

Cross-Education Strength and Activation After Eccentric Exercise

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Context: After injury, eccentric exercise of the injured limb is often contraindicated. Cross-education training, whereby the uninvolved limb is exercised, is an alternative that may improve quadriceps muscle strength and activation in the unexercised limb.

Objective: To determine the effect of eccentric exercise on quadriceps strength and activation gains in the unexercised limb.

Patients or Other Participants: Eighteen healthy individuals were randomly assigned to an eccentric training group or a control group.

Intervention(s): Quadriceps strength and activation measures were collected at preintervention, midintervention, and postintervention. Eccentric training participants exercised their dominant limb with a dynamometer in eccentric mode at 60°/s, 3 times per week for 8 weeks.

Main Outcome Measure(s): Quadriceps strength was quantified at 30° and 60°/s in concentric and eccentric modes. Quadriceps activation was assessed using the burst superimposition technique and quantified via the central activation ratio. A 2 × 3 repeated-measures analysis of variance was used to detect the effects of group and testing session on quadriceps strength and activation. Where appropriate, post hoc Bonferroni multiple-comparisons procedures were used.

Results: We found greater eccentric strength in the unexercised limbs of eccentric training participants between preintervention and midintervention and between preintervention and postintervention (preintervention to midintervention: 30°/s $P = .05$; preintervention to postintervention: 30°/s $P = .02$, 60°/s $P = .02$). No differences were noted in concentric strength ($P > .05$). An overall trend toward greater quadriceps activation in the unexercised knee was detected between preintervention and postintervention ($P = .063$), with the eccentric training group demonstrating a strong effect (Cohen $d = 0.83$). Control strength did not change ($P > .05$).

Conclusions: Exercising with eccentric actions resulted in mode-specific and velocity-specific gains in quadriceps strength in the unexercised limb. A trend toward greater quadriceps activation in the unexercised knee was noted, suggesting that strength gains may have occurred because of enhanced neural activity. This type of therapy may be a useful addition to rehabilitation programs designed to improve quadriceps strength.

Key Words: cross-education training, knee, quadriceps muscle, rehabilitation

Key Points

- Five weeks of eccentric cross-exercise led to consistently stronger eccentric contractions in the unexercised limb.
- A trend toward greater quadriceps muscle activation was detected in the unexercised limb.
- To improve the recovery of quadriceps strength and activation after knee injury, clinicians may be able to use eccentric cross-education as an alternative rehabilitation approach for strengthening the involved limb.

The quadriceps muscle group plays a pivotal role in dynamic stabilization of the knee joint. Consequently, after injury, the restoration of quadriceps function is often central to any knee rehabilitation protocol. However, despite the best efforts of clinicians and researchers to improve rehabilitative techniques, quadriceps weakness often persists long after rehabilitation concludes.^{1–3} Given the importance of the quadriceps muscle to knee-joint health, it is critical that rehabilitation approaches that are capable of maximizing postoperative quadriceps function be identified.

It has been well established that the potential to improve muscle strength by overloading the tissue is greater with eccentric strengthening than with concentric strengthening.^{4,5} Yet the application of early eccentric resistance to the injured or surgical limb is often contraindicated because of the potential for injury to the graft, articular cartilage, or surrounding soft tissue structures.⁶ Although some evidence

has recently shown that early eccentric exercise can be used safely post–anterior cruciate ligament (ACL) reconstruction,⁷ the long-term safety and effectiveness of this intervention are unknown. As a result, there is still a clear need to identify a rehabilitative protocol that can be used to safely overload the quadriceps muscle early to induce strength.

Cross-education training of the uninvolved limb is an alternative to early eccentric exercise of the involved limb that could potentially improve quadriceps function post–knee injury. *Cross-education* describes the ability of exercise of 1 limb to cause an increase in strength of the contralateral unexercised limb.⁸ Protocols using cross-education have been shown to successfully improve quadriceps strength in the limbs of healthy, uninjured participants.^{9–11} Although the exact mechanism of cross-education has yet to be identified, the strength gains that are produced in the unexercised limb are thought to occur as a

Table 1. Participant Demographics (Mean ± SD)

Group	Participants, No.	Sex, Women/Men, No.	Age, y	Height, m	Mass, kg	Preintervention Activity Level	
						Tegner Scale	Marx Scale
Eccentric exercise	9	4/5	23.3 ± 2.4	1.73 ± 0.1	70.6 ± 14.3	5.67 ± 1.1	8.89 ± 3.9
Control	9	6/3	22.6 ± 3.6	1.72 ± 0.1	66.9 ± 10.0	6.11 ± 1.1	7.67 ± 3.4

result of alterations in neural activity.^{12,13} Because deficits in quadriceps strength after injury are hypothesized to occur, in part from alterations in quadriceps activation,¹⁴ identifying if cross-education training can improve quadriceps activation could help researchers to develop targeted interventions for populations with volitional muscle-activation failure.

To date, limited evidence shows that gains in quadriceps strength in the unexercised limb of healthy individuals can be improved through an eccentric exercise protocol,^{10,11} and we are unaware of any data that document the effectiveness of a single-legged eccentric exercise protocol on volitional quadriceps muscle activation in the unexercised leg. Recent authors¹⁵ have shown that eccentric exercise in the ACL-reconstructed limb at 9 months after surgery improves quadriceps muscle activity, warranting further questioning as to whether or not eccentric training results in neuromuscular gains of the unexercised limb after cross-education training. Also, if greater quadriceps strength and muscle activation can be achieved with an eccentric training protocol in the unexercised limb of healthy individuals, future investigators may be able to use this training protocol with populations in whom eccentric exercise in the injured limb may be contraindicated (eg, meniscal injury or repair, acute quadriceps injury, ACL injury, total knee arthroplasty). Therefore, the primary purpose of our study was to determine the cross-education benefits of a single-legged eccentric exercise program on quadriceps muscle strength and activation of the unexercised limb in a healthy population. A secondary objective was to determine the dose of eccentric exercise necessary to elicit quadriceps strength and activation gains in the unexercised knee.

METHODS

Participants

Eighteen healthy individuals were randomly assigned into 1 of 2 groups: an eccentric training group (EX) and a control group (CNTRL). No differences in participant demographics and activity levels existed between groups before enrollment (Table 1). Potential participants were excluded if they had a previous history of knee surgery, had suffered a lower extremity injury within the past 6 months, were currently suffering from knee pain, or had a known heart condition. Pregnant females were also excluded. We obtained written informed consent from all participants before testing. The study was approved by the university's institutional review board.

Testing Protocol

Regardless of group assignment, all participants were required to report for testing on 3 occasions over the duration of the 8-week intervention (preintervention,

midintervention, postintervention). Before testing, the dominant limb was determined to be the leg used to kick a soccer ball.¹⁶ At each testing session, measurements of quadriceps strength and activation were recorded in the dominant and nondominant limbs. Participants in EX also had quadriceps strength and activation measured in the nondominant or unexercised limb once a week, after the last training session of that week.

Training Protocol

Participants who were randomized into EX were required to report for 3 training sessions per week, for a total of 24 training sessions. Participants began each training session by performing a warm-up series of 10 concentric, isokinetic knee actions in an isokinetic dynamometer (HUMAC NORM; Computer Sports Medicine, Inc, Stoughton, MA) with the dominant limb at 60°/s. After the warm-up trial, all EX participants performed 4 sets of 10 maximal eccentric isokinetic actions of the dominant limb at 60°/s. Repetitions were continuous, and sets were separated by a rest of 2 minutes. Participants performed all actions through approximately 90° of knee flexion. The nondominant or unexercised limb hung freely during training.

Quadriceps Strength Measurements

To assess quadriceps strength, we positioned participants with the hips flexed to 90°, the back supported, and the testing leg and torso strapped securely in an isokinetic dynamometer. Participants were asked to perform 3 concentric knee actions at a speed of 30°/s to serve as a warm-up and to familiarize themselves with the testing procedure. After the warm-up, each participant performed 3 maximal concentric and eccentric trials at 30° and 60°/s with a 2-minute rest between trials. The order in which the limbs were tested was counterbalanced. The average torque across the 3 trials was normalized to body weight (Nm/kg) and used for statistical analysis.

Quadriceps-Activation Measurements

Quadriceps activation was quantified using the central activation ratio assessed via the superimposed-burst technique (Figure).¹⁷ Superimposed-burst testing was initiated by asking participants to perform a minimum of 3 maximal voluntary isometric knee-extension contractions (MVICs) while the hip and testing knee were flexed to 90° and with 2 minutes of rest between trials. There was no limit on the number of MVIC trials a participant could perform, but trials were ceased when torque stopped improving. This procedure helped to ensure that each participant's maximum voluntary contraction was achieved and has been used by others.^{18,19} Oral encouragement and visual feedback of the real-time torque output were provided to help facilitate maximal effort. Once the maximal knee-extension torque output had been achieved,

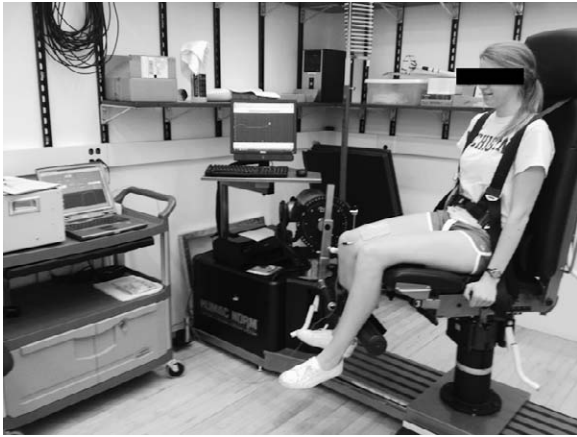


Figure. The experimental setup for measurement of quadriceps activation using the superimposed-burst technique. Participant is positioned in the dynamometer with the testing knee locked at 90° of flexion and with stimulating electrodes placed on the quadriceps. The real-time torque output is projected onto the laptop computer that is visible to the participant to help facilitate maximal effort.

participants were asked to perform an additional MVIC and maintain this contraction for approximately 5 seconds. A custom-written LabVIEW program (version 8.5; National Instruments Corporation, Austin, TX) was set to deliver a supramaximal electrical stimulus (100 pulses/s, 600- μ s pulse duration, 100-millisecond train duration, and 130 V) to the quadriceps once the maximal knee-extension torque was reached and then subsequently dropped by 1 Nm.^{17,19} Automatic instead of manual delivery of the stimulus was chosen because it has been shown to reduce measurement error by improving stimulus timing.²⁰ The electrical stimulus provided to participants during the superimposed-burst technique was delivered through 2 self-adhesive stimulating electrodes (Dura-Stick II; 7 \times 13 cm; Chattanooga Group, Hixson, TN) applied over the vastus lateralis muscle proximally and the vastus medialis distally using a Grass S88 Dual Output Square Pulse Stimulator (Natus Neurology Incorporated—Grass Products, Warwick, RI) with an SIU8T Transformer Stimulus Isolation Unit (Natus Neurology Incorporated—Grass Products) attached. Volitional activation of the quadriceps was determined using the central activation ratio (CAR) formula (Equation 1), wherein the participant's peak torque generated immediately before the delivery of the stimulus was divided by the peak torque generated as a result of the electrical stimulus (superimposed burst). A CAR of 1.00 was used to represent complete quadriceps activation.²¹ The average CAR across 3 trials was used for statistical analysis.

$$\text{CAR} = \frac{\text{MVIC}}{\text{MVIC} + \text{superimposed burst}} \quad (1)$$

Scales to Assess Activity Level

All participants were encouraged to maintain their normal activity level during the study. To monitor this and to ensure activity level did not change over the course of the intervention, participants in both groups were required to complete the Marx²² and Tegner²³ scales weekly. The EX group completed the scales during the last

training session of each week. Participants in CNTRL were e-mailed weekly and provided an electronic copy of the scales to complete and return to the primary investigator. We selected the Marx²² activity scale because it takes into account the frequency of participation and the intensity of the activity. Four separate activities are rated: running, cutting, decelerating, and pivoting. Frequency of participation is then classified for each activity: *none*, *1 time a month*, *1 time per week*, *2 to 3 times per week*, and *4 or more times per week*. We selected the Tegner²³ activity level scale because it quantifies activity levels in both sport and work activities into a 10-level gradient, wherein levels 8 to 10 account for competitive sport, level 7 describes recreational and competitive sports, level 6 represents “other recreational sports,” and levels 1 to 5 combine work and sport. All participants rated their level before study enrollment and their current level at the end of each week.

Statistical Analysis

To ensure group randomization was successful, we compared participant demographics (sex, age, height, and mass) and preintervention activity levels between groups using a Student *t* test. To determine the magnitude of change in each limb associated with eccentric training, the unexercised/nondominant knee was compared with the exercised/dominant knee using a 2 \times 2 \times 3 (limb \times group \times time) repeated-measures analysis of variance. To determine the cross-education benefits of a single-legged eccentric exercise program in the unexercised knee, a 2 \times 3 repeated-measures analysis of variance was used to detect the main effects of group and testing session on quadriceps strength and activation measurements. Activity levels were also monitored within the 2 \times 3 repeated-measures analysis of variance to ensure that participants' activity did not change over the course of the intervention. To detect the dose of eccentric exercise necessary to elicit sustained gains in quadriceps strength and activation in the unexercised knee, paired *t* tests were used within EX. Where appropriate, we conducted post hoc Bonferroni multiple-comparison procedures. Standardized effect sizes (Cohen *d* = [preintervention – postintervention/pooled SD]) and 95% confidence intervals were calculated to assess gains in quadriceps strength and activation in the unexercised and exercised limbs. Effect sizes were interpreted using the guidelines described by Cohen,²⁴ with values less than 0.5 interpreted as *weak*, values ranging from 0.5 to 0.79 interpreted as *moderate*, and values greater than 0.8 interpreted as *strong*. The α level was set a priori at $P \leq .05$. Statistical analysis was performed using SPSS (version 19.0; IBM Corporation, Armonk, NY).

RESULTS

Demographics

No differences in participant sex ($t_{16} = 0.918$, $P = .372$), age ($t_{16} = -0.535$, $P = .600$), height ($t_{16} = -0.277$, $P = .786$), mass ($t_{16} = -0.634$, $P = .535$), or preintervention activity levels (Tegner: $t_{16} = 0.977$, $P = .343$; Marx: $t_{16} = -0.704$, $P = .491$) were noted between groups, suggesting successful randomization (Table 1).

Table 2. Average Isokinetic Torque, Nm/kg (Mean ± SD)

Group	Velocity, %s	Exercised/Dominant Limb			Unexercised/Nondominant Limb		
		Preintervention	Midintervention	Postintervention	Preintervention	Midintervention	Postintervention
Eccentric exercise	E 30	2.23 ± 0.5	3.48 ± 1.3 ^{a,c}	3.85 ± 1.4 ^{a,c}	2.17 ± 0.7	2.82 ± 1.1 ^a	3.27 ± 1.3 ^a
	C 30	2.08 ± 0.5	2.48 ± 0.7	2.66 ± 0.9	1.85 ± 0.6	2.22 ± 0.8	2.45 ± 0.8
	E 60	2.15 ± 0.6	3.58 ± 1.1 ^b	3.86 ± 1.3 ^a	2.26 ± 0.7	3.00 ± 1.3	3.31 ± 1.3 ^a
	C 60	1.58 ± 0.5	2.18 ± 0.7	2.22 ± 0.9	1.51 ± 0.6	1.93 ± 0.8	2.26 ± 0.8
Control	E 30	2.72 ± 0.7	2.80 ± 0.7	2.98 ± 0.6	2.76 ± 0.6	2.77 ± 0.5	2.58 ± 0.5
	C 30	2.33 ± 0.5	2.39 ± 0.4	2.51 ± 0.5	2.25 ± 0.4	2.22 ± 0.5	2.35 ± 0.5
	E 60	2.76 ± 0.7	2.91 ± 0.6	3.02 ± 0.7	2.91 ± 0.6	2.88 ± 0.5	2.84 ± 0.5
	C 60	1.70 ± 0.4	1.85 ± 0.4	2.10 ± 0.5	1.87 ± 0.5	1.85 ± 0.5	2.06 ± 0.7

Abbreviations: C, concentric; E, eccentric.

^a Different than preintervention ($P < .05$).

^b Different than preintervention ($P \leq .001$).

^c Different than the unexercised limb ($P < .05$).

Eccentric Training Compliance

Eccentric training participants were required to attend a minimum of 90% of the scheduled training sessions (21 of 24 scheduled sessions). All EX participants met the required number of training sessions, with the average number of training sessions attended being (mean ± SD) 23.4 ± 0.73 .

Activity Levels

All participants were able to maintain their preintervention activity level over the course of the intervention (Tegner: $F_{2,32} = 2.118$, $P = .137$; Marx: $F_{2,32} = 0.130$, $P = .879$).

Magnitude of Crossover Effect on Quadriceps Strength and Activation

A significant 3-way interaction was found for eccentric quadriceps strength at 30°/s ($F_{2,32} = 3.417$, $P = .045$), wherein EX demonstrated greater strength in the exercised limb as compared with the unexercised limb at the midintervention ($F_{1,8} = 30.211$, $P = .001$) and postintervention ($F_{1,8} = 16.186$, $P = .004$; Table 2) time points. We saw no difference in eccentric quadriceps strength at 30°/s in CNTRL ($P > .05$). Additionally, no other significant 3-way interactions were identified for eccentric quadriceps strength at 60°/s, concentric strength at 30° and 60°/s, or quadriceps activation ($P > .05$).

Quadriceps Strength and Dose Response in the Unexercised Limb

Benefits of cross-education training were noted in the unexercised limb of the EX participants between the preintervention and midintervention and between the preintervention and postintervention time points. Eccentric strength was greater within the unexercised limb at 30°/s between the preintervention and midintervention time points ($F_{1,8} = 5.374$, $P = .049$; Table 2) and at 30° and 60°/s between the preintervention and postintervention testing sessions (30°/s: $F_{1,8} = 8.218$, $P = .021$; 60°/s: $F_{1,8} = 8.212$, $P = .021$; Table 2). Gains in eccentric strength at 30° and 60°/s were associated with large effect sizes and confidence intervals that did not cross zero (Table 3). No differences were observed in EX between the midintervention and postintervention time points or

for concentric strength over the course of the intervention ($P > .05$).

Eccentric training participants had consistently greater eccentric quadriceps strength in the unexercised limb compared with preintervention strength, at week 5 through the end of the 8-week intervention ($P = .029$; Table 4).

Quadriceps Strength in the Exercised Limb

Training had a positive effect on eccentric quadriceps strength in the exercised limb for participants in EX between the preintervention and midintervention and preintervention and postintervention time points. Specifically, EX participants demonstrated greater eccentric strength in the exercised limb at 30° and 60°/s (preintervention to midintervention: 30°/s: $F_{1,8} = 13.379$, $P = .006$; 60°/s: $F_{1,8} = 25.090$, $P = .001$; preintervention to postintervention: 30°/s: $F_{1,8} = 17.230$, $P = .003$; 60°/s: $F_{1,8} = 19.452$, $P = .002$; Table 2). Large effect sizes and confidence intervals that did not cross zero were associated with gains in eccentric strength at 30° and 60°/s (Table 3). We saw no change in quadriceps strength in CNTRL ($P > .05$, Table 2). Additionally, concentric strength did not differ in EX over the course of the intervention or between the midintervention and postintervention time points in the exercised limb ($P > .05$, Table 2).

Quadriceps Activation

An overall trend toward greater quadriceps activation occurred in the unexercised limb ($F_{2,32} = 3.022$, $P = .063$). No difference was detected in the exercised limb ($F_{2,32} = 0.466$, $P = .632$, Table 5).

DISCUSSION

The primary purpose of our study was to determine if a single-legged eccentric exercise protocol was capable of producing quadriceps strength and activation gains in the unexercised limbs of healthy participants. The greater clinical intent of this research was to determine if this eccentric training regimen could be used in populations with quadriceps strength and activation deficits immediately postinjury (eg, post-ACL injury), when eccentric exercise with the involved limb would be contraindicated. Our findings indicate that eccentric training leads to gains

Table 3. Standardized Effect Size Interpretations, Effect Size (95% Confidence Interval) Extended on Next Page

Group	Exercised Limb				Quadriceps Activation Central Activation Ratio
	Quadriceps Strength (Velocity, °/s)				
	E 30	C 30	E 60	C 60	
Eccentric exercise	1.54 (0.49, 2.59) Strong	0.80 (-0.16, 1.76) Strong	1.69 (0.61, 2.77) Strong	0.88 (-0.09, 1.85) Strong	0.35 (-0.58, 1.28) Weak
Control	0.40 (-0.53, 1.33) Weak	0.36 (-0.57, 1.29) Weak	0.37 (-0.56, 1.30) Weak	0.88 (-0.08, 1.85) Strong	0.00 (-0.92, 0.92) Weak

Abbreviations: C, concentric; E, eccentric.

in eccentric quadriceps strength in both the exercised and unexercised limbs of healthy participants. Further, we note a trend toward greater quadriceps muscle activation in the unexercised limb.

Quadriceps Activation in the Unexercised Limb

A single-legged eccentric exercise protocol improved eccentric quadriceps strength in the unexercised limb and may also lead to gains in quadriceps activation. Given that the underlying mechanism of cross-education is hypothesized to be from alterations in neural activity,^{12,13} we had anticipated that tracking the CAR of EX participants would provide evidence of a change in neural activity. Although we did not find a statistically significant change in quadriceps activation, we did see an overall trend toward greater quadriceps activation ($P = .063$; Cohen $d = 0.83$; 95% CI = -0.13, 1.80; Table 3), with EX participants demonstrating more quadriceps activation in the unexercised limb at the postintervention time point as compared with preintervention and CNTRL (Table 5). The P value is close to $P < .05$ and the effect size is large, but it is important to note that the confidence interval around the effect size crosses zero, suggesting that the effect or result may not be clinically meaningful. Using electromyographic measures to detect changes in neural activity might have provided additional insight, as previous authors¹⁰ have shown an increase in vastus lateralis activity in the unexercised limbs of healthy participants after an eccentric exercise protocol. Further, the effects of eccentric training may be larger in patients who are experiencing quadriceps activation failure, such as those who have undergone an ACL reconstruction.

Quadriceps Strength in the Unexercised Limb

Exercising eccentrically resulted in specific eccentric gains in quadriceps strength in the unexercised limb. Previous authors^{10,11} have found mode-specific gains in quadriceps strength in the unexercised limbs of healthy participants after a single-legged exercise protocol. The transfer of quadriceps strength with concentric and

isometric muscle contractions has been well established. More recently, Hortobagyi et al¹⁰ and Seger et al¹¹ demonstrated that greater mode-specific cross-education training benefits occur from eccentric than concentric exercise. Hortobagyi et al¹⁰ reported eccentric quadriceps strength gains as high as 77% versus 30% with concentric actions at 60°/s, whereas Seger et al¹¹ found eccentric quadriceps strength gains of 15% versus 10% with concentric actions at 90°/s. Our data showed a similar trend at 30°/s, such that EX participants had eccentric quadriceps strength gains of 51% versus 32% concentric gains. Interestingly, at 60°/s, our EX participants demonstrated a greater change in quadriceps strength with concentric actions at an increase of 49% versus a 46% gain in eccentric strength. However, the overall increase in concentric quadriceps strength at 60°/s over time was not statistically significant ($P = .071$), with the mean difference between the preintervention and postintervention time points demonstrating a small increase in concentric quadriceps strength (mean difference at 60°/s: concentric = 0.75 Nm/kg, eccentric = 1.05 Nm/kg).

A few important points can be made based on these strength outcomes. First, our data are in agreement with the current literature,^{10,11} with our EX participants demonstrating mode-specific eccentric gains in quadriceps strength at both 30° and 60°/s. Second, a trend toward greater concentric quadriceps strength at 60°/s appeared to emerge in our EX participants. Given that our EX participants trained at 60°/s, it is possible that velocity-specific gains in quadriceps strength occurred in the unexercised limb. Evidence of cross-education training producing velocity-specific gains in quadriceps strength has previously been reported.^{10,11}

Dose Response in the Unexercised Limb

To provide clinicians with recommendations for the dose of eccentric exercise necessary to elicit gains in quadriceps strength in the unexercised knee, we measured the unexercised limb at the end of each week. The EX participants produced consistently stronger eccentric actions, compared with their preintervention strength, from

Table 4. Dose Response: Quadriceps Strength in the Unexercised Limb, Nm/kg, Mean ± SD

Eccentric Mode, °/s	Week								
	0 (Preintervention)	1	2	3	4 (Midintervention)	5	6	7	8 (Postintervention)
30	2.17 ± 0.7	2.28 ± 0.7	2.43 ± 0.8	2.84 ± 1.1	2.82 ± 1.1	3.17 ± 1.2 ^a	3.33 ± 1.4 ^a	3.36 ± 1.2 ^b	3.27 ± 1.3 ^a
60	2.26 ± 0.7	2.55 ± 0.8	2.74 ± 0.7	2.77 ± 0.9	3.00 ± 1.3	3.30 ± 1.3 ^a	3.45 ± 1.4 ^a	3.36 ± 1.2 ^a	3.31 ± 1.3 ^a

^a $P < .05$.

^b $P \leq .01$.

Table 3. Extended From Previous Page

Unexercised Limb				
Quadriceps Strength (Velocity, °/s)				Quadriceps Activation Central Activation Ratio
E 30	C 30	E 60	C 60	
1.05 (0.07, 2.04) Strong	0.85 (-0.12, 1.81) Strong	1.01 (0.03, 1.99) Strong	1.15 (0.15, 2.15) Strong	0.83 (-0.13, 1.80) Strong
-0.33 (-1.26, 0.60) Weak	0.22 (-0.71, 1.15) Weak	-0.13 (-1.05, 0.80) Weak	0.31 (-0.62, 1.24) Weak	-0.25 (-1.18, 0.68) Weak

week 5 through the end of the 8-week intervention. Based on these results, we recommend that clinicians implementing a cross-exercise eccentric protocol have participants train 3 times per week for at least 5 weeks (Table 4). To our knowledge, we are the first to examine the length of eccentric training required to induce strength gains using cross-education exercise. This finding is critical, as understanding the number of training sessions that elicit improvements in the unexercised limb is necessary to appropriately delivering this type of therapy.

Quadriceps Strength in the Exercised Limb

Similar to the unexercised limb, a mode- and speed-specific response to eccentric strength training also occurred in the exercised leg of EX participants. The increase in quadriceps torque production in the exercised limb during eccentric actions is similar in magnitude to that previously reported in studies with comparable training intensities (3–6 sets of 10–12 repetitions), velocities (60°–90°/s), and durations (10–12 weeks).^{10,11,25} At a velocity of 30°/s, the average torque produced by EX participants increased by approximately 60% with eccentric actions versus 27% with concentric actions. Similar results were also produced at speeds of 60°/s: EX participants increased their eccentric torque by 80% versus 40% with concentric actions. EX participants produced the greatest strength gains at the training velocity (60°/s), which indicates that quadriceps strength gains in the exercised limb were not only mode but also velocity specific, just as we saw with the unexercised limb.^{10,11}

Quadriceps Activation in the Exercised Limb

We found no change in quadriceps activation in the exercised limb of EX participants. Again, the most reasonable explanation for this is that the lack of detection in neural changes was due to an inadequate measurement technique (CAR) in a healthy population, with no deficits in voluntary activation at preintervention. However, it should be noted that limb differences in the CAR appeared to change over time, with little to no change in the exercised limb ($P = .632$) versus marginal improvements in the unexercised limb ($P = .063$, Table 5). Because the relationship between the CAR and strength is curvilinear²⁶

and the greatest strength gains were achieved in the exercised limb, we had expected that CAR improvements would be greatest in the exercised limb. It is possible that improvements in the exercised-limb CAR were not seen because the CAR measurement is taken during an isometric contraction. The greatest quadriceps strength gains achieved in our EX participants were mode and velocity specific, so it is possible that these strength gains did not transfer to the isometric contraction. Hence, electromyography might have been a more appropriate measurement technique, as this has been shown to detect improvements in quadriceps muscle activity after an eccentric exercise protocol.¹⁰

Magnitude of the Crossover Effect: Quadriceps Strength and Activation

Our results indicate that exercising with eccentric contractions leads to greater quadriceps strength in the exercised limb as compared with the unexercised limb at 30°/s. Given that muscle adapts when it is stressed, this finding in the exercised limb is not surprising. In contrast, no difference in quadriceps strength was detected between the exercised and unexercised limbs at 60°/s in eccentric mode. We suspect the lack of difference at 60°/s can be attributed to inadequate statistical power to detect a 3-way interaction ($1 - \beta = 0.325$), rather than revealing equivalent strength gains between limbs. When examining our results, we noted an 80% change from baseline in the exercised limb compared with only a 46% change in the unexercised limb, suggesting that the exercise limb may indeed see greater gains at 60°/s. Future work may be necessary to provide additional insight into the magnitude of strength gains that result for each limb after cross-education training.

Limitations

Our study is not without limitations. First, because we did not measure muscle morphology, we could not detect if changes in quadriceps strength were related to gains in muscle mass. Knowing if quadriceps muscle volume increased after eccentric exercise could have helped to explain if different mechanisms were at work in the exercised versus the unexercised limbs. It seems reasonable

Table 5. Quadriceps Activation: Central Activation Ratio, Mean ± SD

Group	Exercised/Dominant Limb			Unexercised/Nondominant Limb		
	Preintervention	Midintervention	Postintervention	Preintervention	Midintervention	Postintervention
Eccentric exercise	0.91 ± 0.04	0.93 ± 0.05	0.93 ± 0.07	0.92 ± 0.05	0.95 ± 0.01	0.95 ± 0.01
Control	0.95 ± 0.02	0.94 ± 0.03	0.95 ± 0.02	0.93 ± 0.04	0.95 ± 0.02	0.92 ± 0.04

to suggest that gains in quadriceps strength in the exercised limb could have been the result of greater muscle mass, whereas improvements in the unexercised limb's strength were more likely due to neural adaptations. Future investigators with magnetic resonance imaging capability should consider using this measure. Second, our participants exercised using only isokinetics, which resulted in mode- and velocity-specific strength gains. It is unclear if isotonic exercise, which requires only basic resistance equipment, is capable of producing the same results. We can only speculate that if our participants had used isotonic rather than isokinetic exercise, the strength gains would not have been velocity specific. Further, because isokinetic exercise maximally loads the muscle through the entire range of motion, this type of exercise results in greater strength gains than isotonic exercise.²⁷ Hence, it is possible that smaller strength gains would be achieved with isotonic cross-education training. Thus, our results cannot be generalized to isotonic exercise protocols. Third, the quadriceps activation measure in the unexercised limbs of EX participants revealed a strong effect size with a wide confidence interval that crossed zero. We interpret this to mean that beyond using other measurement techniques such as electromyography, a larger sample size might have allowed us to detect a change in quadriceps activation. It is important to note that our sample size was similar to that of other authors^{9–11} examining cross-education training in healthy participants. Lastly, although this study was not powered to consider sex as an independent variable, it is possible that neural changes could have been influenced by it. Thus, future researchers may want to examine if males and females respond differently to a cross-education eccentric training protocol. Readers should take all these limitations into consideration.

Clinical Implications

Identifying interventions aimed at safely overloading the quadriceps muscle early after injury is essential to reducing the consequences of persistent quadriceps weakness. Because the long-term safety and effectiveness of early eccentric exercise on the involved limb are unknown, alternative rehabilitative techniques that are capable of improving quadriceps strength are needed. Our results indicate that a 5-week, single-legged eccentric exercise protocol improved quadriceps strength in the unexercised limb of healthy individuals and may also produce some modest improvements in quadriceps activation. Based on this investigation, we suggest that populations with quadriceps activation and strength deficits may benefit from cross-education training. Furthermore, it appears necessary to exercise the uninvolved limb 3 times per week (4 sets of 10 repetitions) for 5 weeks to realize quadriceps strength gains in the unexercised limb. However, these exercise recommendations are based on data extrapolated from healthy individuals, and future investigators will need to study participants postinjury to make recommendations for specific clinical populations.

CONCLUSIONS

We are the first to provide insight into the neuromuscular response of the unexercised quadriceps muscle to eccentric cross-education training using volitional muscle-activation

testing. In addition, this study is unique because it is the first to determine the dosage of eccentric cross-education training necessary to elicit changes in quadriceps strength of the unexercised limb. Based on these results, we concluded that training with eccentric actions resulted in both mode- and speed-specific gains in quadriceps strength in the exercised and unexercised limbs of healthy participants. We also found that 5 weeks of eccentric cross-exercise led to consistently greater eccentric quadriceps strength in the unexercised limb. A trend toward greater volitional quadriceps activation in the unexercised limb was also detected, suggesting that strength gains may have occurred because of enhanced neural activity.

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