

Muscle oxygenation and plasma growth hormone concentration during and after resistance exercise: Comparison between "KAATSU" and other types of regimen

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We investigated the acute effects of "Kaatsu" resistance exercise and other types of exercise on muscle oxygenation and plasma growth hormone. Six young male bodybuilders performed leg extension exercise according to four exercise regimens: low-intensity [$\sim 30\%$ of one repetition maximum (1RM)] exercise with moderate occlusion (LO-Kaatsu), low-intensity ($\sim 50\%$ 1RM) exercise with slow movement and tonic force generation (3 s for lowering and 3 s for lifting actions, 1-s pause, and no relaxing phase; LST), low-intensity (same as LST) isometric exercise at 45° knee angle (ISO), and high-intensity ($\sim 80\%$ 1RM) exercise with normal movement speed (HN), commonly used for gaining muscular size and strength. The muscle oxygenation level measured with near-infrared continuous-wave spectroscopy (NIRcws) showed the largest changes during and after LO-Kaatsu among all regimens. The minimum oxygenation level during LO-Kaatsu was the lowest among the four exercise regimens. On the other hand, the increases in muscle oxygenation after LO-Kaatsu were the largest among the four regimens. Plasma GH and blood lactate concentrations after LO-Kaatsu, LST and HN were significantly ($P < 0.05$) higher than those after ISO, but there were no significant differences among those after LO-Kaatsu, LST and HN. The results indicate that "Kaatsu" resistance exercise causes marked changes in muscle oxygenation level and circulating growth hormone, both of which may be related to muscular hypertrophy.

Key words: blood flow restriction, hypoxia, blood lactate, muscle hypertrophy

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INTRODUCTION

The exact mechanisms underlying exercise-induced muscle hypertrophy and strength gains are not fully understood, although a number of studies have shown that resistance training successfully caused muscular hypertrophy and increased strength (Aniansson et al., 1981). In general, middle-to-high exercise intensity ($\sim 80\%$ 1RM) has been regarded as essential for these adaptations (McDonagh and Davies, 1984).

However, recent studies have reported that large mechanical stress is not necessarily indispensable for muscular hypertrophy. For instance, low-intensity ($\sim 50\%$ 1RM) resistance training for the knee extensor muscles caused marked increases in muscular size ($\sim 12\%$ gain in cross-sectional area) and strength ($\sim 20\%$ gain) when combined with moderate vascular occlusion, i.e. "Kaatsu" training (Takarada et al., 2002b). Also, a training the knee extensor muscles at 40% maximum voluntary contraction (MVC) under ischemic condition resulted in an increase in muscular strength by $\sim 25\%$ (Shinohara et al., 1998). These effects are likely mediated by the

following processes: (a) stimulated secretion of growth hormone (GH) through an intramuscular accumulation of metabolic sub-products such as lactate (Takarada et al., 2000a); (b) moderate production of reactive oxygen species promoting tissue growth (Takarada et al., 2000b); (c) additional recruitment of fast-twitch fibers in a hypoxic environment (Shinohara and Moritani, 1992; Takarada et al., 2000c). These studies suggest that the muscle-trophic effect of resistance exercise involves not only large mechanical stress but also metabolic, hormonal and neuronal factors.

On the other hand, exercises with sustained force generation would also be effective to make the intramuscular environment hypoxic even without artificial occlusive pressure. Under the normal circulation, continuous force generation at $>40\%$ MVC has been shown to suppress both blood inflow to and outflow from the muscle due to an increase in intramuscular pressure (Bonde-Petersen et al., 1975; Mitchell et al., 1980). A previous study has shown that a low-intensity resistance training ($\sim 50\%$ 1RM) with relatively tonic movement and a short interser

rest period (30 s) causes increases in muscular size and strength (Takarada and Ishii, 2002a). A slow-speed resistance training (10-s lifting and 4-s lowering) has also been shown to be effective for increasing muscular strength (Westcott et al, 2001). In addition, an earlier study by Hettinger and Muller (1953) showed that isometric resistance training at about 50% 1RM intensity caused an increase in muscular strength. However, no study has examined the relationship between the intramuscular oxygen environment and either acute or long-term effects of various types of resistance exercise training, including "Kaatsu" training.

In the present study, we compared the effects of four different exercise regimens on muscle oxygenation levels and plasma growth hormone concentrations. The exercise regimens were: low-intensity [$\sim 30\%$ of one repetition maximum (1RM)] exercise with moderate vascular occlusion (LO-Kaatsu), low-intensity ($\sim 50\%$ 1RM) exercise with slow movement and tonic force generation (3 s for lowering and 3 s for lifting actions, 1-s pause, and no relaxing phase; LST), low-intensity (same as LST) isometric exercise at 45° knee angle (ISO), and high-intensity ($\sim 80\%$ 1RM) exercise with normal movement speed (HN). It is generally known that high-intensity ($\sim 80\%$ 1RM) exercise with relatively short interset rest period (~ 1 min.) like HN strongly stimulates secretion of growth hormone (Kraemaer et.al, 1991). We hypothesized that there is some relationship between the changes in muscle oxygenation levels and the hormonal responses to exercise.

METHODS

Subjects and regimens for exercise training

Six young male bodybuilders and power-lifters

aged 20-22 years volunteered as subjects. Their physical characteristics were as follows: height, 172.7 ± 1.0 (SE) cm; weight, 82.8 ± 6.2 kg. All subjects performed knee extension exercises in a seated position with a nominally isotonic leg extension machine. The range of joint motion was from 0° (0° at full extension).

The subjects performed the four exercise regimens: low-intensity [$\sim 30\%$ of one repetition maximum (1RM)] exercise with rhythmic movement (1 s for lifting and lowering actions) and artificial vascular occlusion (LO-Kaatsu); low-intensity [$\sim 50\%$ of one repetition maximum (1RM)] exercise with slow movement and tonic force generation (3 s for lowering and 3 s for lifting actions, 1-s pause, and no relaxing phase; LST); low-intensity (same as LST) isometric exercise at 45° knee angle (ISO); and high-intensity ($\sim 80\%$ 1RM) exercise with normal speed (1 s for lifting and 1 s for lowering actions, and 1 s for relaxing; HN). Subjects repeated the movement at approximately constant speed and frequency with the aid of a metronome in each exercise session.

For LO-Kaatsu exercise, a specially designed elastic belt (Sato Sports Plaza Co., Tokyo, Japan) was placed around the most proximal portion of both legs. The belt contained a small pneumatic bag along its inner surface that was connected to an electronic pressure meter (MPS-700, VINE, Tokyo Japan). The occlusive pressure was set at 200 mmHg and maintained during the entire session of exercise (Takarada et al, 2002b).

All four exercise sessions consisted of three sets with an interset rest period of 60 s. In LO-Kaatsu exercise, the subjects performed 30 repetitions for the first set and repeated the movements until exhaustion during the second and third sets. In LST and HN exercises, the subjects repeated the

Table 1. Exercise intensity and repetitions in four types of regimen

		LO	LST	ISO	HN
Set 1	Intensity (kg)	52.5 \pm 1.9	81.9 \pm 3.7	81.9 \pm 3.7	142.4 \pm 6.4
	% of 1RM	30.2 \pm 0.0	47.0 \pm 1.0	47.0 \pm 1.0	81.9 \pm 1.5
	Repetitions	30	8	56 s *	8
Set 2	Intensity (kg)	52.5 \pm 1.9	75.8 \pm 2.9	75.8 \pm 2.9	130.5 \pm 5.7
	% of 1RM	30.2 \pm 0.0	43.8 \pm 0.9	43.8 \pm 0.9	75.2 \pm 1.6
	Repetitions	23.3 \pm 3.1	8	56 s *	8
Set 3	Intensity (kg)	52.5 \pm 1.9	69.8 \pm 3.2	69.8 \pm 3.2	120.7 \pm 5.6
	% of 1RM	30.2 \pm 0.0	40.2 \pm 1.4	40.2 \pm 1.4	69.2 \pm 1.9
	Repetitions	15.2 \pm 2.8	8	56 s *	8

Values are means \pm SE; $n = 6$ (same subjects) for each exercise method. Intensity, the weight used for leg extension machine. 1RM, 1 repetition maximum. * Exercise endurance time.

movement until exhaustion (repetition maximum; RM) during each set of exercise. The exercise intensity was determined at 8RM for each set, because RM intensity is used most frequently in the practice of exercise training. Also, the exercise intensities in terms of % 1RM were different between LST (~50% 1RM) and HN (~80% 1RM) are different, because the movements in each type of exercise are different. In ISO exercise, the subjects kept isometric force for 56 s at the same intensity as for LST to match the intensity and impulse with those for LST. The mean intensity and repetitions in each exercise are shown in Table 1. The exercise sessions were separated by one week.

All subjects were fully informed about the experiment procedures to be used as well as the purpose of the study, and their written informed consent was obtained. The study was approved by the Ethics Committee for Human Experiments, Graduate School of Arts and Sciences, University of Tokyo.

Measurement of peripheral muscle (VL) oxygenation by NIRcws

A near-infrared continuous-wave spectroscopic (NIRcws) monitor (BOMLITR, Omegawave, Inc) was used to measure the peripheral muscle oxygenation in the left vastus lateralis (VL) muscle during and after exercise. The wavelengths of emission light were 780, 810 and 830 nm, and the relative concentrations of oxygenated hemoglobin/myoglobin (Oxy-Hb/Mb) in tissues were quantified according to the Beer-Lambert law (Chance et al., 1992). Since the NIRcws signals registered during exercise do not always reflect the absolute levels of oxygenation, the changes of oxygenation in working skeletal muscles are expressed relative to the overall changes in the signal monitored according to the arterial occlusion method (Chance et al., 1992; Hampson and Piantadosi, 1988). In the present study, the resting level and minimum plateau level of Oxy-Hb/Mb obtained during arterial occlusion by cuff pressure (300mmhg) were defined as 100% (baseline) and 0%, respectively (Bae et al., 2000). For measurements, the distance between the incident point and the detector was 30 mm. A laser emitter and a detector were fixed with a sticking tape after shielding with a rubber sheet. The NIRcws signals were stored in a personal computer.

Blood sampling

Venous blood samples (20 ml for each point of measurement) were obtained from the subjects seated in a slightly reclined position through an indwelling cannula in a superficial arm vein for measurement of plasma hormone concentrations. Blood samples (approximately 5 μ l for each point of measurement) were taken from the fingertip using a needle for measurement of blood lactate

concentrations. All of the blood sampling was conducted at the same time of the day to diminish the effects of any diurnal variations on the hormonal concentrations. A resting blood sample was obtained after a 30 min. equilibration period. The exercise session started 30 min. after the resting blood sample was drawn. Thereafter, blood samples were obtained at 0, 15, and 30 min. The subjects refrained from ingesting alcohol and caffeine for 24 h and performing any strenuous exercise for 48 h before the experimental exercise session.

Biochemical analysis

Blood lactate concentration and plasma concentrations of growth hormone (GH) and norepinephrine (NE) were measured using a lactate analyzer (Lactate Pro, Kyoto Primary Science, Japan), with radioimmunoassay (Bando et al., 1992), and with high-performance liquid chromatography (Yoshimura et al., 1993), respectively.

Statistical analysis

All values are expressed as means \pm SE. One-way analysis of variance (ANOVA) with repeated measures followed by Scheffe post-hoc test was used to examine differences between groups and differences between time course variables within the same group. $P < 0.05$ was considered as significant.

RESULTS

Peripheral muscle oxygenation

In all types of regimens, the minimum level of oxygenation during exercise was significantly lower than the resting level. Also, the maximum level of oxygenation after exercise was significantly higher than the resting level. The mean values of minimum oxygenation level during LO-Kaatsu and LST exercises were significantly lower than during HN exercise, and there were no significant differences between those values during LO-Kaatsu, LST and ISO exercises (Fig. 1). The large decrease in the muscle oxygenation level during LO-Kaatsu exercise was likely due to the restriction of muscle blood flow. On the other hand, the decreases in the muscle oxygenation levels during LST and ISO were likely due to the lasting increase in the intramuscular pressure that may also diminish the muscle blood flow. The mean value of maximum oxygenation level after LO-Kaatsu exercises was significantly higher than after ISO exercise (Fig. 2).

Blood lactate concentration

Figure 3-A shows changes in blood lactate concentration measured at rest (pre), immediately after the exercise (post), and 15 and 30 min. after the exercise. All types of regimen caused significant increases in the blood lactate concentration at post,

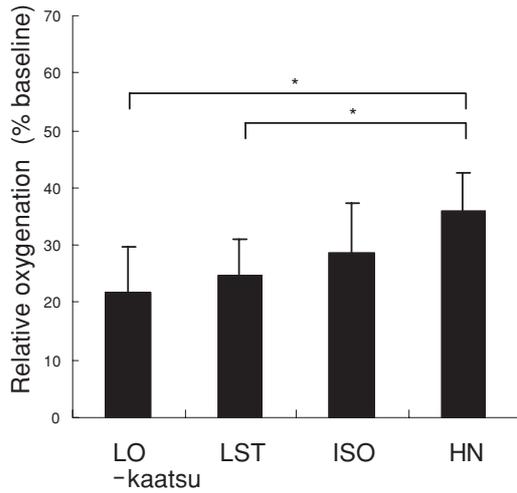


Figure 1. Mean values of minimum oxygenation level during LO-Kaatsu, LST, ISO, and HN exercises. Means \pm SE ($n = 6$, same subjects for each exercise) are shown. *Significant differences ($P < 0.05$) between exercises. When compared to the resting level, all types of exercise caused significant changes ($P < 0.05$).

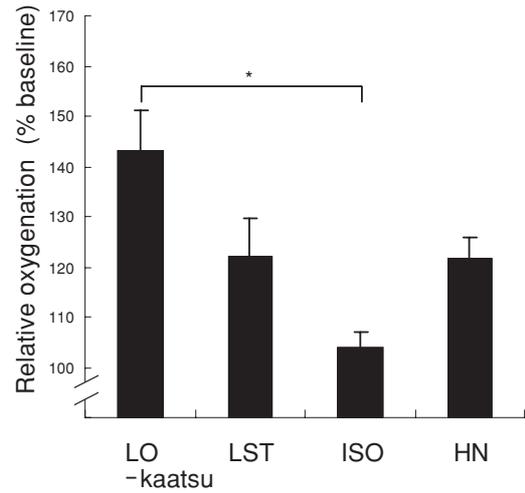


Figure 2. Mean values of maximum oxygenation level after LO-kaatsu, LST, ISO, and HN exercises. Means \pm SE ($n = 6$, same subjects for each exercise) are shown. *Significant differences ($P < 0.05$) between exercises. When compared to the resting level, all types of exercise caused significant changes ($P < 0.05$).

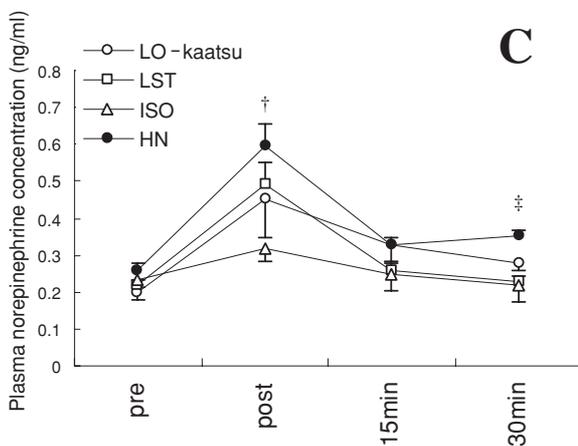
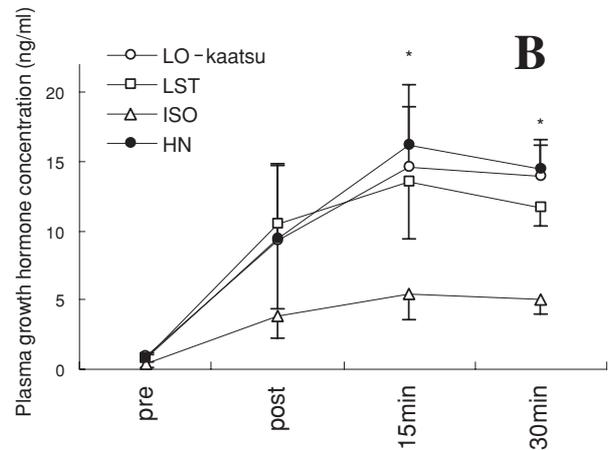
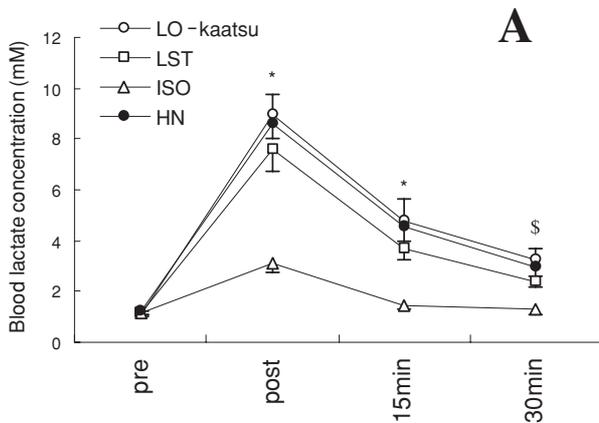


Figure 3. Changes in blood lactate and in plasma growth hormone, and norepinephrine concentrations before and after LO-Kaatsu (\circ), LST(\square), ISO(\triangle), and HN(\bullet) exercises. Means \pm SE ($n = 6$, same subjects for each exercise) are shown. * Significant difference ($P < 0.05$) between ISO and the other exercises. \$ Significant difference ($P < 0.05$) between HN, LO and ISO exercises. † Significant difference ($P < 0.05$) between HN and ISO exercises. ‡ Significant difference ($P < 0.05$) between HN and LST, ISO exercises.

when compared to the resting concentration. Blood lactate concentrations after LO-Kaatsu, LST and HN exercises were significantly higher than after ISO exercise and there were no significant differences between LO-Kaatsu, LST and HN exercises at post, and 15 min. time points. Those after LO-Kaatsu and HN exercises were significantly higher than after ISO exercise at 30 min. time point. Changes in blood lactate concentration were similar after LO-Kaatsu, LST and HN exercises, despite of the much lower exercise intensity in LO-Kaatsu and LST than in HN.

Plasma GH concentration

Figure 3-B shows changes in plasma GH concentration. All types of regimen caused significant increases in the plasma GH concentration at post, 15 min. and 30 min. after the exercises when compared to the resting concentration. Plasma GH concentrations after LO-Kaatsu, LST and HN exercises were significantly higher than after ISO exercise and there was no significant difference among after LO-Kaatsu, LST and HN exercises at 15min and 30 min after the exercises. Changes in plasma GH concentration were similar after LO-Kaatsu, LST and HN exercises, despite of the much lower intensity in LO-Kaatsu and in LST than in HN. In total, the plasma GH concentration showed exercise-regimen dependence similar to that of blood lactate concentration.

Plasma NE concentration

Figure 3-C shows changes in plasma NE concentration. LO-Kaatsu, LST and HN exercises caused significant changes immediately after the exercise (post), whereas ISO exercise did not. Immediately after the exercise, the plasma NE concentration in HN exercise was significantly higher than in ISO exercise. That in HN exercise was significantly higher than in LST and ISO exercises at 30min. time point. HN exercise resulted in higher NE concentration than did the other regimens at 0, 15 and 30 min. after exercise, indicating that it has the strongest impact on the sympathetic activation.

DISCUSSION

The present study showed that resistance exercises combined with restriction of muscular blood flow, including "Kaatsu" exercise, caused changes in the muscle oxygenation levels, an increased production of an anaerobic metabolite, and increased endocrine responses that may be related to the mechanisms necessary for muscular hypertrophy. The increases in blood lactate and plasma GH concentrations after LO-Kaatsu and LST exercises were similar to those after HN exercise, despite of the much lower exercise intensity than in HN. This phenomenon may be related to the reduced muscular blood flow and

resulting hypoxic environment during the exercise.

Among the exercise regimens examined, LO-Kaatsu exercise appeared to cause the greatest changes in muscle oxygenation levels during and after the exercise (Fig1 and 2). This may be due largely to the artificial restriction of muscular blood flow, thereby both the supply of oxygen and the clearance of metabolic sub-products are suppressed for a prolonged period of time. LST exercise had been expected to cause a similar effect. HN exercise, commonly used for promoting muscular size and strength (Kraemer and Ratamess, 2005; Kraemer et al, 1991), appeared to cause small decreases in muscle oxygenation during exercise and relative hyperoxygenation after exercise, both of which may reflect the hyperemia due to repeated contraction and relaxation (Laughlin, 1987).

The decrease in muscle oxygenation levels during exercise was similar between LO-Kaatsu and LST exercises. The lowered muscle oxygenation level and the increased blood lactate concentration during those two types of exercise were likely due to the restriction of muscular blood flow. It has been speculated that local accumulation of metabolic sub-products such as lactate, stimulates the hypophyseal secretion of GH (Kraemer and Ratamess, 2005; Kraemer et al, 1991) and the local secretion of growth factors such as IGF- I (Schott et al., 1995). It has also been shown that plasma GH stimulates synthesis and secretion of IGF- I within a muscle, which then may act on the muscle itself and promote growth (Devol et al., 1990; Isgaard et al., 1989).

The isometric exercise appeared to be a superior method for maintaining constant tension, and the oxygenation level in VL was lowered during ISO exercise similar to LO-Kaatsu and LST exercises. However, it did not cause hyperoxygenation after exercise (Fig. 2). Also, isometric contraction produces no mechanical work, so the blood lactate concentrations after ISO exercise were lower than after the other types of exercise. Consequently, plasma GH concentration after ISO exercise was also lower than after the other types of exercise. These results suggest that, in addition to the restriction of blood flow, energy expenditure is required to cause post-exercise hyperoxygenation of muscle and hormonal responses.

The production of reactive oxygen species (ROS) may play an important role in muscular hypertrophy. The activity of ROS within the muscle has been shown to increase in a hypoxic environment (Korthius et al., 1985). A considerable amount of ROS could be produced when the muscle is kept hypoxic and subsequently exposed to reperfusion (Southard et al., 1987). Among the ROS, Nitric oxide (NO), known as the strongest vasodilator, has also been shown to mediate activation and proliferation of

muscle satellite cells, which are muscle fiber stem cells (Anderson, 2000). Therefore, both lowered and elevated muscle oxygenation levels during and after exercise may cause an enhanced production of ROS, thereby stimulating muscle growth. In LO-Kaatsu exercise, the mean value of minimum oxygenation level during exercise was the lowest and that of maximum oxygenation level after exercise was the highest among the four exercise regimens examined.

In conclusion, LO-Kaatsu and LST exercises, even at low intensities, can cause hypoxic intramuscular environment, increase the production of metabolic sub-products during exercise, and enhanced endocrine responses, which may be especially useful for strength training aged people or those recovering from orthopedic injuries.

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