reaches a feeding vessel, blood

flow in the vessel oscillates. This oscillation becomes oscillation of oxygen supply. The portion occupied by the feeding vessel in the muscle is affected by oxygen supply, and consequently deoxygenation oscillation can be detected by NIRS through the interaction between mitochondria and oxygen supply.

Thus, since NIRS measures deoxygenation concerning hemoglobin in the vessels in the muscle and myoglobin in the muscle, there could be synchronization in deoxygenation in a portion of the muscle. However, it is still unclear whether there is synchronization between different muscle groups. A previous study using impulse exercise suggested that end tidal CO₂ pressure (PETCO₂) in the lungs might interact with deoxygenation in the muscle. This suggestion is based on the condition of frequency of PETCO₂ being similar to that of deoxygenation in the muscle. In the brain, it has been reported that there is an interaction between PETCO₂ and blood oxygen level-dependent (BOLD) [15]. However, this suggestion is not directly examined in an interaction between lungs and muscles yet. Furthermore, estimation of deoxygenation by the Beer-Lambert method in the previous studies has been reported to be affected by skin blood flow under a certain condition [16, 17], though the validity of this method has been reported [18, 19].

The purpose of the present study was to examine whether there is synchronization between PETCO₂ and the tissue oxygen index (TOI) determined by spatially resolved spectroscopy (SRS) after impulse exercise. SRS was used in the present study since it has been shown that estimation of TOI by SRS is not greatly affected by oxygenation dynamics of skin blood flow [20].

Materials and Methods

Ethics statement

Each subject signed a statement of informed consent following a full explanation regarding the nature of the experiment. The Ethics Committee of Hokkaido University Graduate School of Education approved the present study. This study was performed in accordance with the declaration of Helsinki.

Subjects

Seven healthy males participated in this study. The subjects' mean age, height and body weight were 24.7 ± 3.0 (SD) yrs, 173.0 ± 7.7 cm and 69.3 ± 12.4 kg, respectively.

Experimental protocol

Each subject performed a main test consisting of one impulse exercise and incremental exercise on a cycle ergometer (Ergometer 232 CXL, Combi, Tokyo, Japan). After rest for 5 min and 50 sec on the cycle ergometer seat, 10-s impulse exercise with 400 watts work

load at 80 rpm was performed and was followed by 20-min recovery in a resting state. The work load 400 watts is the maximal work rate of the cycle ergometer used in the present study. Incremental exercise was also performed at 50, 100, 150, and 200 watts for 5 min in each step, and the load was increased by 20 watts for each 1 min until the subject could not maintain the revolution rate of pedaling (60 rpm).

Before rest on the cycle ergometer seat prior to 400 watts impulse exercise, each subject sat on a chair to attach electrodes on the subject's chest for monitoring heart rate (HR) and to attach photo probes on the subject's left leg (vastus lateralis and gastrocnemius) for NIRS. Each subject was instructed to relax and to maintain cycle ergometer cranking in a horizontal position at rest and during recovery on the cycle ergometer.

Measurements and determinations

Blood samples (each 100 μ l) were collected from fingertips using a capillary tube at rest, and at 5 min, 10 min and 20 min during recovery. Each subject's hand was pre-warmed in 40-45°C water while sitting on the chair prior to each test in order to arterialize capillary blood. After this warming, the subject's hand was warmed by a heating glove at rest, during exercise and during recovery on the cycle ergometer. It has been shown that such blood samples might not accurately reflect arterial O₂ pressure but can closely reflect arterial CO₂ and pH [21]. Samples were analyzed using a blood gas analyzer (i-STAT1, i-STAT, Abbott Point of Care Inc. IL, USA) to measure CO₂ pressure (PaCO₂), pH and lactate (La).

Data for respiration gas exchange were obtained using a respiratory gas analyzer by the breath-by-breath mode (AEROMONITOR AE-310S, Minato Medical Science CO., LTD., Osaka, Japan). Ventilation ($\dot{V}_E$) was measured by a hot-wire flow meter, and the flow meter was calibrated with a syringe of known volume (2 liters). O₂ and CO₂ concentrations were measured by a paramagnetic oxygen analyzer and photometric gas analyzer, respectively. The gas analyzer was calibrated by known standard gas (O₂ : 15.13%, CO₂ : 5.068%). Respiration gas exchange was measured continuously during rest, exercise, and recovery periods. Heart rate (HR) was recorded using a heart rate monitor installed in the respiratory gas analyzer. $\dot{V}_{O_2}$, PETCO₂ and HR were obtained breath-by-breath. In incremental exercise, breath-by-breath data were outputted as 20-s data. In impulse exercise, breath-by-breath data were converted to 1-sec data according to the method described below.

TOI in the left vastus lateralis and that in the left gastrocnemius were determined using a NIRS system (NIRO200x, Hamamatsu Photonics, K. K. Hamamatsu, Japan). Although NIRO200x can determine oxygenation and deoxygenation by the Modified Beer-Lambert method, TOI determined by the spatially resolved spectroscopy (SRS) method was used in the present study. The NIRS probe consisted of a light source and an optical detector, with a distance of 3.0 cm between the light source and detector. Triple-wavelength light (735, 810 and 850 nm) emitted from the light source penetrates tissue, where it is either absorbed or scattered, and some of the scattered light returns to the optical detector. The sampling frequency of TOI was 1 Hz. TOI was calculated from deoxygenation (HHb) and oxygenation

(O₂Hb) determined by the SRS method using following equation;

$$TOI = O_2Hb / (HHb + O_2Hb).$$

Calculation and statistical analysis

In a previous study [22], in order to obtain 1-s data, breath-by-breath data obtained in repeated exercise with a time interval were converted to 1-sec data in each exercise, and the data obtained in each exercise were summed. However, in this method, the oscillation of measured data is eliminated by the summation. In order to avoid this effect, breath-by-breath data for $\dot{V}O_2$, HR and PETCO₂ were interpolated into 1-sec data using a three-dimensional spline in the present study, but there is also a problem in this method. Higher frequency of oscillation than the respiration rate has no meaning. The 1-sec data for TOI and PETCO₂ were analyzed by fast Fourier transform (FFT) for the period from 5 min to 20 min after impulse exercise. Power spectral density (PSD) for each TOI was calculated. A cross power spectrum (CPS) was calculated using the two TOIs. The CPS reflexes the correlation between the two parameters.

Results are presented as means $\pm$ standard deviations. Blood gas data were analyzed by Dunnett's method. The significant level was set at $p < 0.05$.

Results

One subject was very weak and could only do the incremental exercise up to 150 watts. For that subject, the impulse exercise was therefore carried out at 200 watts. Maximal work rate performed by incremental exercise was 239 ± 59.0 watts. The work load (400 watts including 200 watts for the above subject) in impulse exercise per this maximal work rate performed in incremental exercise was 159 ± 31.0 %. Peak $\dot{V}O_2$ was 2.77 ± 0.78 l/min. Peak $\dot{V}O_2$ was obtained by the maximal value of 20-sec data converted from breath-by-breath data for each subject in incremental exercise.

Figure 1 shows average kinetics of $\dot{V}O_2$ and HR. $\dot{V}O_2$ increased during exercise. After impulse exercise, $\dot{V}O_2$ rapidly decreased and then increased before a decrease during recovery. HR increased during exercise and then decreased after impulse exercise.

Figure 2 shows average TOIs in the vastus lateralis and in the gastrocnemius. During impulse exercise, TOIs in both muscles decreased and then recovered to the resting level. However, TOI in the vastus lateralis overshoot and then recovered to the resting level.

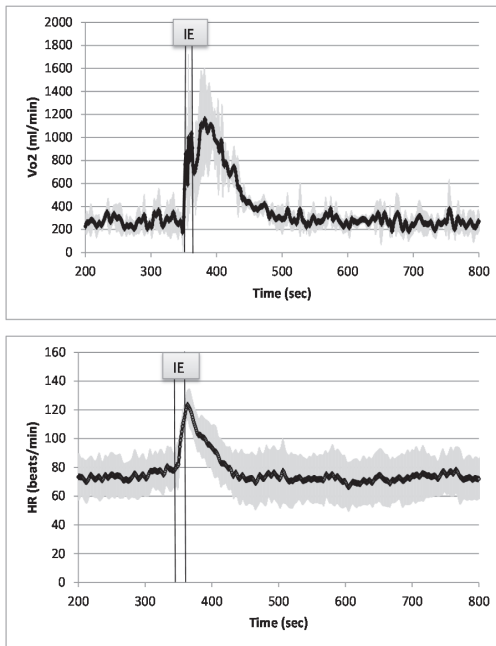


Fig.1. Average values of oxygen uptake ($\dot{V}O_2$) and heart rate (HR) kinetics. The straight lines shows the duration of impulse exercise (IE). Before and after impulse exercise, rest and resting recovery on the bicycle ergometer were carried out.

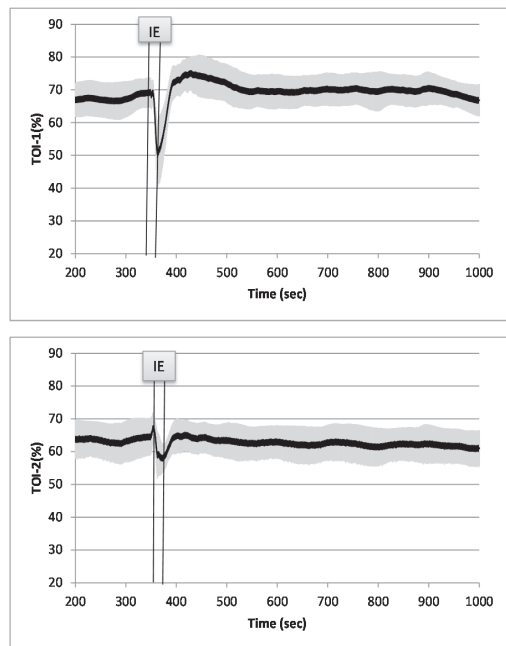


Fig.2. Average kinetics of tissue oxygen index in the vastus lateralis (TOI-1) and in the gastrocnemius (TOI-2). The straight lines shows the duration of impulse exercise (IE).

Figure 3 shows individual kinetics of TOI. Although average TOI did not show oscillation (Fig 2), individual data showed oscillation at rest and after impulse exercise (Figure 3). TOIs in the two muscles showed synchronization. It seemed that oscillation was restarted after reset of preceding oscillation at impulse exercise. However, the effect of work load on TOIs could be seen immediately after impulse exercise (quick recovery and overshooting). Therefore, synchronization of the oscillations of TIOs started after overshoot.

PETCO₂ overshoot after impulse exercise and then recovered to the resting level. PETCO₂ during recovery after overshoot showed fine oscillation, and its amplitude increased and decreased. This pattern of increase and decrease was repeated. These repetitions are unlikely to be oscillation of TOIs. It was thus observed that PETCO₂ did not show remarkable oscillation after overshoot and did not synchronize with TOIs in all of the subjects. Figure 4 shows three examples of PSD for PETCO₂. There were several peaks and there was no certain tendency for these peaks in any of the subjects.

Table 1 shows changes in Paco₂, pH and La. Paco₂ did not significantly change from the resting level to recovery level. La and pH were significantly changed at 5 and 10 min during recovery.

Table 1. Mean values and standard deviation (SD) of arterialized blood pH, blood lactate (La) and carbon dioxide pressure (PaCO₂) at rest and during recovery.

		Rest	Rec 5 min	Rec 10 min	Rec 20 min
pH	Mean	7.404	7.372*	7.389*	7.392
	SD	0.0220	0.0271	0.0235	0.0232
La	Mean (mM)	1.34	2.59*	2.10*	1.47
	SD	0.43	0.74	0.59	0.46
Paco2	Mean (Torr)	40.8	41.9	41.4	40.4
	SD	1.45	2.60	2.23	5.11

*significant difference compared with the rest value in recovery values.

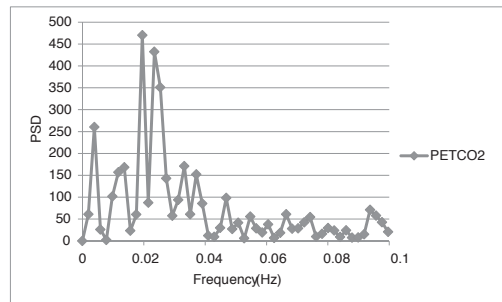
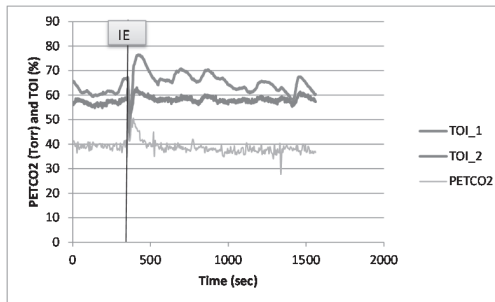
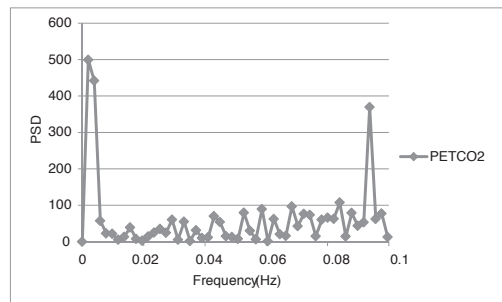
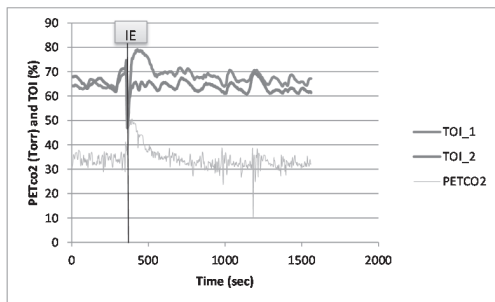
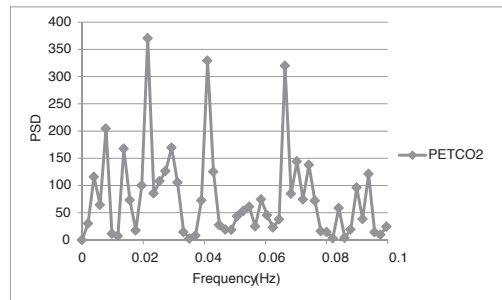
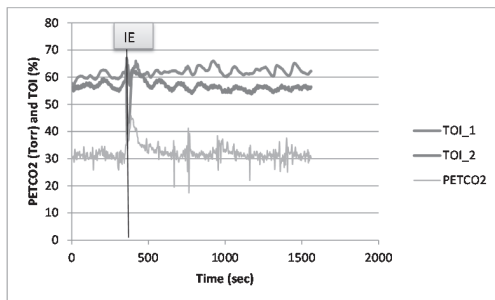


Fig.3. Individual kinetics of tissue oxygen index in the vastus lateralis (TOI-1), in the gastrocnemius (TOI-2) and end tidal CO₂ pressure (PETCO₂) for three subjects were shown. A straight line shows impulse exercise (IE). Before and after impulse exercise, rest and resting recovery on the bicycle ergometer were carried out.

Fig.4. Three examples of power spectra density (PSD) in end tidal CO₂ (PETCO₂).

Figure 5 shows a typical example of the PSD and CPS. In this example, there were two peaks. Some subjects showed several peaks. In these subjects, we chose the highest peak and the second-highest peak. The frequencies of the two peaks are shown in Table 2. Slow frequency ranged from 0.0019 to 0.0078 Hz, and fast frequency ranged from 0.0058 to 0.016 Hz.

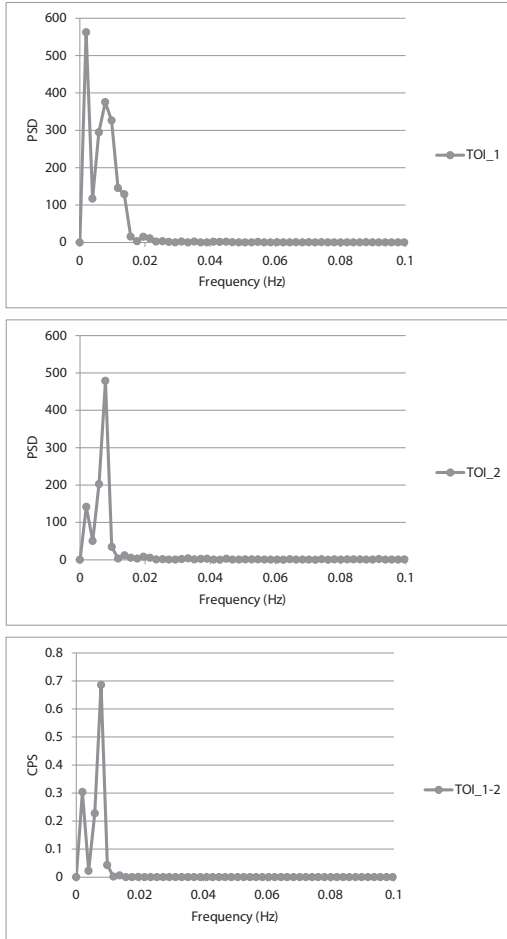


Fig. 5. Power spectra density (PSD) in tissue oxygen index in the vastus lateralis (TOI-1), in the gastrocnemius (TOI-2) and cross power spectra (CPS) in one subject.

Table 2. Individual oscillation frequencies of tissue oxygen index in the vastus lateralis (TOI-1) and in the gastrocnemius (TOI-2). Slow frequencies and fast frequencies are shown.

Subject	TOI-1		TOI-2		TOI1-2	
	slow (Hz)	fast (Hz)	slow (Hz)	fast (Hz)	slow (Hz)	fast (Hz)
1	0.0020	0.0120	0.0039	0.0078	0.0039	0.0058
2	0.0020	0.0078	0.0020	0.0078	0.0020	0.0078
3	0.0020	0.0098	0.0039	0.0098	0.0039	0.0098
4	0.0020	0.0059	0.0059	0.0160	0.0020	0.0059
5	0.0020	0.0058	0.0020	0.0059	0.0019	0.0058
6	0.0059	0.0097	0.0020	0.0059	0.0020	0.0058
7	0.0078	0.0120	0.0078	0.0120	0.0078	0.0120
Mean	0.0034	0.0090	0.0039	0.0093	0.0034	0.0076
SD	0.0024	0.0026	0.0022	0.0037	0.0022	0.0025

Discussion

In the present study, average $\dot{V}O_2$ kinetics coincided with the results of a previous study on impulse exercise [23]. The first increase in $\dot{V}O_2$ is thought to be related to an increase of cardiac dynamics [22]. The second increase is known to be related to oxygen consumption in active muscle [22]. It has been reported that $\dot{V}O_2$ in impulse exercise is a nonlinear dynamic system [23]. However, this did not mean that $\dot{V}O_2$ kinetics involved oscillation. Actual individual $\dot{V}O_2$ kinetics at the lung level involves oscillation [24], though the oscillation is cancelled when $\dot{V}O_2$ is averaged. This oscillation in $\dot{V}O_2$ at lung level suggests oscillation of oxygen consumption at the muscle level. This interference is supported by the finding of oscillation of deoxygenation in the muscle at rest and during light exercise [11, 12]. Further support is provided by the finding that PCr can recover with damped oscillation from exercise [9]. Thus, in a portion of the muscle, there would be an oscillation in mitochondria.

The observed overshooting in average TOI in the vastus lateralis can be explained by the following two possibilities. One possible explanation is that the overshooting is a restarting point of oscillation in TOI. Slow and fast oscillations during late recovery may be reset and restarted by impulse exercise, and they persist after the overshooting. The other possible explanation is that this overshooting is a phenomenon triggered independently of TOI oscillation only by impulse exercise. PETCO₂ also showed overshooting corresponding to the period for TOI. Therefore, the overshooting of TOI may be a response to impulse exercise. However, the former possibility makes it difficult to use data during early recovery. Therefore, in the present study, we used the data after early recovery for calculations of PSD and CSP.

It is known that there are oscillations in cutaneous blood perfusion in humans. Wavelet transform has been used for analysis of signals of blood flow. It has been reported that the signal in the frequency interval from 0.0095 to 1.6 Hz consists of oscillations with five

different characteristic frequencies. It has been shown that these oscillations may represent the influence of heart beat (1.6-0.6 Hz), respiration (0.4-0.16 Hz), intrinsic myogenic activity of vascular smooth muscle (0.16-0.06 Hz), neurogenic activity on the vessel wall (0.06-0.02 Hz) and endothelium-mediated vasodilation (0.02-0.0095 and 0.0095-0.005 Hz) [25, 26]. Thus, direct physiological factors of oscillations in cutaneous blood perfusion have been studied in detail. However, it is not clear why endothelium-mediated vasodilation has a rhythm.

As mentioned in Introduction, the origin of the rhythm in endothelium-mediated oscillation was assumed to be mitochondria metabolism. Accordingly, a certain substance in mitochondria oscillates, and then stimulation of this oscillation can be transmitted to vascular endothelial cells. However, the slow frequency determined in TOI was slower than that determined in vascular endothelial cells. Therefore, it is thought that the slow oscillation in TOI cannot be transmitted to endothelial cells. If the origin of the slow frequency in the fast twitch fibers with low capillary density [27] is as described below, endothelial oscillation would not be easily observed. In fact, Yano et al. [14] suggested that it may be able to expand to the range from 0.002 Hz-0.025 Hz on the basis of the results of a previous study on PCr recovery in the muscle from exercise [9].

Iotti et al. [9] reported that the frequency of PCr oscillation is dependent on cytosolic pH (pHc). The lower pHc is, the lower is the frequency although they reported one oscillation for each pHc. In contrast to that report, two oscillations existed in the present study. The two oscillations can be interpreted as follows. One possible explanation is related to the decrease in blood pH after an increase from the resting state during recovery. If this is the case, slow frequency may exist during early recovery and fast frequency may appear in the late period during recovery. However, as far as a visual inspection concerning TOI kinetics (see Figure 3), this possibility would be very low. The other possibility is that muscle fiber type may be related to the two frequencies: 400 watts is a sufficiently high intensity to recruit all muscle fiber types [28]. Since it has been shown that slow twitch fibers (ST) have high oxidative capacity and that fast twitch fibers (FT) have low oxidative capacity and low capillary density [27], FT could produce much lactate, whereas the energy sources for ST would mainly be PCr and Vo_2 . Consequently, pHc in ST could become higher than that in FT. This could result in the slow frequency in FT and the fast frequency in ST.

We assumed that PETCO_2 affects TOIs in both muscles but that PETCO_2 is not a carrier of information for self-organization between the lungs and muscle. In previous studies in which PSD for PETCO_2 was analyzed, some rectangular windows with 50% overlap [13] or a 128-point Hanning window with an overlap of 56 points [15] were used, but one rectangular window with no overlap was used in the present study because it was necessary to use the same procedure for PSD in order to compare TIOs for PETCO_2 . As a result, there were several peaks and there was no certain tendency for these peaks in PETCO_2 . This makes it difficult to obtain CPS between PETCO_2 and TOIs.

Thus, it seemed that PETCO_2 was not an interactive factor for TOIs in the two muscles. However, since we found synchronization between TOIs in the vastus lateralis and

gastrocnemius, there should be information in order to make the synchronization from the lungs. The interaction may be derived from information through the nervous system or from humoral carriers from the lungs.

In conclusion, synchronization is important evidence of self-organization among several organs directed by work load induced by the brain. There was synchronization between TOIs in the vastus lateralis and gastrocnemius. However, this synchronization was not induced by PETCO₂ fluctuation.

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