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Contralateral Effects by Unilateral Eccentric versus Concentric Resistance Training

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ABSTRACT

TSENG, W.-C., K. NOSAKA, K.-W. TSENG, T.-Y. CHOU, and T. C. CHEN. Contralateral Effects by Unilateral Eccentric versus Concentric Resistance Training. *Med. Sci. Sports Exerc.*, Vol. 52, No. 2, pp. 474–483, 2020. **Purpose:** Unilateral resistance training increases muscle strength of the contralateral homologous muscle by the cross-education effect. Muscle damage induced by second eccentric exercise bout is attenuated, even when it is performed by the contralateral limb. The present study compared the effects of unilateral eccentric training (ET) and concentric training (CT) of the elbow flexors (EF) on maximal voluntary isometric contraction (MVC) strength and muscle damage of the contralateral untrained EF. **Methods:** Young men were placed into ET, CT, ipsilateral repeated bout (IL-RB), and contralateral repeated bout (CL-RB) groups ($n = 12$ per group). The ET and CT groups performed unilateral EF training consisting of five sets of six eccentric and concentric contractions, respectively, once a week for 5 wk by increasing the intensity from 10% to 100% of MVC, followed by 30 maximal eccentric contractions (30MaxEC) of the opposite EF 1 wk later. The IL-RB group performed two bouts of 30MaxEC separated by 2 wk using the nondominant arm, and CL-RB group performed two bouts of 30MaxEC with a different arm for each bout in 1-wk apart. **Results:** The MVC increased ($P < 0.05$) greater for the trained (19% ± 8%) and untrained (11% ± 5%) arms in ET when compared with those in CT (10% ± 6%, 5% ± 2%). The magnitude of changes in muscle damage markers was reduced by 71% ± 19% after the second than the first bout for IL-RB group, and by 48% ± 21% for CL-RB group. Eccentric training and CT attenuated the magnitude by 58% ± 25% and 13% ± 13%, respectively, and the protective effect of ET was greater ($P < 0.05$) than CL-RB, but smaller ($P < 0.05$) than IL-RB. **Conclusions:** These results showed that cross-education effect was stronger for ET than CT, and progressive ET produced greater contralateral muscle damage protective effect than a single eccentric exercise bout. **Key Words:** CROSS-EDUCATION EFFECT, RESISTANCE TRAINING, CONTRALATERAL REPEATED BOUT EFFECT, MUSCLE STRENGTH, DELAYED ONSET MUSCLE SORENESS

Muscle strength increases not only for the trained muscle but also in the contralateral, nontrained homologous muscle after unilateral resistance training, which is known as the cross-education effect (1–3). Munn et al. (2) showed that the average magnitude of cross-education effect from the trained to nontrained limb muscle strength was 35% (95% confidence interval, 20.9%–49.3%). In a recent meta-analysis study of cross-education effect based on 96 studies, Green and Gabrial (4) reported that cross-education effect was present similarly between upper- and lower-limb muscles, and between sexes, and that the magnitude of increase in muscle strength of the nontrained limb was 18% in young adults, 17% in older adults, and 29% in patients with neuromuscular disorders. They also showed that the magnitude of the cross-education effect among nonclinical populations (the ratio between the nontrained and trained muscle strength gain) ranged from 48% to 77%. If such cross-education effect can be maximized, it could be used more effectively for rehabilitation, such as minimizing atrophy and strength loss of immobilized limb, and enhancing recovery from injury. It is not known how to maximize the cross-education effect, but it may be that muscle contraction types (i.e., isometric, concentric, eccentric) in resistance training affect the magnitude of the effect.

Kidgell et al. (5) compared unilateral eccentric and concentric strength training of the wrist flexors for their effects on the cross-education of muscle strength, corticospinal excitability, and inhibition using young men and women. After 12 training sessions over 4 wk, both groups exhibited a significant strength gain in the trained limb similarly (eccentric training [ET], 62%; concentric training [CT], 64%), but the extent of the

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cross-education effect was significantly greater for ET (47%) than CT (28%). They reported that the ET reduced intracortical inhibition (32%), silent period duration (15%–27%) and increased corticospinal excitability (51%) greater when compared with the CT (2%, 4%–8%, 13%, respectively). They concluded that ET uniquely modulated corticospinal excitability and inhibition of the untrained limb to a greater extent than CT. This needs to be confirmed for other muscles, such as the elbow flexors (EF). It is also interesting to examine if a small number of training sessions can still increase muscle strength of the contralateral untrained muscle. Then, the mechanisms underpinning the greater cross-education effect by eccentric than concentric contraction are yet to be clarified.

In relation to the cross-education effect of eccentric exercise, several studies have shown that the magnitude of muscle damage induced by eccentric exercise is reduced when the second exercise bout is performed by the contralateral homologous muscle, which is referred to as the contralateral repeated bout (CL-RB) effect (6–12). For example, Chen et al. (10) reported that the CL-RB effect was evident when the second bout of maximal eccentric exercise of the EF was performed by the opposite arm of the first bout at 1 d (changes in muscle damage markers were attenuated by 51% in average), 1 wk (48%) or 4 wk (26%), but not at 0.5, 6, or 12 h or at 8 wk. The CL-RB effect was also found for the knee extensors at 6 wk after the initial bout (13). However, no previous study has examined whether progressive unilateral ET confers greater protective effect on the contralateral muscle damage than a single bout of eccentric exercise, and whether progressive unilateral CT also provides any protective effect similar to that of the ET. It might be that some of the mechanisms underpinning the cross-education effect and the CL-RB effect are similar.

Therefore, the present study compared 1) ET and CT of one arm for changes in muscle strength and upper arm circumference (CIR) of the contralateral EF, and 2) four different conditions for the magnitude of muscle damage after maximal eccentric exercise of the EF; ET, CT, ipsilateral repeated bout (IL-RB) and CL-RB. Comparison between ET and CT conditions might provide an insight into the mechanisms underpinning the contralateral effect on the strength gain and muscle damage protection. Comparison between ET and CL-RB conditions could potentially clarify how much of the contralateral protective effect is associated with the strength gain. To the best of the authors' knowledge, no previous studies examined the cross-education effect and the CL-RB effect together. The working hypotheses were that 1) the ET would increase muscle strength and upper arm CIR of the nontrained arm greater when compared with the CT; and 2) the contralateral muscle protective effect conferred by ET would be greater than CL-RB and CT, but would be smaller than IL-RB condition.

METHODS

Participants and Study Design

A total of 48 young sedentary healthy men who had not performed any structured regular resistance, aerobic, or flexibility training in the past 1 yr, and who did not carry heavy objects frequently in their daily activities and had no musculoskeletal injuries of the upper extremities, were recruited for this study. They provided informed consent to participate in this study that had been approved by the Research Ethic Committee of National Taiwan Normal University, Taiwan. The study was conducted in conformity with the policy statement regarding the use of human subjects by the Declaration of Helsinki. Their mean (± SD) age, height, body mass, and maximal voluntary isometric contraction (MVC) torque of the EF were 23.2 ± 2.5 yr, 172.6 ± 4.6 cm, 69.4 ± 8.2 kg, and 48.9 ± 4.8 N·m, respectively.

The participants were placed into one of the four groups (n = 12 per group) by matching the baseline peak MVC torque among the groups; an IL-RB, a CL-RB, a progressive ET, and a progressive CT. The ET and CT groups performed unilateral EF training consisting of eccentric and concentric contractions, respectively once a week for 5 wk (five training sessions), in which the load was increased from 10%, 30%, 50%, 80%, and 100% of MVC strength, followed 1 wk later by five sets of six 30 maximal eccentric contractions (30MaxEC) of the opposite EF. IL-RB group performed two bouts of 30MaxEC separated by 2 wk using the nondominant arm, and CL-RB group performed the second bout of 30MaxEC with the opposite arm from that of the first bout at 1 wk later. The 2-wk interval between bouts for the IL-RB group was based on the previous studies (10,11). Because muscle damage markers do not return to the baseline in 7 d (14), we thought that it was better to set a longer interval (i.e., 2 wk) than a week between bouts for the IL-RB group to compare it with the CL-RB group. The choice of the dominant and nondominant arm for the training or for the first exercise bout was counterbalanced among the participants. No significant ($P > 0.05$) differences in age, height, body mass, and baseline MVC torque were observed among the groups.

The sample size was estimated using the data from a previous study (10) in which the contralateral and IL-RB effect were investigated for EF. Based on the effect size of 1 for a possible difference in MVC torque changes between the ipsilateral and contralateral conditions, it was estimated that at least 11 participants were necessary for each condition, with the alpha level of 0.05 and power ($1 - \beta$) of 0.80 by G*Power (G*Power 3.1.9.2, Heinrich-Heine-Universitat Dusseldorf, Dusseldorf, Germany; http://www.gpower.hhu.de/). Thus, considering possible dropouts and calculation error, 12 participants for each group, a total of 48 men were recruited.

Familiarization Session

A familiarization session was set at 3 d before the first exercise session. The participants experienced the muscle soreness (SOR) assessment and performed submaximal (10%, 30%, 50%) isometric contractions at the 90° of elbow flexion on an isokinetic dynamometer (Biodex System 3 Pro; Biodex Medical Systems, Shirley, NY). The investigator demonstrated the eccentric contractions, but no eccentric contractions of the EF were performed by the participants. For the CT group, the participants performed low-intensity (5%–10%) concentric contractions of EF using a dumbbell.

Progressive Training

To determine the dumbbell weight to be used for the progressive ET or CT, MVC strength of the unilateral EF was measured by a loadcell (model DFG51; Omega Engineering, Stamford, CT) that was attached to a cuff surrounding the wrist of the exercise arm. Each participant was seated on a custom-made preacher curl bench, placing the elbow joint angle at 90° and the shoulder joint angle at 45° flexion and 0° abduction. The participant was instructed to flex the elbow joint maximally for 3 s, and this was repeated three times with a 45-s rest between attempts. The peak value was defined as the highest value during the 3-s contraction, and the highest value of the three peak values was used to determine the dumbbell weight (15,16).

For the ET group, each training session consisted of five sets of six eccentric contractions, in which the participants were instructed to lower a dumbbell from an elbow flexed (90°) to a fully extended position (0°) in 3 s, and the investigator removed the dumbbell at the extended position, and the arm was returned to the start position without load. The interval was 15 s between contractions, and 2 min between sets. These were also the case for the participants in the CT group, except for the type of muscle contractions performed in the training (concentric instead of eccentric contractions), and the starting angle was not a fully extended but slightly flexed angle (≈10°) to avoid a possible eccentric contraction at long muscle lengths. After each concentric contraction, the arm was returned to the start position without load, and the investigator spotted a participant if he showed difficulty at long muscle lengths at 80% and 100% MVC loads during weeks 4 and 5. All participants performed five sets of six concentric contractions from the elbow extended to the flexed position (90°) in 3 s. The load for each exercise was increased from 10%, 30%, 50%, 80%, and 100% of MVC strength, which was reassessed at each week.

Maximal Eccentric Exercise

All participants performed at least a bout of five sets of six 30MaxEC with a dumbbell corresponding to the MVC strength. The participants in the ET and CT groups used the opposite arm of the trained arm to perform 30MaxEC. The participants in the CL-RB and IL-RB groups performed two bouts of 30MaxEC as explained previously. Each participant was instructed to lower a dumbbell from an elbow flexed (90°) to an elbow fully extended position (0°) in 3 s, and the investigator removed the dumbbell at the extended position, and the arm was returned to the start position without load. Each contraction lasted for 3 s and was repeated every 15 -s, and a 2-min rest was given between sets (16,17).

Dependent Variables

The dependent variables consisted of MVC torque, range of motion (ROM), upper arm CIR, SOR, and plasma creatine kinase (CK) activity. All variables except for blood samples were taken from both arms. The MVC and ROM measures were taken before; immediately after; and 1, 2, and 3 d after the first to fourth training sessions (10%–80%) for ET and CT groups. Circumference and SOR were measured before, and 1, 2, and 3 d after the first to fourth sessions. Plasma CK activity was measured before and 3 d after the first to four sessions. All variables were measured before, immediately after (except for CIR, SOR, and CK), and 1 to 5 d after the last (fifth) training session for the ET and CT groups. All measures were taken before, immediately after (except for CIR, SOR, and plasma CK activity) and 1 to 5 d after the maximal eccentric exercise (30MaxEC) for all groups.

The test–retest reliability based on intraclass correlation coefficient (R) and coefficients of variation were 0.84% and 9.9% for MVC, 0.99% and 3.0% for ROM, 0.99% and 9.3% for CIR, 1.00% and 0% for SOR, and 0.77% and 9.7% for plasma CK activity.

MVC torque. The participant's trunk was stabilized by a pelvic strap and two shoulder straps to minimize the involvement of other body parts. The shoulder joint angle was set at 45° (0.79 rad) flexion with 0° abduction, the forearm supinated, and the hand grasped on an attachment connected to the level arm of the isokinetic dynamometer. The MVC torque was measured at 90° (1.57 rad) elbow flexion, where the full elbow extension angle was considered as 0° (0 rad) using the dynamometer. Participants were verbally encouraged to generate maximal force for 3 s, with a 45-s rest, and this was repeated three times. The peak value during the 3-s contraction was recorded, and the highest value of the three peak values was used for further analysis (17–19).

ROM. The ROM of the elbow joint was determined as the difference between the elbow joint angles of maximal voluntarily flexion and extension measured by a manual goniometer (10,20). Three measurements were taken for each angle, and the mean of the three measurements was used to calculate ROM (10,20).

Upper arm CIR. While each participant was standing, relaxing, and letting the arm hang down by his side, the upper arm CIR was measured at the midportion of the upper arm, between the acromion process of the clavicle to the lateral epicondyle of the humerus, using a Gulick tape measure (Creative Health Products, Plymouth, MI). The measurements were taken three times by the same examiner, and the mean of the three measures was used for statistical analysis (10).

SOR. Muscle soreness of the EF was quantified using a visual analog scale (VAS) that had a 100-mm continuous line with "not sore at all" on one side (0 mm) and "very, very sore" on the other side (100 mm). The investigator asked the participant to rate his perceived soreness on the VAS when the muscles were passively extended for the ROM (120°–0° of elbow flexion angles) measures (10).

Plasma CK activity. Approximately 5 mL of venous blood was withdrawn by a standard venipuncture technique from the cubital fossa region of the arm and centrifuged for 10 min to extract plasma, and plasma samples were stored at −80°C until analyses. Plasma CK activity was assayed spectrophotometrically by an automated clinical chemistry analyzer (Model 7080; Hitachi, Co. Ltd., Tokyo, Japan) using a commercially available test kit (10,21).

Index of Protection

The index was based on the comparison to the changes after the first bout of the IL-RB and CL-RB groups (average of the two groups; control condition [CON]). It should be noted that the index was based on the groups not individuals, and the magnitude of the repeated bout effect was calculated by comparing the changes in the variables after 30MaxEC among the four groups with those of the control condition. The formula was modified from that of the previous study (10); [change in the control condition − change in each group]/change in the control condition × 100%. The change in the formula was the magnitude of the decrease from the baseline at 1 d postexercise for MVC and ROM, maximal change from the baseline for CIR, SOR, and plasma CK activity.

Statistical Analyses

All dependent variables before the maximal eccentric exercise (the first and second 30MaxEC for IL-RB and CL-RB, 30MaxEC of nontrained EF for ET and CT) were compared among the groups by a one-way ANOVA. Changes in MVC torque, ROM, and CIR after the 5-wk progressive resistance training from the baseline were assessed by a pair *t* test for the ET and CT groups separately. Changes in all dependent variables after 30MaxEC were also compared between the ET and CT groups by a mixed-design of two-way ANOVA. Because the changes in each variable after the first MaxEC were similar between the IL-RB and CL-RB groups, the average of the two groups was considered as the control condition (CON). Changes in the dependent variables over time after 30MaxEC for the ET and CT groups, the second bout of the IL-RB and CL-RB groups, and the control condition were compared by a mixed design of two-way ANOVA. When the ANOVA found a significant interaction effect, a Tukey's *post hoc* test was performed. The average values of index of protection for MVC, ROM, CIR, SOR, and plasma CK activity were compared among the ET, CT, IL-RB, CL-RB groups by one-way ANOVA, followed by a Tukey's *post hoc* test. Eta-squared values (η^2) were calculated as measures of effect size when necessary, and they were considered that a value of ~0.02 is a small effect; ~0.13, a medium effect; and >0.26, a large effect (22). A significant level was set at $P \leq 0.05$. The data were presented as mean ± SD, unless otherwise stated.

RESULTS

Baseline measurements. No significant differences ($P > 0.05$) in the baseline values of any of the dependent variables were found before the progressive ET and CT for the ET and CT groups, and before the maximal eccentric exercise for the CL-RB and IL-RB groups. However, when comparing the four (CL-RB, IL-RB, ET, CT) groups for the dependent variables of the arm used for 30MaxEC (the second MaxEC of the CL-RB and IL-RB groups, nontrained arm of the ET and CT groups), significant differences were found for MVC and CIR. The ET and CT groups showed greater ($P < 0.05$) MVC and CIR when compared with the CL-RB and IL-RB groups due to the training effects as described below, and the MVC and CIR were greater ($P < 0.05$) for the ET than CT group.

Changes in the variables during resistance training sessions. Figure 1 shows changes in the dependent variables before and 3 or 5 d after each training session for the ET and CT groups. Significant ($P < 0.05$) changes in MVC torque, ROM, SOR, and CK activity were seen for the ET group, especially after the third to fifth training sessions. In contrast, the CT group showed significant ($P < 0.05$) changes only for MVC torque and ROM, and these changes were observed only at immediately postexercise.

Changes in MVC torque and CIR of the trained and nontrained arms before and after 5 wk of ET and CT are shown in Figure 2. The MVC torque increased ($P < 0.05$) greater for the trained (19% ± 8%) and nontrained (11% ± 5%) arms of ET, when compared with CT (10% ± 6%, 5% ± 2%). When comparing the arms, the magnitude of the increase was greater ($P < 0.05$) for the trained than the nontrained arm for both groups. The ratio for the magnitude of increase in MVC between the trained and nontrained arm was 0.6 ± 0.6 for the ET and 0.5 ± 0.4 for the CT, without a significant difference between the groups ($P = 0.363$). A significant ($P < 0.05$) increase in CIR was found only for the trained arm of both the ET (3% ± 1%) and CT (2% ± 1%) groups.

Changes in the dependent variables after the first bout of 30MaxEC for the CL-RB and IL-RB groups. As shown in Table 1, all dependent variables changed significantly over time ($P < 0.05$) after the first bout of 30MaxEC without significant differences between the IL-RB and CL-RB groups (MVC: $P = 0.913$, $\eta^2 = 0.030$; ROM: $P = 0.601$, $\eta^2 = 0.065$; CIR: $P = 0.937$, $\eta^2 = 0.026$; SOR: $P = 0.200$, $\eta^2 = 0.121$; plasma CK activity: $P = 0.968$, $\eta^2 = 0.016$). Thus, the average values of the two groups were considered to be the "control" condition that represents normal changes in the dependent variables after 30MaxEC (Figs. 3–4).

Comparison in muscle damage between ET, CT, CL-RB, and IL-RB groups after 30MaxEC. When compared with the changes in the variables after the first bout of 30MaxEC performed by the CL-RB and IL-RB groups, the changes were significantly smaller for the second 30MaxEC of the IL-RB group (interaction effect: MVC, $P < 0.001$; $\eta^2 = 0.619$; ROM, $P < 0.001$; $\eta^2 = 0.654$; CIR, $P < 0.001$; $\eta^2 = 0.745$) as well as the CL-RB group (MVC, $P < 0.001$; $\eta^2 = 0.272$; ROM, $P = 0.001$; $\eta^2 = 0.271$; CIR, $P < 0.001$; $\eta^2 = 0.590$), and ET group (MVC: $P < 0.001$, $\eta^2 = 0.451$, ROM: $P < 0.001$, $\eta^2 = 0.433$, CIR: $P < 0.001$, $\eta^2 = 0.732$) as shown in Figure 3. However, no such effects were found between the CT group and control condition for MVC ($P = 0.979$, $\eta^2 = 0.009$) and ROM ($P = 0.315$, $\eta^2 = 0.099$), but CIR ($P < 0.001$, $\eta^2 = 0.251$) showed smaller changes for the CT group than control condition. When comparing the IL-RB, CL-RB, and ET groups, changes in MVC ($\eta^2 = 0.297$), ROM

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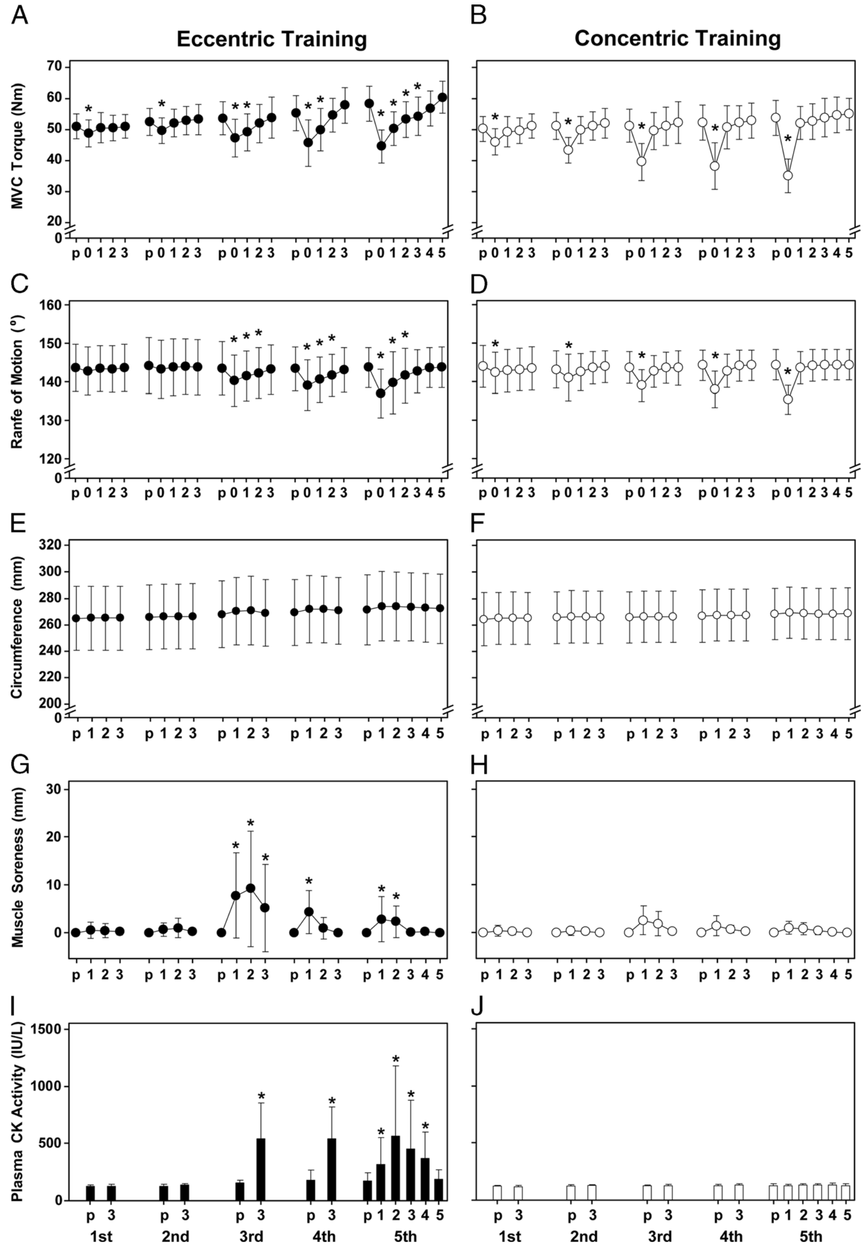

FIGURE 1—Changes (mean ± SD) in MVC torque (A, B), ROM (C, D), upper arm CIR (E, F), SOR (G, H), and plasma CK (I, J) activity before (p), immediately after (0) and 1–3 (1–3) or 1 to 5 d (1–5) after the 1st (10%), 2nd (30%), 3rd (50%), 4th (80%), and 5th (100%) training sessions in the unilateral ET group (left) and CT group (right). * indicates a significant difference ($P < 0.05$) from the prevalue.

($\eta^2 = 0.490$) and CIR ($\eta^2 = 0.170$) for IL-RB group was smaller ($P < 0.001$) than those of the CL-RB group, and changes in MVC ($P = 0.011$, $\eta^2 = 0.117$) and ROM ($P = 0.003$, $\eta^2 = 0.251$) for the ET group were greater than those of the IL-RB group without significant difference in CIR ($P = 0.200$, $\eta^2 = 0.062$) between the ET and IL-RB groups. Changes in MVC ($P = 0.033$, $\eta^2 = 0.097$) and CIR ($P = 0.003$, $\eta^2 = 0.140$) were smaller for the ET group when compared with the CL-RB group, but no differences ($P > 0.05$) in ROM ($\eta^2 = 0.133$) and SOR ($\eta^2 = 0.031$) were evident between ET and CL-RB groups (Fig. 3).

Changes in SOR and plasma CK activity after 30MaxEC are shown in Figure 4. When compared with the changes in the control condition, SOR developed less for the IL-RB ($P < 0.001$, $\eta^2 = 0.655$), CL-RB ($P < 0.001$, $\eta^2 = 0.424$), ET ($P < 0.001$, $\eta^2 = 0.620$) and CT ($P < 0.001$, $\eta^2 = 0.348$) groups, and no significant difference was evident between the IL-RB, CL-RB, and ET groups (IL-RB vs CL-RB: $P = 0.067$, $\eta^2 = 0.088$, IL-RB vs ET: $P = 0.237$, $\eta^2 = 0.059$, CL-RB and ET: $P = 0.628$, $\eta^2 = 0.031$), and these groups showed less (all: $P < 0.001$) SOR than CT group (IL-RB vs CT: $\eta^2 = 0.541$, CL-RB vs CT: $\eta^2 = 0.224$, ET vs CT: $\eta^2 = 0.470$). Regarding plasma CK activity, the increases after 30MaxEC were significantly smaller for the IL-RB ($P < 0.001$, $\eta^2 = 0.767$), CL-RB ($P < 0.001$, $\eta^2 = 0.552$) and ET ($P < 0.001$, $\eta^2 = 0.651$) groups when compared with the control condition, but no significant difference was evident between CT group and control condition

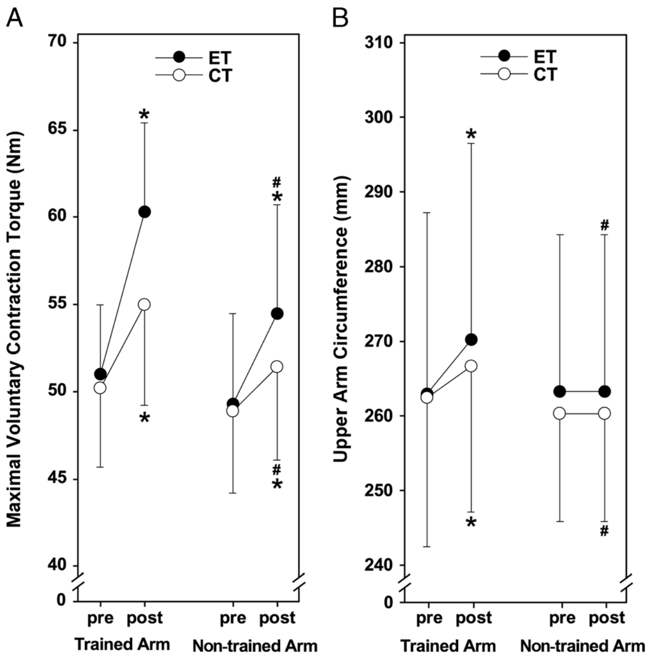

FIGURE 2—MVC torque (A) and upper arm CIR (B) from the baseline (pre) to 5 d after the fifth training session of the 5-wk progressive unilateral ET or CT for the trained and nontrained EF (mean ± SD). *Significant difference ($P < 0.05$) from the prevalue; #Significant ($P < 0.05$) difference from the trained arm.

($P = 0.143$, $\eta^2 = 0.071$). When comparing the IL-RB, CL-RB, and ET groups, changes in CK ($P = 0.045$, $\eta^2 = 0.097$) for the ET group were greater than those of the IL-RB group, and the ET ($P = 0.031$, $\eta^2 = 0.104$) and IL-RB groups ($P < 0.001$, $\eta^2 = 0.336$) showed smaller increases than the CL-RB group.

Magnitude of the protective effect. Figure 5 compares the magnitude of the protective effect for each variable, and the average of the five variables (MVC, ROM, CIR, SOR, and plasma CK activity). The magnitude of the protection is different among the variables, and among the groups. For the average values, the ET (58% ± 25%; $P = 0.026$), CL-RB (48% ± 21%; $P = 0.004$), and CT (13% ± 13%; $P = 0.001$) groups demonstrated less protection than that of the IL-RB group (71% ± 19%). When comparing the three contralateral effect groups (CL-RB, ET, and CT), the effect was smaller for the CL-RB ($P = 0.015$) and CT ($P = 0.004$) groups than the ET group, and the CT group was also smaller ($P = 0.002$) than the CL-RB group.

DISCUSSION

The present study tested the hypotheses that 1) the magnitude of increases in muscle strength and upper arm CIR of the nontrained arm would be greater after eccentric than CT; and 2) the contralateral muscle damage protective effect conferred by the progressive ET would be greater than that by the progressive CT and one bout of maximal eccentric exercise, but would be smaller than the protective effect shown by the repeated bout of the same arm. The results were in line with the first hypothesis, but the ratio in the strength gain between the trained and nontrained arms was not different between the two training protocols. The second hypothesis was also supported by the results, which is best demonstrated in Figure 5, showing that the magnitude of the protective effect was 71% for the IL-RB group, 58% for the ET group, 48% for the CL-RB group, and only 13% for the CT group.

Comparison between ET and CT. As shown in Figure 1, decreases in MVC torque and ROM were observed only at immediately after concentric exercise, although the acute changes became larger with increasing in the intensity from 10% to 100% of MVC strength, suggesting no muscle damage was induced by CT. It is known that concentric exercise does not induce muscle damage, and acute changes in muscle function observed immediately postexercise are probably due to neuromuscular fatigue (23–25). In contrast, significant decreases in MVC torque and ROM lasting more than 1 d postexercise, and increases in SOR and plasma CK activity were observed after eccentric exercise, especially after the third to fifth training sessions. These suggest that the higher-intensity (>50% of MVC) eccentric exercise induced muscle damage, but the magnitude of muscle damage was not large, when compared with typical changes in these markers of muscle damage after maximal eccentric exercise of the EF reported in previous studies (10,12,26). For example, after maximal eccentric exercise of the EF, without any preceding eccentric exercises, MVC torque is still >20% lower than the baseline at 5 d postexercise, plasma CK activity increases above 5000 $IU \cdot L^{-1}$, and peak SOR exceeds 50-mm in the 100-mm VAS (10). It should be noted that the intensity of eccentric exercise even at 100%

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TABLE 1. Changes (mean ± SD) in MVC torque of the EF, ROM, upper arm CIR, SOR, and plasma CK activity before (pre), immediately after (post) and 1–5 d after the first eccentric exercise bout of the IL-RB and CL-RB groups.

		Pre	Post	1 d	2 d	3 d	4 d	5 d
MVC (N·m)	IL	50.0 ± 4.8	33.4 ± 3.6	34.5 ± 3.2	35.5 ± 3.7	37.1 ± 3.9	39.0 ± 4.4	40.4 ± 4.7
	CL	48.2 ± 4.0	31.2 ± 3.9	33.3 ± 2.6	34.3 ± 2.3	35.5 ± 2.3	37.2 ± 2.0	39.2 ± 1.9
ROM (°)	IL	147.2 ± 5.2	133.9 ± 5.1	133.5 ± 7.2	134.4 ± 8.1	135.2 ± 9.4	136.7 ± 9.2	137.4 ± 9.3
	CL	145.4 ± 5.9	130.7 ± 6.9	132.3 ± 5.9	134.4 ± 6.7	135.0 ± 6.8	135.9 ± 6.0	138.1 ± 5.6
CIR (mm)	IL	261.0 ± 26.0	—	265.4 ± 25.5	267.2 ± 25.5	268.8 ± 25.3	270.4 ± 25.2	272.0 ± 25.4
	CL	259.9 ± 27.5	—	264.3 ± 29.0	265.9 ± 28.0	268.0 ± 28.9	269.5 ± 29.6	270.9 ± 29.0
SOR (mm)	IL	0.0 ± 0.0	—	45.0 ± 26.4	63.5 ± 16.1	56.5 ± 16.8	39.3 ± 20.9	27.9 ± 15.5
	CL	0.0 ± 0.0	—	32.1 ± 20.0	51.3 ± 19.1	44.1 ± 18.3	27.6 ± 13.0	14.0 ± 9.6
CK ($IU \cdot L^{-1}$)	IL	118.1 ± 11.8	—	370.8 ± 205.1	1230.7 ± 603.9	3217.2 ± 2255.6	5984.8 ± 3965.8	6047.4 ± 4285.7
	CL	127.0 ± 9.8	—	216.2 ± 96.9	1029.3 ± 375.6	2790.8 ± 1263.6	5404.4 ± 1416.7	6266.3 ± 2131.7

Note: No significant differences ($P > 0.05$) between IL and CL groups for changes in any variables over time.
1d-5d, 1 to 5 d.

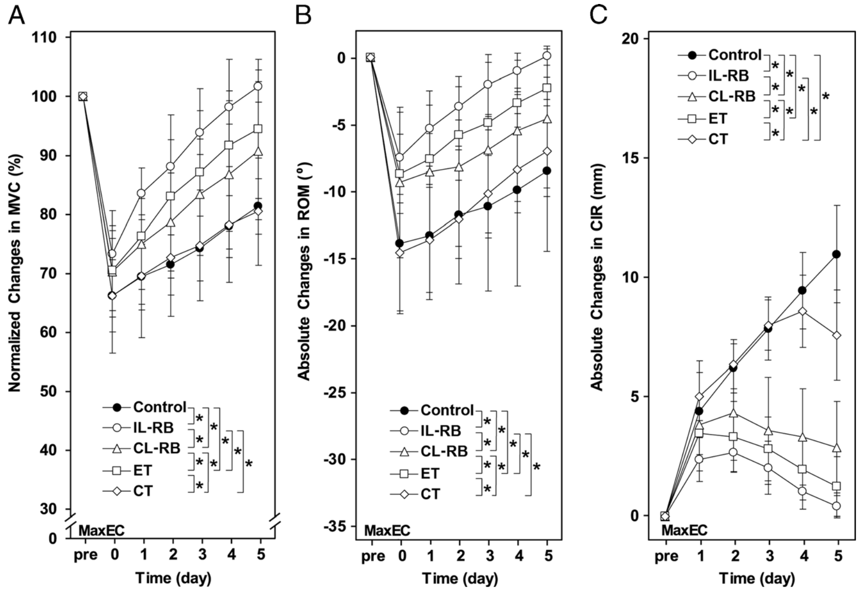

FIGURE 3—Normalized changes (mean ± SD) in MVC torque (A) torque, ROM (B) and upper arm CIR (C) from the baseline (pre) at immediately (0), and 1, 2, 3, 4, and 5 d after maximal eccentric exercise of the EF for the control condition (average of the first bout of IL-RB and CL-RB groups), the second bout the IL-RB and CL-RB groups, and the bout of the progressive ET and CT groups. *Significant ($P < 0.05$) interaction effect by a mixed-design of two-way ANOVA for the corresponding two groups.

was still submaximal, because the intensity was based on maximal isometric contraction strength which was assumed to be lower than maximal eccentric contraction strength, and the absolute intensity was the same between eccentric and concentric exercises in the present study. Chen et al. (27) reported that the magnitude of muscle damage induced by eccentric exercise of the knee extensors was minor, when the intensity of eccentric contractions was progressively increased. This was also the case for the EF as shown in the present study (Fig. 1). However, it is important to note that muscle damage was not completely eliminated in the ET with progressively increased intensity.

The MVC torque increased greater for the trained (19% ± 8%) and nontrained (11% ± 5%) arms after ET when compared with CT (10% ± 6% and 5% ± 2%, respectively), and the magnitude of the increase was greater for the trained than the nontrained arm for both training modalities (Fig. 2A). The greater increase in MVC strength after ET than CT has been reported in previous studies (1,5). For example, Hortobagyi et al. (1) reported that MVC strength increased greater after unilateral maximal isokinetic ($60°\cdot s^{-1}$) knee extensors ET (trained limb: 45%, nontrained limb: 39%) than CT (36%, 22%) training performed 3 d a week for 12 wk. The magnitude of increase in MVC strength found in the present study appears to be smaller when compared with that of the previous studies (1,5). This may be due to the shorter training period and less number of training sessions in the present study. It is possible that the repeated strength measures of the trained arm contributed to the increases in the strength, but it is important to note that the number of the measures was the same between ET and CT groups. It seems that the training protocol used in the present study was very efficient, considering that only five training sessions produced approximately 20% (ET) or 10% (CT) MVC strength increase.

It was found that not only the trained arm but also the nontrained arm showed an increase in strength (Fig. 2A). It has been demonstrated in the review articles that the magnitude of increase in muscle strength of the nontrained muscle is about one thirds (2) or more than 48% of that of the trained

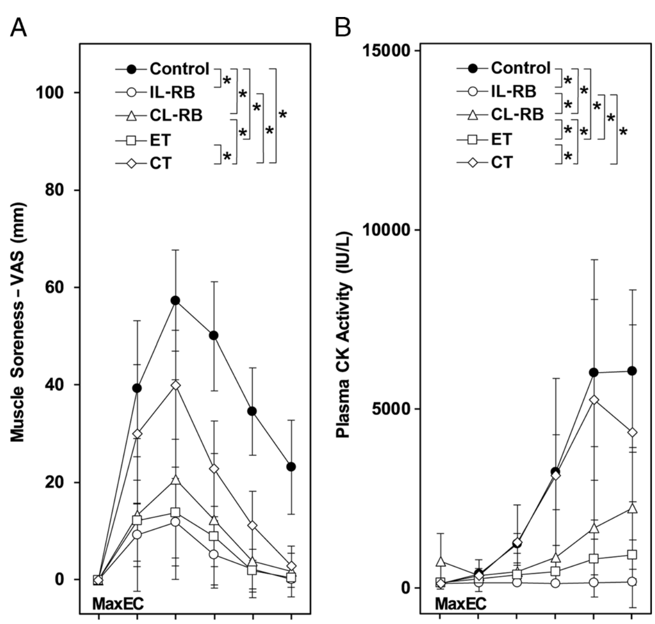

FIGURE 4—Changes (mean ± SD) in SOR (A) and plasma CK (B) activity before (pre), and 1, 2, 3, 4, and 5 d after maximal eccentric exercise of the EF for the control condition (average of the first bout of IL-RB and CL-RB groups), the second bout the IL-RB) and CL-RB groups, and the bout of progressive ET and CT groups. *Significant ($P < 0.05$) interaction effect by a mixed-design of two-way ANOVA for the corresponding two groups.

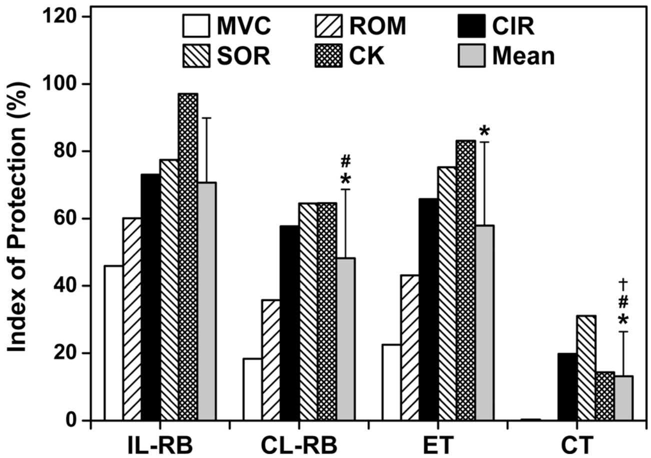

FIGURE 5—Index of protective effect of MVC torque of the EF, ROM, upper arm CIR, SOR, plasma CK activity, and the average, and standard deviation of the five variables (mean) for the ipsilateral repeated bout (IL-RB), CL-RB, progressive ET and CT groups. The index was based on the comparison to the changes after the first bout of the IL-RB and CL-RB groups (average of the two groups: control condition). The formula was modified from that of the previous study (10); [Change in the control condition − Change in each group]/[Change in the control condition × 100%]. The "Change" in the formula refers to the magnitude of the decrease from the baseline at 1 d postexercise for MVC and ROM, maximal change from the baseline for CIR, SOR, and CK. *Significant ($P < 0.05$) difference from IL-RB; #Significant ($P < 0.05$) difference from ET; †Significant ($P < 0.05$) difference from CL-RB.

muscle (4). It should be noted that the training was not necessarily performed eccentrically in the studies included in the review papers (2,4). However, in the present study, the magnitude of increase in the MVC torque of the nontrained arm was approximately 50% of that of the trained arm for both ET and CT groups. Kidgell et al. (5) reported that unilateral resistance training of the wrist flexors performed three times a week for 4 wk with 80% of one repetition maximum concentric strength load resulted in MVC strength increase of 64% for the trained arm, and 28% for the nontrained arm after CT, but 62% and 47%, respectively, after ET. Hortobagyi et al. (1) also reported relatively greater increase in MVC strength in the nontrained leg after ET (87%) than CT (61%). In the present study, when comparing the magnitude of increase in MVC torque between the trained and nontrained arms, no significant difference was found between the ET and CT groups (both was about 50%). Further studies are warranted to examine whether the magnitude of the cross-education effect is different between ET and CT, and it should be investigated further whether the cross-education effect of ET is different between upper- and lower-limb muscles, between males and females, and among different populations (e.g., older adults, clinical populations).

Comparison in muscle damage after 30MaxEC between four conditions. The changes in the muscle damage markers after the first 30MaxEC bout of the IL-RB and CL-RB groups (Table 1) were similar to those reported in previous studies in which a similar 30MaxEC of the unilateral EF was performed by sedentary individuals (10,11). Thus, it seems likely that the responses to the 30MaxEC shown in Table 1 represent typical changes in the dependent variables after the initial bout of 30MaxEC in control condition. If there was no repeated bout effect, the changes in the variables after the second 30MaxEC bout in the IL-RB and CL-RB groups, and the 30MaxEC in the ET and CT groups should have been similar to those shown in Table 1. However, the changes after the second 30MaxEC for the CL-RB group and the 30MaxEC for the ET group (Figs. 3 and 4) were significantly smaller than those shown in Table 1. This was most likely due to the protective effect conferred to the contralateral, nonexercised or nontrained arm.

The new findings of the current study were that the 5-wk unilateral EF ET attenuated muscle damage after 30MaxEC performed by the contralateral arm greater than one bout of 30MaxEC did on the opposite arm, and the CT did not provide such an effect (Figs. 3 and 4). As shown in Figure 5, the magnitude of the protective effect of the ET group (average: 58%) was significantly smaller than that of the IL-RB group (71%), but was greater than that of the CL-RB (48%) group. It should be noted that the interval between the two 30MaxEC bouts for the IL-RB group was longer (2 wk) than that of other groups (1 wk). Thus, it might be that the protective effect could have been greater for the IL-RB group, if the second 30MaxEC bout had been performed 1 wk later. When comparing the CL-RB and ET groups, it appears that the contralateral protective effect was enhanced by the progressive ET. It is interesting that the magnitude difference of the protective effect was smaller between IL-RB and ET groups than between IL-RB and CL-RB groups. It may be that the contralateral protective effect becomes comparable to the ipsilateral protective effect, if the number of the ET sessions (i.e., training period) increases. However, this does not necessarily mean that the mechanisms underpinning the IL-RB and CL-RB effect are the same.

Regarding the CT, it has been shown that CT does not attenuate muscle damage induced by eccentric contractions even for the trained muscle (28,29). Vissing et al. (30) reported that no protective effect against muscle damage of knee extensors was conferred by a bout of concentric exercise of the same muscle. The present study showed that no protective effect against eccentric contraction-induced muscle damage was induced in the contralateral arm after progressive CT that resulted in 5% increase in MVC strength of the contralateral arm. It seems unlikely that the muscle damage protective effect is produced by CT, although the CT produced the cross-education effect. The extent of ipsilateral protective effect conferred by eccentric exercise was associated with the magnitude of muscle damage induced by the initial bout (17). This may explain why the CT, which did not induce any indication of muscle damage, did not produce any protective effect. It is important to note that the muscle damage was minimum in the ET as represented by minor delayed onset muscle soreness, small decreases in strength, and small increases in plasma CK activity (Figs. 3–4), which were much less than those after the first bout of 30MaxEC. However, the magnitude of the protective effect in the ET group was greater than that of the CL-RB group (Fig. 5). Thus, it does not appear that the magnitude of the muscle damage is a key factor determining the magnitude of the muscle damage protective effect for contralateral limb induced by eccentric exercise.

Regarding the mechanisms underpinning the repeated bout or protective effect on muscle damage, Hyldahl et al. (31) described a combination of neural adaptations (i.e., shift in motor unit recruitment, increased α-motorneuron excitability, increased inhibitory feedback), muscle–tendon complex adaptations (i.e., reduced fascicle elongation, increased tendon compliance, smaller displacement of myotendinous junction), extracellular matrix (ECM) remodeling (i.e., initial ECM deadhesion, delayed ECM adhesion, and collagen expression), and modified inflammation response (i.e., attenuated inflammatory signaling in the contralateral homologous muscle). Hody et al. (32) showed that muscle proteome modifications could be linked to a decrease in anaerobic catabolism and a possible isoform shift toward a more resilient, slower-contracting phenotype of trained muscle, after five sessions of submaximal isokinetic eccentric contractions (50%, 60%, 70%, 80%, and 90%) of the knee extensors with 2 to 3 d between sessions. However, it seems likely that the CL-RB effect is more associated with the neural and inflammatory response adaptations than the adaptations at muscle-tendon complex, muscle fibers, and ECM levels, although the possibility of muscle fiber and ECM changes in the nonexercised muscle in response to eccentric exercise cannot be completely ruled out. As for the neural adaptations underpinning the CL-RB effect, it is possible that the shift in motor unit recruitment (7,33,34), increased α-motorneuron excitability (35), and increased inhibitory feedback (5,35) could be induced to the contralateral limb. Kidgell et al. (5) observed that ET modulated the corticospinal excitability and inhibition of the untrained limb to a greater extent than CT. In the present study, the unilateral progressive CT did not induce any protective effect on the contralateral limb (Figs. 3 and 4), although it increased MVC strength of the contralateral arm (Fig. 1). Thus, it does not appear that the cross-education effect mechanisms are the same as the contralateral muscle damage protective mechanisms.

For the inflammatory responses, it seems reasonable to speculate that modified inflammatory responses play a role in the CL-RB effect, but it should be clarified whether the effect is specific to the homologous muscle or systemic (the effect extends to other muscles). It should be investigated further if a unilateral EF eccentric exercise could attenuate muscle damage of elbow extensor or knee extensor muscles of the ipsilateral or contralateral limb. It is known that skeletal muscles produce many different kinds of cytokines (myokines) in response to exercise (36,37). It seems possible that myokines are involved in the CL-RB effect. If so, it may be that myokines are produced greater after eccentric than concentric contractions. If the contralateral muscle damage protective effect is limited to homologous muscle, it is not known how myokines affect the homologous muscle specifically. Interestingly, Xin et al. (9) showed that an increase in inflammatory-related transcription factor nuclear factor kappa–light-chain-enhancer of activated B cells (NF-κB) after the second bout was significantly attenuated not only in the vastus lateralis that was used in the maximal eccentric contractions of the ipsilateral knee extensors (123% ± 3%) but also in the opposite leg that was not used in the exercise (109% ± 3%). The NF-κB is an effector of an upstream mechanistic pathway that could be transferred to the nonexercising muscles (9). The present study showed that the progressive ET with minor muscle damage conferred much greater contralateral muscle damage protective effect than a bout of maximal eccentric exercise that resulted in greater muscle damage.

Hody et al. (38) have articulated beneficial effects and multiple applications of eccentric exercise training and stated that more efforts should be devoted to develop intensity, duration, and modes of ET optimizing efficiency of this method. The findings of the current study provide some practical implications for rehabilitation areas. It should be noted that CT does not provide any protective effect on potential muscle damage after eccentric exercise. Thus, rehabilitation protocols should include eccentric muscle actions, but to minimize muscle damage, the intensity of eccentric contractions should be increased gradually from low-intensity over session. It is clear that training of one limb can affect the nontrained limb (1,4,5), and the magnitude of muscle damage induced by eccentric contractions is attenuated by eccentric exercise of the opposite limb, just like the well-known cross-education effect. Hence, if one of the limbs is not utilized for a while (e.g., broken bone of a limb), it is recommended that before retraining of the injured limb, a progressive ET can be given to the opposite limb to minimize muscle damage when the injured muscle performs eccentric contractions. It is also important to note that ET of a noninjured limb could potentially attenuate muscle strength loss of the injured limb better than CT. Eccentric training appears to be beneficial for rehabilitation in many ways. More studies are warranted to investigate the effects of ET on rehabilitation.

In conclusion, the present study demonstrated that minor muscle damage was induced after the third to fifth ET sessions when the intensity was higher, and the progressive ET produced greater increases in muscle strength not only for the trained arm but also the nontrained arm. The magnitude of muscle damage of the nontrained arm was reduced by more than 50% by the progressive ET, and this effect was greater than the CL-RB effect conferred by one bout of maximal eccentric exercise.

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Conflict of interest: The authors declare that they have no conflict of interest. The results of the present study do not constitute endorsement by American College of Sports Medicine. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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