INTRODUCTION

Whole-body circulation during physical exercise is highly organized. Exercise-induced activation of sympathetic nerve activity leads to increased heart rate (HR), cardiac output (Q), and stroke volume (SV). At the same time, dynamic exercise induces changes in the redistribution of whole-body organ-tissue blood circulation, including cutaneous blood circulation. We hypothesized that limb exercise combined with the restriction of muscular blood flow (KAATSU) may influence cutaneous blood flow redistribution. To examine this hypothesis, forehead (supraorbital) cutaneous blood flow was compared in women performing exercises with and without KAATSU. Ten young and middle-aged female subjects in the supine position performed three sets of 15 repetitions of unloaded unilateral knee extension exercises (30-s rest between sets). Blood flow was calculated from blood velocity and red blood cell mass (blood flow = velocity * mass) determined by laser blood flowmetry. While exercise without KAATSU did not induce alterations in velocity and mass (hence, no alterations in blood flow) throughout the entire exercise series, exercise with KAATSU induced increases (P<0.05) in blood flow owing to increases in velocity. These increases were not eliminated during the rest periods between exercise sets. Heart rate (HR) increased (P<0.05) with the second and third sets of exercises with KAATSU compared with HR before exercise initiation, and was higher than the HR resulting from a corresponding set of exercises without KAATSU. There were no changes in blood lactate and hematocrit in both types of exercises. Norepinephrine increased (P<0.05) at the completion of the exercise sets. These results suggest that forehead cutaneous blood circulation was increased by unloaded KAATSU leg exercise.

Key words: cutaneous blood flow, laser blood flowmetry, knee extension exercise, norepinephrine

Effect of knee extension exercise with KAATSU on forehead cutaneous blood flow in healthy young and middle-aged women

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Dynamic exercise induces changes in the redistribution of whole-body organ-tissue blood circulation, including cutaneous blood circulation. We hypothesized that limb exercise combined with the restriction of muscular blood flow (KAATSU) may influence cutaneous blood flow redistribution. To examine this hypothesis, forehead (supraorbital) cutaneous blood flow was compared in women performing exercises with and without KAATSU. Ten young and middle-aged female subjects in the supine position performed three sets of 15 repetitions of unloaded unilateral knee extension exercises (30-s rest between sets). Blood flow was calculated from blood velocity and red blood cell mass (blood flow = velocity * mass) determined by laser blood flowmetry. While exercise without KAATSU did not induce alterations in velocity and mass (hence, no alterations in blood flow) throughout the entire exercise series, exercise with KAATSU induced increases (P<0.05) in blood flow owing to increases in velocity. These increases were not eliminated during the rest periods between exercise sets. Heart rate (HR) increased (P<0.05) with the second and third sets of exercises with KAATSU compared with HR before exercise initiation, and was higher than the HR resulting from a corresponding set of exercises without KAATSU. There were no changes in blood lactate and hematocrit in both types of exercises. Norepinephrine increased (P<0.05) at the completion of the exercise sets. These results suggest that forehead cutaneous blood circulation was increased by unloaded KAATSU leg exercise.

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INTRODUCTION

Whole-body circulation during physical exercise is highly organized. Exercise-induced activation of sympathetic nerve activity leads to increased heart rate (HR), cardiac output (Q), and stroke volume (SV). At the same time, dynamic exercise induces changes in the redistribution of whole-body blood circulation; blood flow into working muscles to meet oxygen demand precedes flow into inactive regions. It has been suggested that cutaneous circulation is controlled by sympathetic nerve activity, which regulates vasoconstriction and the active vasodilation tone system (Kellogg et al., 1991, Kellogg, 2006, Johnson et al., 1986).

Exercise combined with the restriction of muscular blood flow (KAATSU) is a distinctive type of exercise training that results in obvious hypertrophy and increased muscle strength. KAATSU is extremely low intensity and is characterized by its short training duration (Abe et al., 2005, 2006, Takarada et al., 2000) One of the most striking characteristics of this training method is the restriction of blood flow in the exercising limbs using a restriction cuff belt during exercise, which leads to alteration in circulation dynamics. It has been proposed that exercise with KAATSU may lead to acidic and anaerobic intramuscular states, while restriction-induced elevation in metabolites, such as lactate and growth hormone, might stimulate hypertrophy (Takano et al., 2005b).

KAATSU has been suggested to induce alterations in hemodynamic parameters, such as Q and SV, as well as changes in HR and blood pressure (BP), both at rest and during exercise. Iida et al. (2005) demonstrated that application of a KAATSU belt to both legs during rest restricted venous blood flow and caused venous blood pooling in the legs distal to the belt, resulting in pressure-dependent reduction of arterial blood flow. Consequently, decreases in Q and SV, a slight increase in HR, and no change in BP were demonstrated. In exhaustive knee extension exercise with KAATSU, HR and BP as well as Q have been demonstrated to increase; on the other hand, SV decreased (Takano et al., 2005a). These studies suggest that these parameters play a role in controlling whole-body circulation in response to KAATSU with and without exercise.

In the aforementioned studies (Iida et al., 2005,
Takano et al, 2005b), blood pooling in the exercising limbs has been clearly demonstrated. On the other hand, it is unknown how circulation in other parts of the body responds to KAATSU in the exercising limbs. In the present study, we investigated the response of cutaneous circulation in the forehead (suparorbital region) to knee extension exercise combined with KAATSU-induced blood flow restriction.

**METHODS**

**Subjects**

Ten healthy female aged 23 to 47 years (mean age, 34.5 (SD 10.0) years) volunteered to participate in the study (Table 1). All subjects led active lives, with 8 of 10 participating in KAATSU training for the last 2 years. All subjects were informed of the procedures, risks, and benefits of the study, and signed an informed consent document before participation. The study was approved by the Ethics Committee for Human Experiments, The University of Tokyo.

**Exercise protocol**

The subjects assumed a supine position and performed three sets of knee extension exercises following a warm-up period, with a 30-s rest period between sets (Figure 1). In each set, subjects performed 15 repetitions of left knee extension exercises at 12 repetitions per minute, taking approximately 75 s to perform the entire set. The subjects performed this three-set series of exercises twice – for the first time without KAATSU, and for the second time with KAATSU. The KAATSU belt (Kaatsu-Master, Sato Sports Plaza, Tokyo, Japan) was placed around the most proximal portion of the subject's left leg. Before starting the exercise with the KAATSU belt, the air pressure in the belt, ranging from an initial 140 mm Hg to the final pressure of 200 mm Hg, was repeatedly held for 30 s and then released for 10 s. The final restriction pressure of 200 mm Hg was selected for its ability to serve as an occlusive stimulus, as described previously (Abe et al, 2006). Before starting to exercise with the final restriction pressure, subjects rested for 1 min. The restriction of muscular blood flow was maintained throughout the second exercise set, including the 30-s rest periods. The belt pressure was released immediately upon completion of the session.

**Cutaneous blood flow measurement.**

Cutaneous blood flow in the forehead (supraorbital region) was measured using laser blood flowmetry (Omega Wave, Tokyo, Japan), multiplying blood velocity (the velocity of red blood cells) by mass (the number of red blood cells passing through a given surface area in a specific unit time). The laser probe was placed in the middle of the region, and the circulation at ~1 mm in depth was measured (Figure 2.). Facial skin thickness varies from 0.4 to 1.4 mm (epidermis + dermis) depending on the region; the laser beam is able to penetrate to the dermis. Blood flow measurement was performed at the beginning of the rest period (with and without KAATSU) and lasted through the entire exercise series, both with and without KAATSU. The data obtained for the last 30 s were used for analysis.

**Blood sampling and biochemical analysis**

Venous blood samples were obtained four times from nine subjects in a supine position before and immediately after exercise both with and without KAATSU. All blood samples were processed to plasma before storage at -20°C. Blood lactate (LA)

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**Table 1.** Descriptive characteristics of subjects.

<table>
<thead>
<tr>
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<tr>
<td>Age, y</td>
<td>34.5 (10.0)</td>
</tr>
<tr>
<td>Standing height, cm</td>
<td>161.1 (5.8)</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>51.3 (4.3)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>19.8 (1.3)</td>
</tr>
<tr>
<td>Midthigh girth, cm</td>
<td>46.9 (3.3)</td>
</tr>
</tbody>
</table>

Values are means (SD); BMI, body mass index.
concentrations were determined using a portable analyzer (Lactate Pro, Arkray, Kyoto Primary Science, Kyoto, Japan), and hematocrit was measured in duplicate by microcentrifugation. Plasma norepinephrine (NE) concentration was measured at SRL, Inc. (Tokyo, Japan). HR during exercise was measured using a finger probe (Onyx, Nonin Medical, MN, USA). The data obtained from the last 30 s were used for analysis.

**Statistical analysis**
Results are expressed as mean ± standard deviation (SD) for all values. The effects of exercise with KAATSU compared with exercise without KAATSU on changes in cutaneous blood flow and in blood parameters over time (pre- and postexercise) were tested by a two-factor ANOVA for repeated measurement. Further analysis used Student’s paired t test, if interaction, KAATSU x group was significant. Statistical significance was set at $P<0.05$.

**RESULTS**

**Forehead cutaneous blood flow**
Figure 3 shows changes in mass, velocity, and blood flow. Exercise without KAATSU did not show any changes in mass, velocity, and blood flow for all three measurements. On the other hand, exercise with KAATSU increased ($P<0.05$) the velocity and blood flow in all exercise sets compared with the velocity and blood flow measurements made before the start of exercise. Significantly, these KAATSU-induced increases in both velocity and blood flow were not eliminated following the 30-s rest period between sets.

**Heat rate and blood parameters**
HR increased significantly ($P<0.05$) at the second and third exercise sets with KAATSU compare with pre-exercise HR without KAATSU (Figure 4). Also, HR is significantly higher than HR measurements made during the corresponding exercise sets without KAATSU.

Table 2 shows changes in plasma NE concentration. NE increased ($P<0.05$) from 0.21 (SD 0.08) ng/mL at rest to 0.30 (SD 0.15) ng/mL at the end of exercise.
with KAATSU. There were no changes in either blood LA or hematocrit values (Table 2).

**DISCUSSION**

The main findings of the present study are as follows: 1) Unloaded knee extension exercise with KAATSU significantly stimulated cutaneous circulation in peripheral regions; an elevation in blood flow mainly due to increased velocity was observed. Further, this increase was maintained during rest periods between exercising. 2) Exercise with KAATSU increased HR and circulating NE. 3) No alterations were found in plasma LA and hematocrit values in exercise both with and without KAATSU.

In the present study, subjects performed free extra-load knee extension exercises. In spite of its extremely low intensity, exercise with KAATSU resulted in changes in cutaneous circulation, with an elevation in NE secretion, suggesting that exercise with KAATSU stimulates sympathetic nerve activity and cutaneous circulating dynamics.

Although a significant elevation in velocity and blood flow in response to exercise with KAATSU was observed in almost all subjects, in some subjects the increase was very slight, as illustrated in Figure 5. Subjects who did not show a clear elevation also showed a sluggish increase in NE concentration (<0.04 ng/mL). This suggests that even if exercise with KAATSU is performed in the same way by all subjects, there might be differences among subjects in their sensitivity to these stimuli. In other words, in subjects who showed clear increases in velocity and blood flow, those increases might relate to NE elevation.

In addition to increasing cutaneous circulation dynamics, KAATSU exercise had a potent effect during the rest periods. The exercise-induced increase in velocity and blood flow was maintained during rest periods (rest 1 and rest 2), and there were no significant differences in these parameters during exercise and at rest. In addition, during the rest period before the start of the first exercise set with KAATSU, velocity was already showing a tendency to increase (Figure 3). The main factor behind the increase in velocity and blood flow is currently unknown. If the impact of KAATSU on cutaneous circulation dynamics precedes the impact of exercise, the effect of the extremely low exercise intensity might be obscured by the effect of the blood flow restriction itself.

The KAATSU-induced increase in venous blood pooling has been demonstrated in both legs distal to the KAATSU belt during rest (Iida et al, 2005). This restriction resulted in decreases in Q and SV, a slight increase in HR, and no change in BP. On the other hand, during exhaustive leg extension exercises in a seated position, an increase in Q, HR, and BP and a

| Table 2. Blood norepinephrine and lactate concentration, and hematocrit in response to low-intensity knee extension exercise with and without KAATSU. |
|-------------------------------------------------|---------|---------|
|                     | Control-Exercise | Kaatsu-Exercise |
|                     | Pre | Post | Pre | Post | Pre | Post |
| NE (pg/mL)         | 0.23 (0.16) | 0.19 (0.09) | 0.21 (0.08) | 0.30 (0.15)* |
| Hematocrit (%)     | 39.3 (2.4) | 38.3 (2.3) | 38.4 (3.0) | 39.3 (2.7) |
| Lactate (mM)       | 0.82 (0.04) | 0.81 (0.03) | 0.82 (0.04) | 0.81 (0.03) |

NE, norepinephrine
* Significantly higher than preexercise in the same exercise style (P<0.05).
decrease in SV have been demonstrated (Takano et al., 2005a). Both studies suggest that KAATSU induces a decrease in SV owing to decreased venous return during both rest and exercise. Further, as Takano et al. (2005a) elucidated, an increase in Q during exercise is controlled mainly by an increase in HR. In the present study, a slight but significant increase in HR, possibly induced by elevation of NE, was found in exercise with KAATSU. Thus, the increase in HR might be a response to decreased SV to satisfy blood flow for increasing Q demand. However, measurement of Q, SV, and BP was not done in the present study, so precise interaction of these parameters in response to KAATSU is still uncertain. Additionally, postural effect on the hemodynamic system during exercise with KAATSU also should be considered when evaluating the interaction of these parameters because unlike in previous studies, exercise in the present study was performed in the supine position. In this position, the reduced hydrostatic pressure causes a shifting of blood volume toward the heart, thereby increasing SV and Q. Leyk et al. (1994) have demonstrated that in the supine position, Q increased further in response to right or moderate cycle exercise, and this increase was mainly mediated by an increase in SV but not HR. In the present study, a shifting of blood volume toward the heart might also have occurred, and thus Q might increase too. However, because of KAATSU, HR might increase instead of SV as a compensatory response to increased Q. It is therefore necessary to understand that in interpreting the response of the hemodynamic system to exercise with KAATSU, the increase in HR in the present study might be influenced by both postural effect and an exercise-induced NE increase.

The mechanism that induced an increase in blood flow via an increase in velocity in response to exercise with KAATSU is unidentified. In a previous paper (Takano et al., 2005a), BP has been demonstrated to increase in response to exercise with KAATSU. In the present study, if an increase in BP occurs in the same way during exercise with KAATSU, peripheral vascular resistance is expected to increase. Also, it is logically assumed that the pooling of blood in one part of the body leads to a shortage of blood flow through the rest of the body, even though blood continues to circulate. Therefore, it seems unlikely that cutaneous blood flow in peripheral regions would increase via acceleration of velocity in response to exercise with KAATSU. A possible explanation of accelerated velocity might be found in changes in vessel diameter. If a signal leading to vasodilation is activated independently from BP modulation, peripheral vascular resistance would decrease and blood flow might increase, with a possible combined increase in velocity. NE has also been suggested to be related to both vasoconstriction and vasodilation regulation (Kellogg, 2006). Elucidation of the vasodynamic system in conjunction with BP alteration in response to exercise with and without KAATSU is required.

There was a wide range in the ages (23-47 years) of the subjects in the present study. Since all subjects had an active life with no symptoms demonstrating decreased circulatory function due to aging, such as hypertension or arteriosclerosis, it seems that the effect of age on the hemodynamic system in response to exercise with KAATSU may be minor. However, if KAATSU is to be applied to people of different ages or people with different health conditions, further examination to clarify the effect of KAATSU on whole-body hemodynamics is required.

In conclusion, unloaded knee extension exercise with KAATSU increased forehead cutaneous blood flow. HR increased owing to elevation of NE in response to exercise with KAATSU, possibly influenced by modulation of cutaneous circulation dynamics.

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