CASE REPORT

Day-to-day change in muscle strength and MRI-measured skeletal muscle size during 7 days KAATSU resistance training: A case study

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The purpose of this study was to examine the daily skeletal muscle hypertrophic and strength responses to one week of twice daily KAATSU training, and follow indicators of muscle damage and inflammation on a day-to-day basis, for one subject. KAATSU training resulted in a 3.1% increase in muscle-bone CSA after 7 days of training. Both MRI-measured maximum quadriceps muscle cross-sectional area (Q-CSA max) and muscle volume can be seen increasing after the first day of KAATSU training, and continuously increasing for the rest of the training period. Following 7 days KAATSU resistance training, the increases in Q-CSA max and muscle volume were 3.5% and 4.8%, respectively. Relative strength (isometric knee extension strength per unit Q-CSA max) was increased after training (before, 3.60 Nm/cm^2; after, 4.09 Nm/cm^2). There were very modest increases in CK and myoglobin after a single bout of KAATSU exercise in the first day of the training, but the values were return towards normal at 2 days after the training. IL-6 remained unchanged throughout the training period. In conclusion, our subject gained absolute strength and increased muscle size after only one week of low intensity KAATSU resistance training. Indicators of muscle damage and inflammation were not elevated by this training. KAATSU training appears to be a safe and effective method to rapidly induce skeletal muscle strength and hypertrophy.
Key words: muscle hypertrophy, strength gain, short duration, IL-6, muscle damage

INTRODUCTION

It is clear that high intensity resistance training over a period of time causes increases in skeletal muscle mass in humans [McDonagh and Davies, 1984; Ikai and Fukunaga, 1970; Hakkinen et al., 1985; MacDougall et al., 1977; Jones and Rutherford, 1987]. Typically, the time course that results in significant increases in skeletal muscle mass in humans is on the order of 8-12 weeks, [Kraemer et al., 2002], with occasional reports of significant hypertrophy in as little as 6 weeks [Abe, et al., 2000]. However, a single bout of high intensity resistance exercise in humans results in small but significant increases in synthesis of muscle protein, i.e. a hypertrophic response [Biolo et al., 1995; Phillips et al., 1999].

It is reported that high intensity resistance training produces indicators of muscle damage and inflammation in the plasma [Clarkson and Hubal, 2002; Sorichter et al., 1999]. For example, the proinflammatory plasma cytokine interleukin-6 (IL-6) is increased after high intensity resistance exercise [Smith et al., 2000] and the magnitude of increase has been reported to be proportional to exercise duration [Febbraio and Pedersen, 2002; Pedersen et al., 2001] and intensity [Helge et al. 2003]. In fact,

recent studies have suggested additional biological functions for IL-6 during exercise that may not be related to inflammation [Febbraio and Pedersen, 2002; Febbraio and Pedersen, 2005]. Serum myoglobin and creatine kinase (CK), also thought to be produced in skeletal muscle, increases following high intensity resistance exercise [Clarkson and Hubal, 2002; Sorichter et al., 1999].

We recently reported that the use of KAATSU training (exercise training combined with restriction of muscular venous blood flow from the working muscle) resulted in a rapid (2 weeks) skeletal muscle hypertrophic and strength response (~ 8% increase in thigh muscle volume, ~ 20% increase in maximum leg strength) using 20% of one repetition maximum (1-RM) as the training intensity [Abe et al., 2005]. It would be of interest to know the day-to-day changes in muscle size following even shorter bouts of this type of training. Also, we have reported that in previously untrained subjects, indicators of muscle damage (CK and myoglobin) were not elevated at 1 and 2 weeks during KAATSU training [Abe et al., 2005]. However, in our previous study, we did not examine whether indicators of muscle damage and inflammation were increased during the early phase of the training, as is commonly reported [Clarkson

and Hubal, 2002]. Thus the purpose of our current study was to examine the daily skeletal muscle hypertrophic and strength responses to one week of twice daily KAATSU training, and follow indicators of muscle damage and inflammation on a day-to-day basis, for one subject.

METHODS

The subject was a 47 year old male (height, 1.78 m; weight 80.5 kg) with previous resistance training and aerobic training experience; however, the subject had not resistance trained in the previous three months. During the experiment, the subject did not perform any strenuous exercise other than KAATSU training session.

The subject participated in low-intensity resistance training combined with restriction of leg muscle blood flow. Training was conducted twice per day for 7 consecutive days. Following a warm up, the subject performed 30 repetitions of knee extension exercise without rest, and after a 30 sec rest, he performed three sets of 15 repetitions, with 30 sec rest between sets. The intensity of exercise was 20% of one repetition maximum (1-RM). The subject wore a pressure belt (Kaatsu Master, Tokyo) on both legs during training. On the first day of the training (day 1), the belt pressure was 160 mmHg, and the pressure was increased 20 mmHg each day until a final belt pressure of 220 mmHg (day 4) was reached. The restriction pressure of 160-220 mmHg was selected for the occlusive stimulus as this pressure has been suggested to restrict venous blood flow and cause pooling of blood in capacitance vessels distal to the belt, and ultimately restrict arterial blood flow [Takarada et al. 2000]. The estimated coefficient of variation (CV) of this pressure measurement was 2.2%. The restriction of muscular blood flow was maintained for the entire exercise session, including the rest periods. The belt pressure was released immediately upon completion of the session.

Maximum dynamic knee extension strength (1-RM) was assessed prior to (one week before) and 2 and 6 days after the final training. After warming up, the load was set at 80% of the predicted 1-RM. Following each successful lift the load was increased by ~5% until the subject failed to lift the load through the entire range of motion. A test was considered valid only when the subject used proper form and completed the entire lift in a controlled manner without assistance. Approximately 2-3 min of rest was allotted between each attempt to ensure recovery.

Maximum voluntary isometric strength of the knee extensors was determined using an isokinetic dynamometer (Biodex System 3). The subject was seated on a chair with his hip joint angle flexed at 85°. The center of rotation of the knee joint was visually aligned with the axis of the lever arm of the dynamometer. The ankle of the right leg was firmly attached to the lever arm of the dynamometer with a strap. After a warm-up consisting of submaximal (~50% of maximal strength) contractions, the subject was instructed to perform a maximal isometric knee extension (3~4 sec) at knee joint angles of 75°. A knee joint angle of zero corresponded to full extension of the knee. This test was used every morning throughout the training period, 2 days before the training, and 2 days after the final training.

Muscle-bone cross-sectional area (CSA) for the mid-thigh was estimated using following anthropometric equation:

$$\text{Muscle-bone CSA} = \pi \left[r - (Q\text{-}AT + H\text{-}AT) / 2 \right]^2$$

where r was the radius of the thigh calculated from mid-thigh girth of the right leg, and Q-AT and H-AT were ultrasound-measured anterior and posterior thigh adipose tissue thickness, respectively. We have previously determined that the CV of this measurement was 1.2% [Bemben et al., 2005]. This measurement was completed every morning throughout the pre-training (from 1 week before training), during the training (prior to the morning training session) and detraining (until 10 days after the training).

Magnetic resonance imaging (MRI) images were prepared using a General Electric Signa 1.5 Tesla scanner (Milwaukee, Wisconsin, USA). A T1 weighted, spin echo, axial plane sequence was performed with a 1500 millisecond repetition time and a 17 millisecond echo time. The subject rested quietly in the magnet bore in a supine position with his legs extended. Contiguous transverse images with 1.0 cm slice thickness (0 cm interslice gap) were obtained from the knee joints to the upper portion of the thigh. For each slice, the quadriceps muscle CSA was digitized, and the quadriceps muscle volume (cm^3) was calculated by multiplying muscle tissue area (cm^2) by slice thickness (cm). The estimated CV of quadriceps muscle CSA measurement was 0.3%. This measurement was completed every morning (prior to the morning training session) throughout the training period (except the weekend), 1 week before the training and 2 days after the final training.

Resting venous blood was drawn from the subject at baseline (prior to the training), 24 and 48 hrs after the first training session and 2 days after the final training. All blood samples at rest were obtained at the same time of day (9:00-10:00 AM) following an overnight fast (12-13 hours). A blood sample was also drawn before and after the first and second training sessions (first training day). Serum activity of creatine kinase (CK) was measured at S.R.L. Inc (Tokyo) by the use of spectrophotometry for NADPH formed by a hexokinase and D-glucose-6-phosphate-

dehydrogenase-coupled enzymic system. Serum concentration of myoglobin and IL-6 were measured using a commercially available radioimmunoassay (Daiichi Radioisotope Laboratory, Chiba, Japan) and chemiluminescent enzyme immunoassay, respectively.

RESULTS

Changes in estimated muscle-bone cross sectional area are depicted in Figure 1. KAATSU training resulted in a 3.1% increase in muscle-bone CSA after 7 days of training. Ten days of detraining resulted in a CSA loss of about 1%, i.e. one-third the muscle-bone CSA gained.
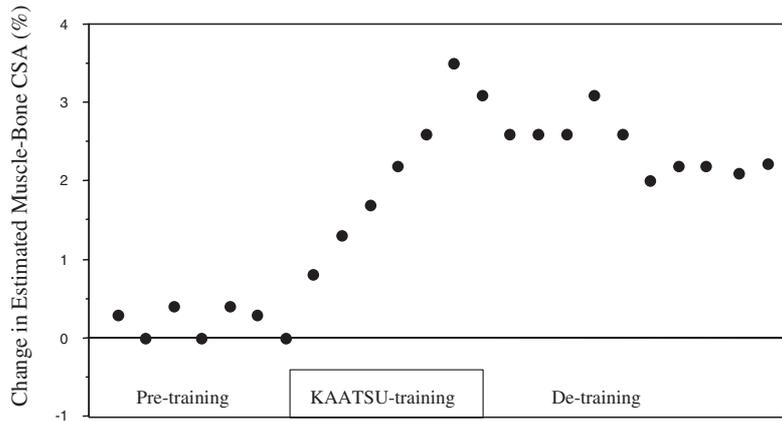
Figure 1. Percent change in estimated muscle-bone cross-sectional area (CSA) before and during KAATSU training and detraining
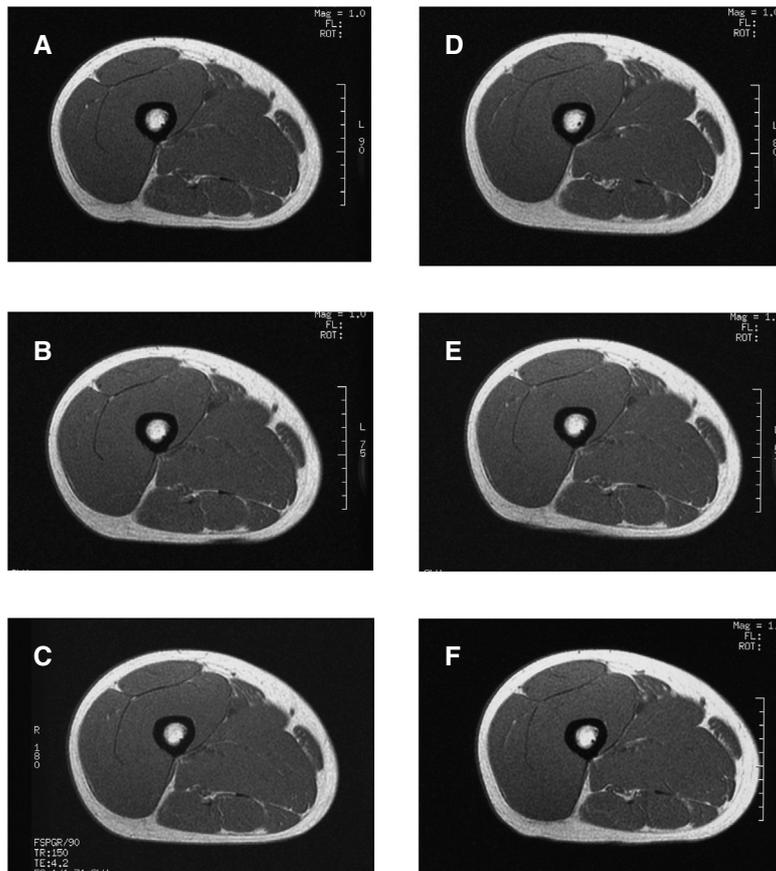
Figure 2. Day-to-day change in MRI images during KAATSU training (before [A], 1 day [B], 2 days [C], 3 days [D], 4 days [E], and 7 days [F] after training).

Table 1. Changes in quadriceps muscle size and isometric knee extension strength during low-intensity resistance training with KAATSU

| | Quadriceps femoris | | | | Absolute and relative strength Isometric knee extension | |
	CSAmax (cm^2)	change (%)	Volume (cm^3)	change (%)	(Nm)	(Nm/cm^2)
1-W before	71.8	0.3	1621	1.8	257	3.58
Before	71.6	0	1593	0	259	3.62
1 day after	72.6	1.4	1647	3.4	273	3.76
2 days after	73.2	2.2	1660	4.2	270	3.69
3 days after	73.4	2.5	1650	3.6	273	3.72
4 days after	74.0	3.4	1665	4.5	280	3.78
5 days after	----	----	----	----	299	4.04*
7 days after	74.1	3.5	1670	4.8	303	4.09

*relative strength was calculated using the value of 4 days after muscle CSA

Table 2. Changes in indicators of muscle damage and inflammation during KAATSU training

	CK(IU/L)	Myoglobin(ng/ml)	IL-6 (pg/ml)
Prior to 1st Ex (AM)	134	35	0.8
Immediately after 1st Ex	164	45	1.0
Prior to 2nd Ex (PM)	123	85	0.7
Immediately after 2nd Ex	173	75	0.7
1 day after	144	65	0.6
2 days after	151	42	0.7
8 days after	120	33	0.7

The resulting day-to-day MRI images are shown in Figure 2. The images show identical sections of muscle midway along the femur. Changes in MRI-measured maximal quadriceps muscle CSA (Q-CSA max) and quadriceps muscle volume are shown in Table 1. Both Q-CSA max and muscle volume can be seen increasing after the first day of KAATSU training, and continuously increasing for the rest of the training period (Figure 2). Following 7 days KAATSU resistance training, the increases in Q-CSA max and muscle volume were 3.5% and 4.8%, respectively.

The changes in absolute and relative isometric strength are also presented in Table 1. Compared with baseline data (before training or 1 week before training), there were small changes (~3% increase) in isometric strength in the first 4 days after training. Isometric strength increased 17% following 7 days KAATSU training. Similarly, dynamic knee extension strength (1-RM) increased 18% after training (2 days after the final training session). After 6 days of detraining, the knee extension 1-RM was still increased 14% compared to before the training. Relative strength (isometric knee extension strength

per unit quadriceps muscle CSA) was increased after training (before, 3.60 Nm/cm^2; after, 4.09 Nm/cm^2).

The subject had normal values of CK, myoglobin, and IL-6 at baseline (Table 2). There were very modest increases in CK and myoglobin after KAATSU training, with the tendency to return towards normal in between bouts (Table 2). IL-6 remained unchanged throughout the training period.

DISCUSSION

We have previously reported [Abe et al., 2005] that 2 weeks of low-intensity twice daily KAATSU resistance training can produce substantial (~8%) muscle hypertrophy, as measured by MRI. In that study, however, muscle size was not measured daily with MRI, instead muscle-bone CSA was estimated daily. MRI was used to determine muscle volume at the beginning and end of the study. Here we report for the first time, evidence of muscle hypertrophy after only one week's resistance training as determined by daily measurements of muscle volume by MRI. Similar increases in muscle size have previously been reported to take ~ 6 weeks of

traditional high-intensity resistance training [Abe et al., 2000]. Our results indicate that because of the low-intensity nature of KAATSU training (e.g. 20% of 1 RM training load, lack of response of indicators of muscle damage, etc.), daily repeated bouts of the exercise appear well tolerated and can lead to faster than previously reported skeletal muscle hypertrophy.

Previous reports with high intensity resistance training (~ 70-100% of 1 RM) indicate that typically 8-12 weeks of training are needed in order to show signs of significant skeletal muscle hypertrophy as measured by non-invasive methods (e.g., MRI, ultrasound, limb circumference). However, one study did report significant hypertrophy at 6 weeks of resistance training [Abe et al., 2000]. It has been shown that even one bout of high-intensity resistance training can result in increases in protein accretion, as measured by invasive methods, i.e., stable isotope labeling [Biolo et al., 1995; Phillips et al., 1999]. This suggests that muscle hypertrophy is occurring even after one session of resistance training at level/rate that is not measurable by most non-invasive methods. What is interesting in the present study is that we were able to measure skeletal muscle hypertrophy via a non-invasive method and identify significant changes after only one week of low-intensity resistance training.

It could be hypothesized that the changes we saw are due, in some respect, to increased water, either in the inter - or intra - vascular space or in the muscle itself. However, we do not believe this to be the case. If changes in the water content of the muscle or surrounding area were responsible for the majority or all of the muscle hypertrophy noted, then no changes in absolute strength would have been likely. Also, changes in relative strength would have been apparent. That is, the ratio of strength per muscle CSA would have decreased. This would have been due to a "diluting" of the number of cross bridges (the force generating mechanism of skeletal muscle) by the increased water. However, both relative strength and absolute strength increased in the present study. Therefore our study suggests that the changes we noted were likely due to hypertrophic changes.

Furthermore, it has recently been noted in humans that cell swelling (i.e. via saline infusion) results in a reduction in proteolysis [Berneis et al., 1999, Keller et al., 2003]. A reduction in proteolysis could contribute to increased net protein balance and subsequently an anabolic response of skeletal muscle. This may be due to activation of a signaling mechanism like h-sgk, which is known to be triggered by cell swelling in vitro [Waldegger et al., 1997]. We hypothesize that KAATSU training, which is known to result in temporary (~3 hours) swelling of skeletal muscle [Abe, 2004], but also skeletal

muscle hypertrophy [Abe et al., 2005], might work via these same mechanisms.

Also in agreement with our previous study, and other published results, we found little to no change in serum indicators of muscle damage and inflammation [Abe et al., 2005; Takarada et al., 2000]. Although these indicators are not definitive measures of skeletal muscle damage, it is commonly known that in untrained subjects, markers of skeletal muscle damage such as CK and myoglobin rise by over 100% after one bout of high intensity exercise [Clarkson and Hubal, 2002; Sorichter et al., 1999]. These markers can remain elevated for several days [Clarkson and Hubal, 2002; Sorichter, et al., 1999]. We noted very little change in CK and myoglobin in this subject, even though he was training two times per day. This confirms that it is the intensity of the exercise, not the number of training sessions, that is the trigger for release of these indicators.

We also noted no change in circulating levels of IL-6, however, a previous study [Takarada et al., 2000] reported that plasma IL-6 concentration increased after acute low-intensity KAATSU resistance exercise. IL-6 release from working muscle is related to the intensity and duration of endurance exercise [Helgo et al., 2003; MacDonald et al., 2003]. The previous KAATSU trial [Takarada et al., 2000] used five sets of exercise compared to three sets in the present study and the difference in exercise duration may explain the difference in the IL-6 data between the trials. The IL-6 data further demonstrate that KAATSU exercise uses a very low exercise intensity, which can allow for faster recovery and greater training frequency. It is interesting to note that IL-6 released from working muscle during exercise may have other important biological functions that are not related to inflammation [Febbraio and Pedersen, 2002] and its relationship to KAATSU intensity and duration warrants further study.

We should acknowledge however, that our subject had previous experience with resistance training. It is known that subjects with previous history of resistance training (even one prior bout) have a blunted response of plasma indicators of muscle damage and inflammation [Clarkson and Hubal, 2002]. However, coupled with previous results from untrained subjects [Abe, et al., 2005; Takarada et al., 2000], we can conclude that after the first or subsequent exposures to KAATSU training, indicators of skeletal muscle damage and inflammation are not elevated, either in untrained people, or people with resistance training experience.

In conclusion, our subject gained absolute strength and increased muscle size after only one week of low intensity KAATSU resistance training. Indicators of muscle damage and inflammation were not elevated by this training. The results of the present study are

probably because with KAATSU training, a very low intensity can be used, which allows for a faster recovery and an ability to train more frequently. Our data taken together with previous KAATSU training studies suggest that KAATSU training appears to be a safe and effective method to rapidly induce skeletal muscle strength and hypertrophy.

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