# **Cross-Transfer Effects of Resistance Training** with Blood Flow Restriction

HARUHIKO MADARAME<sup>1</sup>, MITSUO NEYA<sup>1</sup>, EISUKE OCHI<sup>2</sup>, KOICHI NAKAZATO<sup>2</sup>, YOSHIAKI SATO<sup>3</sup>, and NAOKATA ISHII<sup>1</sup>

<sup>1</sup>Department of Life Sciences, Graduate School of Arts and Sciences, The University of Tokyo, Tokyo, JAPAN; <sup>2</sup>Graduate School of Health and Sport Science, Nippon Sport Science University, Tokyo, JAPAN; and <sup>3</sup>Sato Institute for Rehabilitation and Fitness, Tokyo, JAPAN

### ABSTRACT

MADARAME, H., M. NEYA, E. OCHI, K. NAKAZATO, Y. SATO, and N. ISHII. Cross-Transfer Effects of Resistance Training with Blood Flow Restriction. Med. Sci. Sports Exerc., Vol. 40, No. 2, pp. 258-263, 2008. Purpose: This study investigated whether muscle hypertrophy—promoting effects are cross-transferred in resistance training with blood flow restriction, which has been shown to evoke strong endocrine activation. Methods: Fifteen untrained men were randomly assigned into the occlusive training group (OCC, N = 8) and the normal training group (NOR, N = 7). Both groups performed the same unilateral arm exercise (arm curl) at 50% of onerepetition maximum (1RM) without occlusion (three sets, 10 repetitions). Either the dominant or nondominant arm was randomly chosen to be trained (OCC-T, NOR-T) or to serve as a control (OCC-C, NOR-C). After the arm exercise, OCC performed leg exercise with blood flow restriction (30% of 1RM, three sets, 15-30 repetitions), whereas NOR performed the same leg exercise without occlusion. The training session was performed twice a week for 10 wk. In a separate set of experiments, acute changes in blood hormone concentrations were measured after the same leg exercises with (N = 5) and without (N = 5) occlusion. Results: Crosssectional area (CSA) and isometric torque of elbow flexor muscles increased significantly in OCC-T, whereas no significant changes were observed in OCC-C, NOR-T, and NOR-C. CSA and isometric torque of thigh muscles increased significantly in OCC, whereas no significant changes were observed in NOR. Noradrenaline concentration showed a significantly larger increase after leg exercise with occlusion than after exercises without occlusion, though growth hormone and testosterone concentrations did not show significant differences between these two types of exercises. Conclusion: The results indicate that low-intensity resistance training increases muscular size and strength when combined with resistance exercise with blood flow restriction for other muscle groups. It was suggested that any circulating factor(s) was involved in this remote effect of exercise on muscular size. Key Words: GROWTH HORMONE, ISCHEMIA, RESISTANCE EXERCISE, STRENGTH TRAINING

I thas been well known that resistance training for one side of the limbs can cause increase in muscular strength not only in the trained limb, but also in the contralateral, untrained limb (5,8,9,11,12,17,20,24). This phenomenon is called cross-education or cross-transfer effect (5,11,17). Whereas the increase in muscular strength in trained limb is caused by both neural adaptation (2,11,17,18) and muscle hypertrophy (17,18), it has been thought that cross-transfer of strength increase is caused only by neural factors (5,11). Previous studies have shown that a period of unilateral resistance training results in

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increases in iEMG (24) and motor neuron-discharge rate (20) during contractions of contralateral limb muscles. On the other hand, no study has so far shown a cross-transfer effect with regard to muscular hypertrophy.

Hansen et al. (6) have demonstrated that increases in arm strength were enhanced when leg training was added to the arm training. They (6) also have demonstrated that acute, postexercise changes in plasma testosterone and growth hormone (GH) increased when the leg training was combined. Although no information about muscle size was presented, they suggested that larger increase in arm strength was attributable to muscular hypertrophy caused by these hormones. It has been demonstrated that endogenous (14) as well as exogenous (4,10) testosterone plays an important role in muscular hypertrophy. Although a muscle hypertrophy-promoting effect of endogenous GH is controversial (22,30), it has been shown that acute changes in plasma concentration of GH after an exercise session are positively correlated with the extent of muscular hypertrophy after the period of exercise training (15).

Recent studies have shown that resistance training at an intensity as low as 20% of the one-repetition maximum (1RM) can effectively cause increases in muscular size and

Address for correspondence: Haruhiko Madarame, Department of Life Sciences, Graduate School of Arts and Sciences, The University of Tokyo, Komaba, Meguro-ku, Tokyo 153-8902, Japan; E-mail: h\_madarame@hotmail.com.

strength when combined with moderate blood flow restriction (27,28). This type of resistance training with blood flow restriction ("occlusive exercise") has been shown to evoke enhanced endocrine responses, which are supposed to play a part in muscular hypertrophy (1,21,25,26,29). Takarada et al. (26) have demonstrated that low-intensity occlusive exercise for the lower extremities caused a larger increase in the plasma concentration of GH than did normal exercise of the same intensity and volume. If increases in the systemic concentrations of anabolic hormones promote muscular hypertrophy, resistance training with blood flow restriction for a given muscle is expected to induce muscular hypertrophy not only in the same muscle but also in other muscles trained without blood flow restriction and/ or untrained ("cross-transfer of muscle hypertrophy"). To see whether such a cross-transfer of muscle hypertrophy occurs, the present study investigated the effects of resistance exercise with blood flow restriction for leg muscles on arm muscles that were either untrained or trained in a normal fashion at a low intensity.

## METHODS

**Subjects.** Fifteen healthy men without prior experience of regular resistance training volunteered to participate in the study. They were randomly assigned into the occlusive training group (OCC, N = 8) and the normal training group (NOR, N = 7). Mean age, height, and body mass were  $21.6 \pm 2.4$  yr,  $171.0 \pm 3.7$  cm, and  $58.8 \pm 3.8$  kg in OCC, and  $21.9 \pm 4.2$  yr,  $168.7 \pm 4.2$  cm, and  $60.7 \pm 5.1$  kg in NOR, respectively. All subjects were fully informed about the experimental procedures and the purpose of the study and gave their written informed consent. The study was approved by the ethics committee for human experiments, Graduate School of Arts and Sciences, University of Tokyo.

**Training program.** The exercises used for training were dumbbell curl, knee extension, and knee flexion. Both OCC and NOR performed three sets of single-arm dumbbell curl without blood flow restriction according to the same protocol. Ten repetitions per set were performed at 50% of 1RM with a 180-s rest period between sets. A relatively long rest period was set for arm exercises to diminish hormonal responses to exercise. Either the dominant or nondominant arm was randomly chosen to be trained (OCC-T, NOR-T) or to serve as a control (OCC-C, NOR-C). After the arm exercise, knee extension and knee flexion exercises were performed. In each exercise, one set with 30 repetitions was followed by two sets with 15 repetitions. The rest period between sets was 30 s. The intensity of the exercise was kept at 30% 1RM. The training load was determined according to the pretraining measurement of 1RM (see below) and was kept unchanged throughout the period of training. In OCC, the subjects performed the leg exercise with the proximal portions of both sides of their thighs compressed by specially designed elastic belts (width, 4 cm; length, 175 cm). According to the study by Takarada

et al (27), the occlusive pressure was set at 160 mm Hg during the first 2 wk, and increased by 20 mm Hg for every 2 wk. The compression was kept throughout the session of leg exercise and was released after the end of session. In NOR, the subjects performed the same leg exercise at the same relative intensity and volume without blood flow restriction. The training was performed twice a week and lasted for 10 wk.

**Measurements of muscular strength.** Maximal isometric torques of elbow flexor, knee extensor, and knee flexor muscles were measured, using a torque meter (VINE Medical Instruments, Tokyo, Japan). The output from the torque meter was amplified and stored with a data-acquisition system (Mac Lab/4S, AD Instruments, Colorado Springs, CO). Joint angle was set at 90° for elbow flexion, 80° for knee extension, and 50° for knee flexion. Three trials at maximal effort were made with a 90-s recovery period, and the highest value obtained was used for further analyses.

The 1RM tests were performed for dumbbell curl, knee extension, and knee flexion. The 1RM was determined by gradually increasing the weight until the subject could not lift the weight through a full range of motion using a strict form. The measurements were made before and after the 10-wk training period. On a separate day before the pretraining measurements, the subjects were familiarized with the measurement procedure. The posttraining measurements were made 5–7 d after the final training session, to exclude any impact of the last exercise. The subjects were refrained from ingesting alcohol and caffeine and from performing any strenuous exercise for 24 h before strength measurements.

Magnetic resonance imaging. Cross-sectional images of the right and left upper arms and right thighs were obtained by using a 0.3-T permanent magnet system (AIRIS mate, Hitachi Medical Corporation, Tokyo, Japan). The coil covered the whole upper arm and thigh, including markers attached to the skin. Spin-echo and multislice sequences were used with a repetition of 200 ms and an echo time of 20 ms. For each subject, the range of serial sections was deliberately determined on longitudinal images along the humerus and femur, to obtain sections of identical portions before and after the period of training. Among the photographs of the 15 cross-sectional images obtained, those of two portions near the midpoint of the upper arm and thigh were chosen, and their mean values were used for measurements of muscle cross-sectional area (CSA). On each cross-sectional image, an outline of biceps brachii, brachialis, quadriceps femoris, and hamstring were traced, and the traced images were transferred to a computer for calculation of the anatomic CSA using digitizing software (Scion Image, Scion Corporation, Frederick, MD). The measurements were repeated three times for each image, and their mean values were used. Deviations in these three sets of measurement were less than 2%. The images were obtained before and after the 10-wk training period. The posttraining measurement was made 5-7 d after the final training session.

TABLE 1. Isometric torque, 1RM, and cross-sectional area (CSA) of thigh muscles, measured before and after the training.

		000		NOR	
		Pre	Post	Pre	Post
Isometric torque (N·m)	Knee extensors	169.2 ± 15.2	186.9 ± 12.3*	156.1 ± 15.6	163.2 ± 18.6
	Knee flexors	$69.6 \pm 4.1$	81.5 ± 7.8*	72.6 ± 12.6	$74.7 \pm 13.3$
1RM (kg)	Knee extensors	$94.7 \pm 11.0$	113.2 ± 13.6*	84.2 ± 17.5	93.3 ± 16.1*
	Knee flexors	$43.1 \pm 5.1$	$51.0 \pm 3.8^{*}$	$41.5 \pm 6.6$	$45.4 \pm 7.3^{*}$
CSA (cm <sup>2</sup> )	Knee extensors	$82.8 \pm 10.6$	$86.4 \pm 9.2$	89.4 ± 11.4	88.2 ± 11.9
· ·	Knee flexors	$34.8\pm4.4$	$36.8\pm5.4^{\star}$	$32.4\pm3.5$	$32.5~\pm~3.3$

OCC, occlusive training group; NOR, normal training group.

Values are means  $\pm$  SD; N = 8 for OCC, N = 7 for NOR. \* Significantly different from pretraining (P < 0.05).

Blood sampling and analyses. In a separate set of experiments, acute changes in blood hormone concentrations after single exercise sessions were measured with 10 men. They were randomly assigned into the occlusive training group (OCC, N = 5) and the normal training group (NOR, N = 5). Mean age, height, and body mass were  $25.8 \pm 2.3$  yr,  $177.0 \pm 3.9$  cm, and  $82.6 \pm 18.4$  kg in OCC, and  $25.8 \pm 3.2$  yr,  $173.6 \pm 4.6$  cm, and  $72.7 \pm 6.3$  kg in NOR, respectively. The exercises for leg muscles were performed with a same regimen in the 10-wk training experiments. The occlusive pressure for OCC was 200 mm Hg (26). The subjects refrained from ingesting alcohol and caffeine for 24 h and from performing any strenuous exercise for 48 h before the experimental exercise session. Venous blood samples were taken from the antecubital vein in a seated position. A preexercise blood sample was obtained after 30 min of rest. The exercise session started 10 min after the resting blood sample was drawn. After the exercise sessions, the occlusive pressure was released and blood samples were obtained at 0 (immediately after the exercise), 15, and 30 min after the exercise. Blood samples were analyzed for GH, testosterone, and noradrenaline. All blood samples were processed and stored at -20° until analysis. Plasma concentrations of GH and testosterone were measured with standard radio immunoassay, and plasma concentrations of noradrenaline were measured with high-performance liquid chromatography (Institute for public health, Tokyo, Japan).



FIGURE 1—Isometric elbow flexion torque, measured before and after the training. Values are means and SD. \* Significantly different from pretraining (P < 0.05). OCC-T, trained arm of the occlusive training group; OCC-C, untrained arm of the occlusive training group; NOR-T, trained arm of the normal training group; NOR-C, untrained arm of the normal training group.

**Statistics.** All values are shown as means  $\pm$  SD. The arm muscle data were analyzed with a three-factor ANOVA (group  $\times$  arm  $\times$  time), with Fisher's protected least significant difference test. The leg muscle data were analyzed with a two-factor ANOVA (group  $\times$  time) with Fisher's protected least significant difference test. The hormonal data were analyzed with a two-factor ANOVA (group  $\times$  time) with Scheffe's *post hoc* analysis. The significance level was set at *P* < 0.05.

# RESULTS

Table 1 shows the changes in strength and CSA of the thigh muscles. Isometric knee extension and flexion torques increased significantly in OCC (P < 0.05), whereas no significant changes were observed in NOR. 1RM strengths of knee extension and flexion significantly increased in both OCC and NOR (P < 0.05). CSA of the knee flexor muscles significantly increased in OCC (P < 0.05).

After the 10-wk period of training, isometric elbow flexion torque increased significantly in OCC-T (P < 0.05), whereas no significant changes were observed in OCC-C, NOR-T, and NOR-C (Fig. 1). 1RM strength of the elbow flexor muscles increased significantly in both OCC-T and NOR-T (P < 0.05) (Fig. 2). The CSA of the elbow flexor muscles increased significantly only in OCC-T (P < 0.05) compared with its pretraining value (Fig. 3). When relative



FIGURE 2—1RM strength of elbow flexion, measured before and after the training. Values are means and SD. \* Significantly different from pretraining (P < 0.05). OCC-T, trained arm of the occlusive training group; OCC-C, untrained arm of the occlusive training group; NOR-T, trained arm of the normal training group; NOR-C, untrained arm of the normal training group.



FIGURE 3—Cross-sectional area (CSA) of elbow flexor muscles, measured before and after the training. Values are means and SD. \* Significantly different from pretraining (P < 0.05). OCC-T, trained arm of the occlusive training group; OCC-C, untrained arm of the occlusive training group; NOR-T, trained arm of the normal training group; NOR-C, untrained arm of the normal training group.

changes in CSA were compared between groups, the increase of the CSA in OCC-T was significantly larger than in the other groups (P < 0.05) (Fig. 4). Typical examples of cross-sectional magnetic resonance images of an identical portion of the upper arm are shown in Figure 5.

Figure 6 shows changes in plasma concentrations of GH, testosterone, and noradrenaline. GH concentration increased significantly at 15 min after the exercise in both groups compared with their resting concentrations (P < 0.05). However, no significant differences were observed for GH concentration at any time point or for the area under the GH concentration–time curve (AUC) between occlusive exercise and normal exercise groups. Testosterone concentration did not change significantly in either group. Postexercise noradrenaline concentration showed significant increases in both groups, and the increase was larger in the occlusive exercise group than in the normal exercise group (P < 0.05). When AUC for noradrenaline concentration was compared between groups, it was significantly higher in the occlusive exercise group ( $182.2 \pm 79.0$  nM for 30 min) than in



FIGURE 4—Percent changes in CSA of elbow flexor muscles, measured before and after the training. Values are means and SD. \* Significantly different from other groups (P < 0.05). OCC-T, trained arm of the occlusive training group; OCC-C, untrained arm of the occlusive training group; NOR-T, trained arm of the normal training group; NOR-C, untrained arm of the normal training group.





FIGURE 5—Typical magnetic resonance images showing transverse sections of the trained upper arm taken before (A) and after (B) the 10-wk training.

the normal exercise group (79.4  $\pm$  16.0 nM for 30 min) (P < 0.05).

# DISCUSSION

The main finding of the present study was that CSA and isometric torque of the trained arm muscles increased only when combined with resistance exercise with blood flow restriction for leg muscles. This result suggests that the exercise intensity used for arm muscles was not sufficient for inducing muscular hypertrophy, but a combination of the exercise stimulus and some factors associated with the resistance exercise with blood flow restriction caused muscular hypertrophy. This result is valuable in practical applications. Although direct application of the blood flow restriction is limited to extremities, it may indirectly enhance training effects on proximal muscles, which cannot be subjected to blood flow restriction, such as abdominal and back muscles.

One of the possible factors responsible for the muscle hypertrophy in OCC-T is an effect of systemic hormones. Resistance exercise with blood flow restriction has been shown to cause marked increases in plasma concentrations of GH and noradrenaline, possibly through a reflex against

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FIGURE 6—Changes in plasma concentrations of GH (*A*), testosterone (*B*), and noradrenaline (*C*) before and after the exercises with (**■**) and without occlusion ( $\Box$ ). \* Significantly different from preexercise (P < 0.05); # significantly different between groups (P < 0.05).

local accumulation of metabolic subproducts, such as lactate and proton (13,25,26,29). It has been reported that the increase in circulating anabolic hormones such as testosterone, GH, and/or insulin-like growth factor-I plays a role in exercise-induced muscular hypertrophy (1,6,13–15). For example, McCall et al. (15) have demonstrated that acute changes in plasma concentration of GH after exercise are positively correlated with the extent of muscular hypertrophy after the period of exercise training. However, the precise roles played by GH in exercise-

induced muscular hypertrophy are still controversial (22,30).

Compared with GH, testosterone is thought to have a consistent anabolic effect on skeletal muscle (4,10,14). It has been demonstrated that both endogenous (14) and exogenous (4,10) testosterone play a crucial role in muscular hypertrophy. However, few studies have conducted on the changes in endogenous testosterone after the resistance exercise with blood flow restriction.

Contrary to the prospected roles of GH and testosterone, the present study shows that only noradrenaline concentration after the exercise was significantly higher in OCC than in NOR. Although postexercise GH concentration tended to be higher in OCC than in NOR, the difference was not statistically significant (P = 0.12), probably because of the small number of subjects and large individual differences. Thus, the present results suggest that noradrenaline is likely related to the enhancement of muscle hypertrophy with occlusion, but that GH and testosterone are not. Although precise roles played by noradrenaline in exercise-induced muscular hypertrophy remain unclear, it has been demonstrated that several beta-adrenergic agonists have an anabolic effect on skeletal muscle (3,7,23). However, subjects for the hormonal measurements were different from those for the 10-wk training study, so the results obtained for hormonal measurements cannot be directly related to the results of training. In addition, systemic factors other than those measured in the present study may be involved in the present enhancement of muscle hypertrophy.

In OCC-C, no significant changes were observed in CSA and isometric torque of elbow flexor muscles. This suggests that circulating muscle hypertrophy–promoting factors, if any, do not cause hypertrophy in untrained muscle, and combinations of circulating factors and exercise stimulus are essential for muscular hypertrophy.

Although isometric torque and CSA of the arm and thigh muscles increased significantly only in OCC, 1RM strengths of dumbbell curl, knee extension, and knee flexion increased significantly in both OCC and NOR. These results may be attributable to training specificity (19). It is well known that the greatest training effects are detected when the same exercise mode is used for both testing and training (19). This phenomenon is thought be caused by neural adaptations such as increased taskdependent motor unit activation and/or decreased coactivation of the antagonist muscles. Moore et al. (16) have demonstrated that 8 wk of resistance training at 50% 1RM caused a significant increase in 1RM irrespective of blood flow restriction, whereas isometric torque increased only when blood flow restriction was combined.

## CONCLUSION

The present study shows that resistance exercise with blood flow restriction for leg muscles caused increases in

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the size and strength of arm muscles subjected to normal resistance exercise, the intensity of which was lower than that which would induce muscular hypertrophy. On the other hand, the occlusive exercise for leg muscles did not cause any changes in untrained arm muscle. It was suggested that any systemic factors released after the

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occlusive exercise may be involved in this cross-transfer effect, but local exercise stimulus, even at low intensity, is indispensable for muscular hypertrophy.

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