

The Influence of Oral L-Glutamine Supplementation on Muscle Strength Recovery and Soreness Following Unilateral Knee Extension Eccentric Exercise

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The study aimed to examine the effects that L-glutamine supplementation has on quadriceps muscle strength and soreness ratings following eccentric exercise. It was hypothesized that glutamine ingestion would quicken the recovery rate of peak force production and decrease muscle soreness ratings over a 72-hr recovery period. Sixteen healthy participants (8♀/8♂; 22 ± 4 years) volunteered in a double-blind, randomized, placebo-controlled crossover study. Supplement conditions consisted of isoenergetic placebo (maltodextrin, $0.6 \text{ g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$) and L-glutamine ($0.3 \text{ g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1} + 0.3 \text{ g}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$ maltodextrin) ingestion once per day over 72 hr. Knee extensor peak torque at 0° , 30° , and 180° per second and muscle soreness were measured before, immediately following, 24, 48, and 72 hr posteccentric exercise. Eccentric exercise consisted of 8 sets (10 repetitions/set) of unilateral knee extension at 125% maximum concentric force with 2-min rest intervals. L-glutamine resulted in greater relative peak torque at $180^\circ/\text{sec}$ both immediately after ($71 \pm 8\%$ vs. $66 \pm 9\%$), and 72 hr ($91 \pm 8\%$ vs. $86 \pm 7\%$) postexercise (all, $p < .01$). In men, L-glutamine produced greater ($p < .01$) peak torques at $30^\circ/\text{sec}$ postexercise. Men also produced greater normalized peak torques at $30^\circ/\text{sec}$ (Nm/kg) in the L-glutamine condition than women (all, $p < .05$). In the entire sample, L-glutamine resulted in lower soreness ratings at 24 (2.8 ± 1.2 vs. 3.4 ± 1.2), 48 (2.6 ± 1.4 vs. 3.9 ± 1.2), and 72 (1.7 ± 1.2 vs. 2.9 ± 1.3) hr postexercise ($p < .01$). The L-glutamine supplementation resulted in faster recovery of peak torque and diminished muscle soreness following eccentric exercise. The effect of L-glutamine on muscle force recovery may be greater in men than women.

Keywords: isokinetic muscle torque, delayed onset muscle soreness, sex

Glutamine is an important conditionally essential amino acid involved with the immune response to muscle damage and is used as an energy source by lymphocytes and macrophages (Walsh et al., 1998). The immune response created from prolonged (i.e., > 2 hr) or intense exercise has been demonstrated to decrease intramuscular and plasma concentrations of glutamine (Castell & Newsholme, 1997; Gleeson, 2008), which consequently may lead to impaired immune system function (Rohde et al., 1998). However, it has recently been shown in men that oral glutamine supplementation ($0.3 \text{ g}\cdot\text{kg}^{-1}$ body mass) can attenuate short-term (i.e., within 1 hr) strength loss following an acute bout of eccentric-based exercise (Street et al., 2011). This notion has led to the idea that exogenous L-glutamine supplementation during periods of intense exercise may accelerate the recovery of muscle strength following exercise (Castell & Newsholme, 1997; Gleeson et al., 1998). Theoretically, these therapeutic

benefits of L-glutamine supplementation could have an impact on athletic training and performance and may explain the recent increase in the popularity of oral L-glutamine supplements among strength and endurance athletes (Antonio & Street, 1999; Candow et al., 2001).

Although L-glutamine supplementation has been well documented to restore plasma glutamine concentrations and improve systemic immune system function (Castell, 2003; Kuhn et al., 2010), few studies support the effectiveness of L-glutamine supplementation on improving muscle function and reducing muscle soreness (Rahmani et al., 2013; Street et al., 2011). Street et al. (2011) randomly assigned fourteen physically active men to a control group or a glutamine group ($0.3 \text{ g}\cdot\text{kg}^{-1}$ body mass $\cdot\text{day}^{-1}$). Following a bout of eccentric exercise, consisting of 100 drop jumps, participants ingested their supplement at 0, 24, 48, and 72 hr postexercise. The findings of this study demonstrated that L-glutamine supplementation resulted in a greater preservation of peak torque over the 72-hr postexercise measurement period at both slower ($30^\circ/\text{sec}$) and faster ($180^\circ/\text{sec}$) knee extension contraction speeds, as well as, lower ratings of perceived muscle soreness. Conversely, Rahmani et al. (2013) observed that a chronic L-glutamine

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supplementation (0.1 g×kg⁻¹ body mass of L-glutamine, 3 days×week⁻¹ for 4 weeks) had no effect on perceived muscle soreness and strength loss 24 and 48 hr posteccentric exercise. Rahmani Nia et al. (2013) used a smaller dosage of L-glutamine and a different exercise protocol (eccentric leg extensions at 75% 1-RM), which could be factors responsible for the discrepancy between these two studies. Furthermore, Street et al. (2011) provided a postexercise supplement only, which may have allowed glutamine concentrations to drop below preexercise concentrations for a brief period of time during and following the eccentric exercise protocol. Nosaka et al. (2006) reported reduced soreness of the elbow flexors at 24 and 48 hr posteccentric exercise when a 3.6 g supplement containing 12 amino acids (including L-glutamine) was ingested pre, immediately post, and on eight more occasions over 4 days posteccentric exercise. Thus, ingestion of a preexercise L-glutamine supplement may provide a greater benefit in assisting with muscle recovery by allowing physiological concentrations of glutamine to be maintained throughout the exercise period. Both of these studies (Rahmani et al., 2013; Street et al., 2011) were conducted in men only. Therefore, whether the benefits of oral L-glutamine supplement exist in women is currently unknown. To date, there is a paucity of information available on sex differences in the response of oral glutamine supplementation. However, Esbjörnsson et al., (2012) recently observed that women, but not men, had increased plasma concentrations of glutamine following three, 30 s Wingate bouts. This finding was coupled with decreased postexercise plasma ammonia concentrations in the women, which suggests that women have a greater capacity to buffer ammonia, and subsequently, synthesize glutamine following strenuous exercise. As such, women may not experience the same degree of benefit from oral glutamine supplementation as men.

The primary purpose of this study was to determine if oral L-glutamine supplementation can improve posteccentric exercise muscle recovery in both men and women. We tested the hypotheses that L-glutamine supplementation would result in 1) a faster return of peak dynamic (30°/sec and 180°/sec) and isometric (at 45° flexion) knee-extensor torques to preexercise values in men versus women, and 2) lower muscle soreness ratings in men than women over a 72-hr posteccentric exercise recovery period.

Methods

Participants

Sixteen healthy, recreationally active (i.e., not engaged in resistance or aerobic exercise more than 3 days per week), normotensive men ($n = 8$) and women ($n = 8$) volunteered with informed consent to participate in this study, which was approved by the Health Sciences Research Ethics Board at Dalhousie University. To minimize the influence of estrogen on the magnitude of muscle damage, women were tested within 4 days from the onset of menstruation

or the placebo phase of oral contraceptive use. Women using any and all forms of birth control were permitted into the study. Participants had not consumed any dietary supplements including, but not exclusive to, protein supplements, creatine, and branched chain amino acids within the previous 6 months. Volunteers avoided therapeutic treatments for the symptoms of muscle damage experienced by the eccentric exercise bout (see below) and maintained their normal physical activity routine throughout the duration of the study. During the first randomly assigned supplement condition, participants were required to record a 4-day diet log and replicated the same dietary intake during the second supplement condition.

Muscle Soreness

Participants rated their perceived level of muscle soreness in the knee extensors using a 7-point Likert scale of muscle soreness (e.g., 0: *a complete absence of pain* and 6: *a severe pain that limits my ability to move*) for the lower limb after the performance of a single unloaded squat movement (Impellizzeri & Maffiuletti, 2007). Participants performed the single unloaded squat movement starting from a standing position with feet shoulder width apart, then bent the knees to 90° while keeping the back straight, and then returned to full knee extension.

Dynamic and Isometric Peak Torque

Peak knee extensor torque was measured using the Cybex NORM isokinetic dynamometer with CSMi HUMAC 2004 software. The test-retest reliability for the measurement of knee extensor peak torque (at 60°/sec and 120°/sec) for this system has been reported previously for both men (0.84–0.86) and women (0.83–0.84) (Li et al., 1996). Dynamic peak torque was measured at angular velocities of 180°/sec and 30 °/sec through a range of motion from ~90° knee flexion to 0° of knee extension. Three repetitions were performed at each speed, with 30 s of rest between each repetition and two minutes of rest between each speed. Isometric peak torque was measured with the knee positioned at a 45° of flexion following a 2-min rest period after the dynamic peak torque measures. Three repeated, 5-s maximum voluntary contractions were performed separated by 30 s of rest. To minimize absolute strength differences between the sexes, all 1-RM force and peak torque data were normalized to the participant's body mass.

L-Glutamine Supplementation

A 5-day “washout” period has been shown to be effective in a population of middle-aged and elderly individuals who supplemented with 0.5 g·kg body mass⁻¹·day⁻¹ of glutamine (Galera et al., 2010). To be conservative and minimize any crossover effect, a minimum 2 week “washout” period separated each supplement condition. Participants ingested four identical supplement beverages during each experimental condition. Two supplement beverages on day 1 (~1 hr pre- and immediately postex-

ercise) and one supplement beverage before testing on days 2, and 3. The L-glutamine supplement consisted of 0.3 g·kg body mass⁻¹·day⁻¹ of maltodextrin and 0.3 g·kg body mass⁻¹·day⁻¹ of L-Glutamine (Micronized L-Glutamine: GNC Pro Performance®, Mississauga, Canada) and the placebo supplement consisted of 0.6 g·kg body mass⁻¹·day⁻¹ of maltodextrin. Supplement allocation was randomized, counterbalanced and double blinded. The order of dominant versus non-dominant leg used for exercise was also randomized and counterbalanced. This dose has previously been shown to produce an acute increase in plasma glutamine concentrations (Ziegler et al., 1990) without producing any adverse effects (Wernerman, 2008). To minimize differences in taste, both supplements were dissolved in 750 ml of water with the addition of a 3.6 g packet of sugar-free lemon-lime powder.

Experimental Design

On the first testing day, participants arrived at the research facility where they immediately ingested their first supplement beverage. Participants' perceived level of muscle soreness in the quadriceps of the involved leg was then collected before a 5-min warm-up on a Monark cycle ergometer with a 1.0 kg load (empty double weight pan) at a pedaling frequency of 60 rpm. Following the warm-up, preexercise values of knee extensor dynamic and isometric peak torque were determined. After baseline measures were completed, the 1-RM of the involved leg was determined and 125% of this value was calculated and added to the weight stack of a Cybex VR2 leg extension machine. Briefly, the 1-RM procedure involved an initial warm-up set of 10 repetitions at 50% of the participant's perceived maximum value. Following 1 min of rest, they performed 5 repetitions with a resistance at 70% of their perceived maximum. A 3-min rest period

was provided before they performed 1 repetition equal to 90% of their perceived maximum. If required, 3-min rest was followed by a 5 lb increment on the weight stack. This final step was repeated ~3–5 times until the participant could not lift the weight through their complete range of motion. Participants then performed the eccentric exercise protocol consisting of 80 eccentric contractions of the involved leg (8 sets of 10 repetitions, 2 min rest between sets). To isolate the eccentric phase of the motion, the lever arm was assisted to full knee extension and then released. The participants were instructed to lower the weight to the starting position in a slow, controlled manner. Immediately following the eccentric exercise protocol, participants ingested their postexercise supplement beverage and were retested for muscle soreness, knee extensor dynamic and isometric peak torques. The participants were evaluated for the same measures after ingestion of another supplement beverage at 24, 48, and 72 hr postexercise. A schematic of the experimental design is presented in Figure 1.

Statistical Analysis

All values are presented as means ± SD. Data were analyzed using SPSS Statistical Software version 20.0 (SPSS Inc., Chicago, IL). To evaluate differences between sex and experimental conditions, dependent variables including dynamic and isometric peak torque, and muscle soreness, were analyzed using a split-plot (Sex × Time × Condition) repeated measures analysis of variance (ANOVA). Separate two factor (Time × Condition) repeated-measures ANOVAs were also conducted for each sex separately. Bonferonni's correction was applied to all within and between-subjects multiple comparisons. The Shapiro-Wilk test of normality ($p > .05$) was used to confirm that all data were normally distributed. Mauchly's

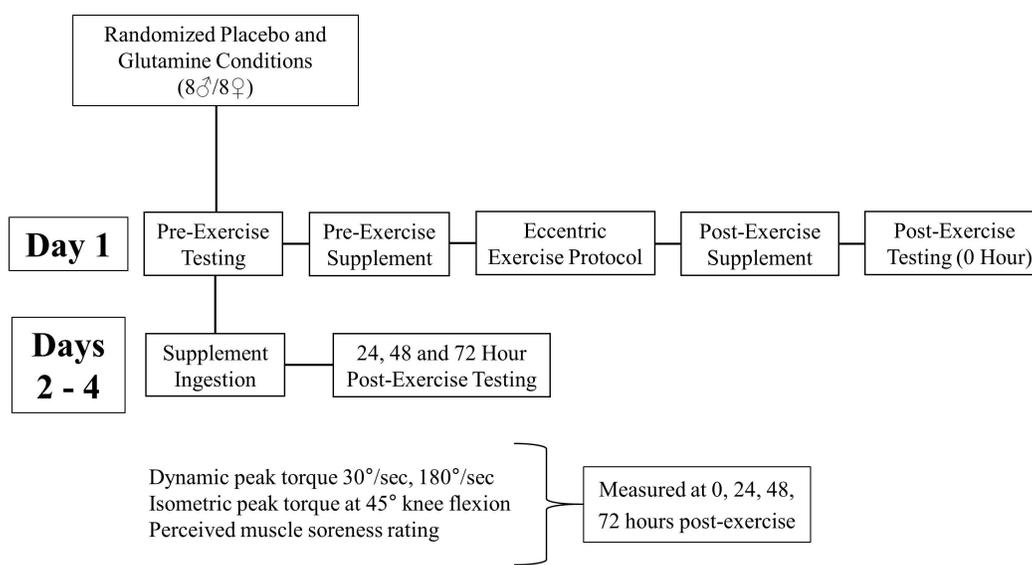


Figure 1 — Schematic representation of the experimental design.

test was used to evaluate if the assumption of sphericity was violated. If a significant Mauchley's test was determined, the Greenhouse-Geisser correction factor was used to adjust the degrees of freedom accordingly. Statistical significance was set at $p \leq .05$.

Results

Participant Descriptive Statistics

Sixteen young, healthy individuals participated in the study. Descriptive data for this sample can be found in Table 1. Age and body mass index were similar between men and women. Height, body mass, and normalized 1-repetition maximum values in both the dominant and nondominant limbs were higher in men than women (all, $p < .01$).

Knee Extensor Peak Torque Results at 180°/sec

Normalized Torque (Nm/kg) There was a main effect of Sex [$F(1,14) = 12.1, p = .004$] with men producing significantly higher normalized peak torques than women (Table 2). There was also a main effect of Time [$F(4,56) = 105.6, p < .001$] such that normalized peak torque (Nm/kg) decreased from preexercise values in both supplement conditions at 0, 24, 48, and 72 hr postexercise (Table 2). These results were consistent for the entire sample and both sexes (Table 2).

Relative Torque (% Preexercise) For the entire sample, there was a Supplement \times Time interaction [$F(1,14) = 6.0, p = .03$] such that L-glutamine resulted in higher peak torque values than placebo immediately postexercise (Figure 2). However, this effect was observed in the men [$F(1,7) = 5.4, p = .05$], but not in the women [$F(1,7) = 1.4, p = .27$].

For the entire sample, there was no main effect of L-glutamine [$F(1,14) = 4.0, p = .065$] on postexercise relative peak torques (Figure 2). However, there was a main effect of L-glutamine [$F(1,7) = 5.32, p = .05$] on postexercise relative peak torque in the men but not in the women [$F(1,7) = 0.34, p = .58$].

For the entire sample, and both sexes, there was also a main effect of Time [$F(4,11) = 55.8, p < .001$] such that relative peak torque (% Preexercise) decreased in both supplement conditions at 0, 24, 48, and 72 hr postexercise (Figure 2).

Knee Extensor Peak Torque Results at 30°/sec

Normalized Torque (Nm/kg) There was a Sex \times Supplement \times Time interaction [$F(1,14) = 6.0, p = .29$] in which men produced higher normalized peak torque values at 30°/sec during the Preexercise time point in both supplement conditions (Table 2). Furthermore, men produced higher torque outputs than women during all postexercise time points in the L-glutamine condition (Table 2).

For the entire sample, there was also a main effect of Time [$F(4,56) = 32.5, p < .01$] such that normalized peak torque (Nm/kg) decreased from preexercise values in both supplement conditions at 0, 24, 48, and 72 hr postexercise (Table 2). This effect was consistent among the men and women (Table 2).

Relative Torque (% Preexercise) For the entire sample, there was no main effect of L-glutamine [$F(1,14) = 2.0, p = .17$] on postexercise relative peak torques (Figure 3). However, there was a main effect of L-glutamine [$F(1,7) = 5.3, p = .05$] on postexercise relative peak torque in the men but not in the women [$F(1,7) = 0.29, p = .61$].

For the entire sample, and both sexes, there was also a main effect of Time [$F(4,56) = 76.7, p < .001$] such that relative peak torque (% Preexercise) decreased in both supplement conditions at 0, 24, 48, and 72 hr postexercise (Figure 3).

Knee Extensor Peak Torque at 0°/sec and 45° Knee Flexion

Normalized Torque (Nm/kg) There was a Sex \times Supplement \times Time interaction [$F(1,14) = 4.7, p = .04$], which demonstrated that men produced a higher normalized peak torque at 0°/sec during the 24 hr postexercise time point in the L-glutamine condition (Table 2).

Table 1 Participant Descriptive Data for the Entire Sample and Separated Between Men and Women

Variable	Men ($n = 8$)	Women ($n = 8$)	Total ($N = 16$)
Age (years)	24 \pm 6	21 \pm 1	22 \pm 4
Height (cm)	179 \pm 5*	167 \pm 3	173 \pm 8
Body mass (kg)	75 \pm 12*	66 \pm 6	71 \pm 10
BMI (kg/m ²)	23 \pm 4	24 \pm 2	24 \pm 3
1-RM Dom leg (kg/kg body mass)	0.79 \pm 0.19*	0.53 \pm 0.08	0.66 \pm 0.19
1-RM Non-Dom leg (kg/kg body mass)	0.81 \pm 0.16*	0.48 \pm 0.10	0.64 \pm 0.21

Note. Data are presented as means \pm SD. BMI = Body mass index; 1-RM = one repetition maximum; Dom = dominant; Nondom = nondominant
* $p < .01$ between men and women.

Table 2 The Effect of L-glutamine Supplementation on Normalized Knee Extensor Peak Torque (Nm/kg Body Mass) Over the 72 hr Posteccentric Exercise Recovery Period for the Entire Sample and Separated Between Men and Women

Test	Supplement	Preex	Postex	24 Hr	48 Hr	72 Hr
Total						
180°/sec	placebo	1.6 ± 0.5	1.0 ± 0.3*	1.1 ± 0.3*	1.3 ± 0.4*	1.3 ± 0.4*
	glutamine	1.6 ± 0.5	1.1 ± 0.3*	1.1 ± 0.3*	1.3 ± 0.4*	1.4 ± 0.4*
30°/sec	placebo	2.6 ± 0.6	1.7 ± 0.5*	1.9 ± 0.4*	2.0 ± 0.4*	2.2 ± 0.4*
	glutamine	2.6 ± 0.6	1.9 ± 0.4*	2.0 ± 0.5*	2.2 ± 0.5*	2.4 ± 0.5*
0°/sec	placebo	2.7 ± 0.8	1.9 ± 0.6*	2.0 ± 0.6*	2.2 ± 0.6*	2.5 ± 0.7*
	glutamine	2.7 ± 0.7	1.9 ± 0.5*	2.0 ± 0.5*	2.3 ± 0.6*	2.6 ± 0.7*
Men						
180°/sec	placebo	1.8 ± 0.5	1.2 ± 0.3*	1.3 ± 0.3*	1.4 ± 0.3*	1.5 ± 0.4*
	glutamine	1.9 ± 0.4	1.3 ± 0.2*	1.3 ± 0.2*	1.5 ± 0.2*	1.6 ± 0.3*
30°/sec	placebo	2.9 ± 0.7§	1.8 ± 0.5*	2.0 ± 0.4*	2.0 ± 0.5*	2.4 ± 0.5*
	glutamine	3.0 ± 0.6§	2.1 ± 0.3*§	2.3 ± 0.4*§	2.4 ± 0.5*§	2.7 ± 0.6*§
0°/sec	placebo	3.0 ± 0.7	2.0 ± 0.6*	2.0 ± 0.4*	2.3 ± 0.5*	2.6 ± 0.6*
	glutamine	3.0 ± 0.7	2.0 ± 0.4*	2.1 ± 0.4*	2.5 ± 0.6*§	2.8 ± 0.7*
Women						
180°/sec	placebo	1.3 ± 0.3	0.9 ± 0.2*	0.9 ± 0.3*	1.1 ± 0.3*	1.1 ± 0.3*
	glutamine	1.2 ± 0.4	0.9 ± 0.3*	0.9 ± 0.3*	1.0 ± 0.3*	1.2 ± 0.3*
30°/sec	placebo	2.3 ± 0.4	1.7 ± 0.5*	1.7 ± 0.4*	2.1 ± 0.3*	2.1 ± 0.4*
	glutamine	2.3 ± 0.3	1.7 ± 0.4*	1.7 ± 0.4*	2.0 ± 0.3*	2.1 ± 0.3*
0°/sec	placebo	2.5 ± 0.8	1.8 ± 0.7*	2.2 ± 0.8*	2.3 ± 0.8*	2.3 ± 0.8*
	glutamine	2.4 ± 0.6	1.8 ± 0.5*	1.9 ± 0.5*	2.0 ± 0.5*	2.3 ± 0.6*

Note. Data are presented as means ± SD. Preex = preexercise, Postex = postexercise. **p* < .05 from preex; †*p* < .05 versus placebo at the same time point; §*p* < .05 versus women (same condition and time point).

For the entire sample, there was also a main effect of Time [*F*(4,56) = 85.5, *p* < .001] such that normalized peak torque (Nm/kg) decreased from preexercise values in both supplement conditions at 0, 24, 48, and 72 hr postexercise (Table 2). This effect was similar between the men and women (Table 2).

Relative Torque (% Preexercise) For the entire sample, and both sexes, there was a main effect of Time [*F*(4,11) = 82.7, *p* < .001] such that relative peak torque (% Preexercise) decreased in both supplement conditions at 0, 24, 48, and 72 hr postexercise (Figure 4).

L-glutamine resulted in higher peak torque values versus Placebo for the entire sample and Men only at the 48, and 72 hr postexercise time points. However, there were no differences in absolute isometric peak torque between supplement conditions in the Women.

Perceived Knee Extensor Muscle Soreness Ratings

For the entire sample, there was a Supplement × Time interaction [*F*(4,56) = 6.7, *p* < .001] for ratings of per-

ceived knee extensor muscle soreness (Figure 5). Specifically, L-glutamine supplementation produced lower ratings of knee extensor soreness than placebo at the 24, 48 and 72 hr postexercise time points (Figure 5). This interaction was similar for women [*F*(4,56) = 5.0, *p* = .004]. However, in men, muscle soreness ratings with L-glutamine supplementation were only lower than placebo at the 48 and 72 hr postexercise time points (Figure 5).

For the entire sample, there was a main effect of Supplement [*F*(1,14) = 13.3, *p* = .003] such that muscle soreness ratings were lower in the L-glutamine versus placebo condition (Figure 5). There was also a main effect for Time [*F*(4,56) = 57.1, *p* < .001] such that all postexercise muscle soreness ratings were higher than preexercise values in both supplement conditions. This effect was similar between men [*F*(4,56) = 36.7, *p* < .001] and women [*F*(4,56) = 36.3, *p* < .001].

Discussion

The major finding of this study is that oral L-glutamine supplementation resulted in significantly less strength

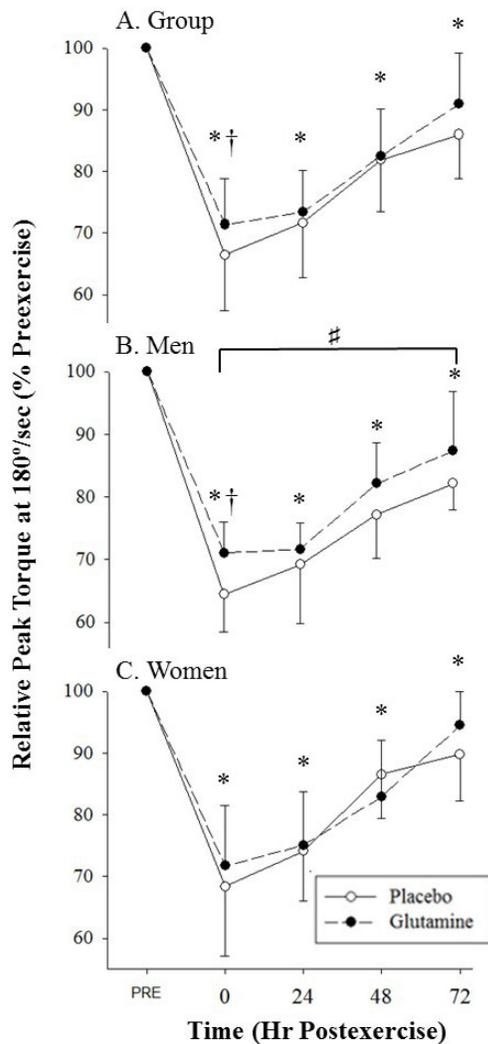


Figure 2 — Changes in concentric knee extensor peak torque at 180°/sec following a bout of eccentric exercise expressed as a percentage of preexercise (Pre) values for the entire sample (A) and separated between men (B) and women (C). * $p \leq .01$ versus preexercise for both supplement conditions; † $p < .01$ between supplement conditions at the same time point; ‡, main effect ($p = .05$) of supplement (L-glutamine > placebo) on postexercise peak torques. All data are expressed as means \pm SD. Data from the placebo condition are represented by open circles. Data from the L-Glutamine condition are represented by the black filled circles.

loss and muscle soreness compared with the placebo condition. The benefit of L-glutamine supplementation on knee extensor peak torque recovery was greater in men than women. To our knowledge, this study represents the first test of the effectiveness of glutamine supplementation ameliorating the symptoms of eccentric exercise-induced muscle damage (i.e., force loss and muscle soreness) in a group that included women.

A possible mechanism for the observed effect that L-glutamine supplementation had on peak torque recov-

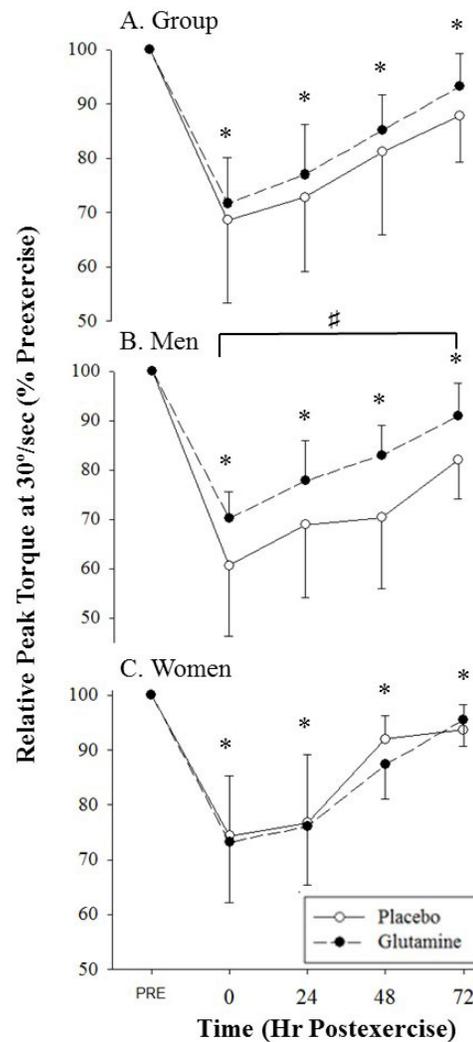


Figure 3 — Changes in concentric knee extensor peak torque at 30°/sec following a bout of eccentric exercise expressed as a percentage of preexercise (Pre) values for the entire sample (A) and separated between men (B) and women (C). *, $p \leq .01$ versus preexercise for both conditions; †, main effect ($p = .01$) of supplement (L-glutamine > placebo) on postexercise peak torques. All data are expressed as means \pm SD. Data from the placebo condition are represented by open circles. Data from the L-Glutamine condition are represented by the black filled circles.

ery following eccentric exercise is an attenuation of the inflammatory response (Antonio et al., 2002). A local inflammatory response is observed in skeletal muscle posteccentric exercise (Clarkson & Hubal, 2002) with the timing and magnitude of leukocyte infiltration associated with decrements in muscle function (Street et al., 2011). Glutamine, like other amino acids, promotes an anabolic state in the muscle; enhancing protein synthesis (MacLennan et al., 1987; Wu & Thompson, 1990). A basic hypothesis is that glutamine supplementation may

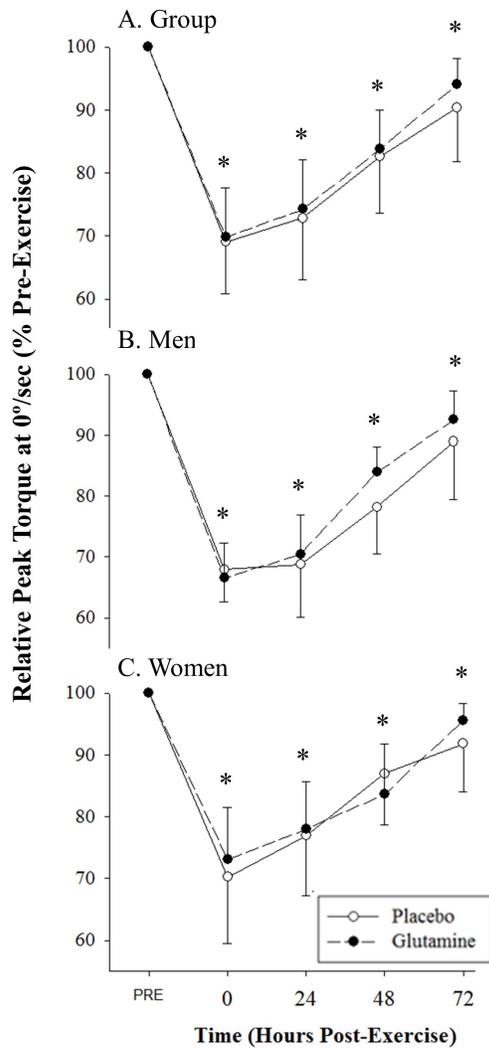


Figure 4 — Changes in isometric knee extensor peak torque at 45° knee flexion following a bout of eccentric exercise expressed as a percentage of preexercise (Pre) values for the entire sample (A) and separated between men (B) and women (C). *, $p \leq .01$ versus preexercise for both conditions; † $p < .01$ between supplements at the same time point: All data are expressed as means \pm SD. Data from the placebo condition are represented by open circles. Data from the L-Glutamine condition are represented by the black filled circles.

improve muscle function by attenuating the inflammatory response to eccentric exercise (Street et al., 2011). After mitigating the inflammatory response, the increased availability of glutamine promotes protein synthesis and the recovery process as demonstrated by decreased strength loss (i.e., quicker recovery to preexercise values) and perceived muscle soreness. However, these protein synthesis results were based on studies in which glutamine was infused directly into the rat hind limb (MacLennan et al., 1987) or chick skeletal muscle (Wu & Thompson, 1990). Whether oral glutamine supplementation has the same beneficial effect on skeletal muscle protein syn-

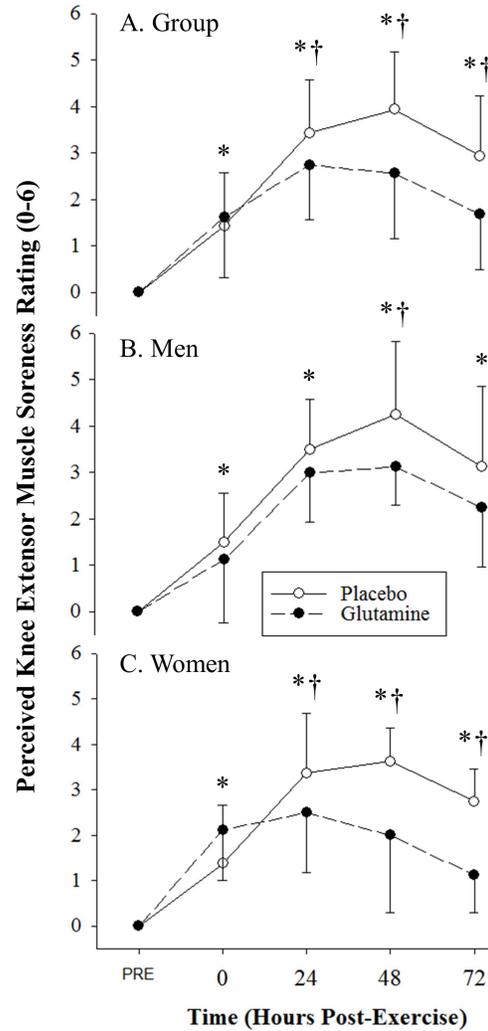


Figure 5 — Changes in perceived muscle soreness ratings on active movement of the knee extensors following a bout of eccentric exercise for the entire sample (A) and separated between men (B) and women (C).*, $p < .01$ versus preexercise (Pre) for both conditions; † $p < .01$ between supplements at the same time point. All data are expressed as Means \pm SD. Data from the placebo condition are represented by open circles. Data from the L-Glutamine condition are represented by the black filled circles.

thesis in healthy humans is not known. Furthermore, it has been documented that ~70% of orally administered glutamine may be degraded by the splanchnic tissues in the first pass (Wu, 1998), thus potentially minimizing its bioavailability in the systemic circulation. However, a 50% increase in plasma glutamine concentrations within 30 min of ingestion have been reported with an acute oral dose of 0.1 g·kg body mass⁻¹ (Castell & Newsholme, 1997), which is a third of the dose used in the current investigation. A limitation of the current study included the lack of venous blood measurements of plasma glutamine concentrations. Therefore, we cannot conclude

that the improved peak torque recovery observed in the L-glutamine condition was associated with a concurrently elevated plasma glutamine concentration.

Our findings are in agreement with the study conducted by Street et al. (2011) in which the greatest benefit of glutamine supplementation on peak torque recovery of the knee extensors was observed at higher (180°/sec) but not lower (30°/sec) angular velocities or peak isometric contractions. This may be due to the standardized order of the muscle torque testing protocol. Specifically, participants performed the same order of testing each day (i.e., 180°/sec, 30°/sec, and then 0°/sec). Randomizing the order of the testing protocol would have removed the order effect and the influence of fatigue on peak torque measures during the subsequent tests.

L-glutamine supplementation resulted in lower perceived muscle soreness ratings at 24, 48, and 72 hr compared with the placebo condition. Glutamine supplementation was also effective in reducing muscle soreness, and perhaps damage, experienced immediately after the exercise protocol as observed by significantly greater peak torque of dynamic knee extension at 180°/sec compared with the placebo supplement. Although reduced muscle soreness might indicate less muscle damage, direct measurements are required to confirm this hypothesis.

Glutamine can be synthesized by branched-chain amino acid metabolism. As such, it is possible that protein and/or amino acid supplementation may promote glutamine synthesis and release following eccentric exercise (Negro et al., 2008). Preexercise supplementation of amino acids has been shown to attenuate the symptoms of eccentric-exercise induced muscle damage (Shimomura et al., 2006; Nosaka et al., 2006). Shimomura et al. (2006) reported branched chain amino acid supplementation before squat exercise delayed the onset muscle soreness as early as 24 hr postexercise. It has also been reported that branched chain amino acid supplementation before exercise attenuates the breakdown of muscle proteins during exercise (Matsumoto et al., 2009; Shimomura et al., 2004; Howatson et al., 2012) and may promote protein synthesis (MacLean et al., 1994; Matsumoto et al., 2007) in skeletal muscle, suggesting that an L-glutamine supplementation may alleviate exercise-induced muscle damage and promote recovery from the damage. Currently there is no general consensus on the underlying mechanism of muscle soreness following eccentric exercise making it difficult to speculate the role glutamine may play in ameliorating muscle soreness. A potential etiological factor is the increased activation of nociceptors induced by mechanical deformation or swelling (side effects of muscle damage) which may lower the threshold for the stimulation of pain (Clarkson & Hubal, 2002).

There appears to be a potential sex difference in response to L-glutamine supplementation in which men are driving the response of the entire sample. There was an interaction effect in men with significant differences between conditions at 0 and 72 hr postexercise in dynamic peak torque at 180°/sec (Figure 2b). There was also a

main effect of supplement (L-glutamine > Placebo) in men during dynamic peak torque at 30°/sec (Figure 3b). In women, there was no main effect of supplement nor an interaction effect during any of the peak torque measurement protocols. This study provides rationale for future investigations to explore the potential mechanisms related to sex differences in the therapeutic response to L-glutamine supplementation. Animal studies have consistently described differences between males and females in the response to eccentric exercise with female animals demonstrating less muscle damage as indicated by diminished serum creatine kinase, myofibrillar disruption and inflammatory responses (Clarkson & Hubal, 2001). These differences have been attributed to the effects of estrogen on diminishing plasma creatine kinase efflux in skeletal muscle (Clarkson & Hubal, 2001). Only a few studies have examined sex differences in skeletal muscle inflammatory responses following strenuous eccentric exercise (MacIntyre et al., 2000; Stupka et al., 2000). Results demonstrated from Stupka et al. (2000) and MacIntyre et al. (2000) proposed that women have a greater initial inflammatory response to exercise, as observed by significantly higher neutrophil accumulation 2 and 4 hr after high-force eccentric exercise. However, women appear to have an attenuated long-term inflammatory response, which was demonstrated by greater leukocyte and antigen-positive inflammatory cells 48 hr after high-force eccentric exercise in men versus women (Clarkson & Hubal, 2001). Based on this evidence, women in the current study would have only benefited from exogenous L-glutamine during the acute (<24 hr) phase of the postexercise recovery period.

Esbjörnsson et al. (2012) reported a pronounced sex difference in the accumulation of plasma ammonia after sprint exercise with significantly lower plasma ammonia concentrations in women. This observation was linked with the greater amount of adipose tissue in women and the ability of adipocytes to buffer plasma ammonia, which combines with glutamate to form glutamine via the enzyme glutamine synthetase. This hypothesis was supported by the finding that plasma glutamine concentrations increased significantly in women, but not in men, following the sprint exercise (Esbjörnsson et al., 2012). Therefore, the effect of exogenous glutamine supplementation in the current study might have been minimized in women due a greater buffering of plasma ammonia and endogenous production of glutamine by adipocytes.

Conclusions

In conclusion, the current study supports previous research by Street et al. (2011) in the efficacy of oral glutamine supplementation providing a therapeutic benefit by promoting recovery from eccentric exercise induced muscle damage. L-glutamine supplementation attenuated the magnitude of strength loss, improved the time course of strength recovery, and diminished muscle soreness more rapidly in comparison with an isoenergetic placebo. Mechanisms explaining our observations for a

sex difference in the therapeutic response to exogenous glutamine supplementation, with men demonstrating a faster recovery of peak torque, requires further investigation.

Acknowledgments

Infrastructure for this project was supported through a Canadian Foundation for Innovation: John R. Evans Leaders Fund awarded to D.S. Kimmerly. The authors have no conflicts of interest to report.

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