Skeletal Muscle Hypertrophy Induced by Novel KAATSU Rehabilitation and Prevention of Sarcopenia

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Sarcopenia, the loss of muscle mass, is an important problem in the older population.

Muscle strength is decreased with age. Muscle volume is quickly decreased 0.45 Kg/year at ages >50 years old. (1%/day in space, 0.6%/day bed rest). Especially, fast twitch fiber decreased to 50% by 80 years old.

To prevent it, high-intensity resistance exercise is usually required, but it cannot be performed in the elderly people. In this symposium, I present our recent data of KAATSU training in elderly persons and basic researches using rat KAATSU model.
Conditions necessary for muscle hypertrophy

(American Sports of Medicine, 2000)

- **Strength**: 70〜80% 1RM (8〜15RM)
  (lower than 65% : unreliable effects)
- **Number**: until exhaustion
- **Sets**: 3 sets
- **Frequency**: 2〜3 times/week

It is impossible to apply such a high-intensity exercise for older subjects or patients.
KAATSU training
The KAATSU training developed by Dr. Sato is a unique technique of performing low-load exercise with restricted muscle blood flow, by using a specially designed KAATSU belt.

It can induce muscle hypertrophy and strengthen muscle even by using a short-term and low-intensity exercise as equal as high-intensity exercise.

Muscle stimuli
Muscle hypertrophy and strength

20-30% 1RM
3-4 sets

Low-intensity, short-term

KAATSU belt

70-80% 1 RM

High-intensity training
Thus, it is likely that KAATSU training mobilizes many muscle fibers including fast fibers.
【Research 1】 Effects of KAATSU training in elderly subjects

【Subjects】 Healthy elderly subjects 19 cases
(Mean age 71 years old)
→ KAATSU group (9 cases), control group (10 cases)

【Exercise】 Knee Extension & Leg Press

【KAATSU pressure】 120 ~ 250 SKU

【Period】 12 weeks (2 times/week)

Knee Extension
(≈20% 1RM)

Leg Press
(≈30% 1RM)

84 years old

Extension Press

<example>

Mon Thur

1 W 2 W 3 W ...... 11 W 12 W

Examination
A typical example of the effects of KAATSU training on cross sectional area of thigh 50% position (MRI)

Case: YN (70 years old)

Pre training

3 months after training

Effects of KAATSU training on muscle size (Thigh 50% position)

**Quadriceps**

<table>
<thead>
<tr>
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<th>Muscle cross sectional area (cm²)</th>
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<tr>
<td>KAATSU</td>
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<td>control</td>
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P<0.01

**Adductor**

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<td>control</td>
<td>5.0</td>
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P<0.05

Increasing muscle strength and muscle mass can improve life function test measured by chair stand test.
Similar results were observed in upper limbs using an elastic band in elderly subjects

YN (71 year old)

The process leading up to muscle hypertrophy from resistance training

Resistance training

Initial stimulus factors
1) Mechanical stress
2) Metabolic stress
3) Hormone (catecholamine)
4) Growth factor (GH), Cytokine (IL-6)
5) Nerve factor
6) Local circulation
7) Local oxygen environment (hypoxia)
8) Cell swelling, stretch et al.

Need 1RM > 65% to induce hypertrophy

Adaptation
1) Protein synthesis ↑
2) Protein degradation ↓

Mechanisms of the hypertrophic effects of KAATSU training?
Several mechanisms underlying hypertrophic effects of KAATSU training

① Increase of muscle activity → Recruitment of fast fibers with a high degree of training effect
② Growth hormone secretion  GH/IGF-1 ↑ → Amino acid uptake, protein synthesis ↑
③ Protein synthesis speed ↑ → Muscle hypertrophy
④ Recruitment of muscle satellite cells?
⑤ Decrease in myostatin → muscle hypertrophy

○ Maintenance of skeletal muscle mass is dependent on the relationship of muscle protein balance (protein synthesis and breakdown). A negative protein balance induces muscle atrophy, whereas a positive balance induces muscle hypertrophy.

○ After muscle disuse, during long-term bed rest, spaceflight and simulated models of no-bearing activity, severe skeletal muscle atrophy develops due to the altered protein metabolism leading to decreased muscle contractile protein content.

To prevent it, resistance exercise, an established and potent stimulus for enhancing muscle protein synthesis and subsequent muscle hypertrophy, is usually used.
On the other hand, skeletal muscle is a plastic organ that adapts its mass to the different conditions by affecting pathways that regulate protein and cellular turnover.

Takarada et al. (2000): Repetitive application of KAATSU (repetitive KAATSU) diminished the post-operation disuse atrophy of knee extensors in patients who underwent an operation for the reconstruction of the anterior cruciate ligament.

From the paper, repetitive KAATSU appears to be a novel stimulus for skeletal muscle to induce a net positive protein balance and prevent atrophy. However, the underlying mechanism of repetitive KAATSU has not been investigated.
Therefore, we investigated the effects of repetitive KAATSU on muscle O$_2$ partial pressure (PmO$_2$), mammalian target of rapamycin (mTOR) signaling pathways involved in translation initiation of skeletal muscle in rat KAATSU model.

(presented at 2013 AHA meeting, Nakajima T et al., submitted)
Methods:
Wistar rats (10 weeks, male) underwent repetitive KAATSU under isoflurane anesthesia.

Repetitive KAATSU
- Repetitive KAATSU to the right lower extremity was induced by compressing the proximal end of the right thigh with a Durable Digit Cuff.
- Repetitive KAATSU stimulus, which consisted of an external compressive force of 100 mmHg for 5 min, followed by 3 min of rest, was repeated six times during a 48-minute interval.

Muscle oxygen partial pressure:
Methods: Wistar rats (10 weeks, male) underwent repetitive KAATSU under isoflurane anesthesia.

Muscle oxygen partial pressure:
Measurement of PmO2: Phosphorescence quenching

Muscle sampling (protein, total RNA)
Pre 0 h 1 h 3 h 6 h

Real-time RT-PCR
Western blotting
Effects of repetitive KAATSU on muscle pO2 (PmvO2) (Aa, b), total muscle weight (Ba) and total muscle weight/body weight (Bb).

**A** Effects of repetitive KAATSU on muscle pO2 (PmvO2)

- **KAATSU**
  - 5min 5min 5min 5min 5min 5min

- **PO2 (Torr)**
  - 0 10 20 30 40 50

- **Time**

- **KAATSU**
  - 1st 2nd 3rd 4th 5th 6th

**B** Total muscle weight of the tibialis anterior muscle (Ba) and total muscle weight/body weight (Bb)

- **Total muscle weight** (mg)
  - Pre Post 0h 1h 3h 6h

- **Left KAATSU**
  - mg

- **Right KAATSU**
  - mg

- **Total muscle weight/body weight**
  - Pre Post 0h 1h 3h 6h

- **Left KAATSU**
  - mg

- **Right KAATSU**
  - mg

* indicates a significant difference.
2 months Time-up go (TUG test)  6 months  Time-up go

Improvement of cognitive function

KAATSU training in a patient with dementia
Conclusion

KAATSU rehabilitation may be a novel useful method to promote muscle strength and hypertrophy safely in patients with elderly subjects, patients, and astronauts.
Thank you very much for your attention.

Collaborators

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