Nutraceutical Effects of Branched-Chain Amino Acids on Skeletal Muscle 1,2,3

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ABSTRACT BCAA catabolism in skeletal muscle is regulated by the branched-chain α-keto acid dehydrogenase (BCKDH) complex, located at the second step in the BCAA catabolic pathway. The activity of the BCKDH complex is regulated by a phosphorylation/dephosphorylation cycle. Almost all of BCKDH complex in skeletal muscle under normal and resting conditions is in an inactive/phosphorylated state, which may contribute to muscle protein synthesis and muscle growth. Exercise activates the muscle BCKDH complex, resulting in enhanced BCAA catabolism. Therefore, exercise may increase the BCAA requirement. It has been reported that BCAA supplementation before exercise attenuates the breakdown of muscle proteins during exercise in humans and that leucine strongly promotes protein synthesis in skeletal muscle in humans and rats, suggesting that a BCAA supplement may attenuate muscle damage induced by exercise and promote recovery from the damage. We have examined the effects of BCAA supplementation on delayed-onset muscle soreness (DOMS) and muscle fatigue induced by squat exercise in humans. The results obtained showed that BCAA supplementation prior to squat exercise decreased DOMS and muscle fatigue occurring for a few days after exercise. These findings suggest that BCAAs may be useful for muscle recovery following exercise. J. Nutr. 136: 529S–532S, 2006.

KEY WORDS: • BCKDH complex • exercise • branched-chain amino acids • muscle fatigue
• muscle soreness

Leucine, isoleucine, and valine possess a similar structure with a branched-chain residue and therefore are referred to as BCAAs. All are essential amino acids for animals and share a common membrane transport system and enzymes for their transamination and oxidative decarboxylation (see below) (1,2), indicating that they are closely related in their metabolic fate.

BCAAs account for 35–40% of the dietary essential amino acids in body protein and 14–18% of the total amino acids in muscle proteins (3,4). The muscle mass of humans is ~40% of the body weight; the muscle protein pool therefore represents a very large reservoir of BCAA in the body. On the other hand, animals have a free amino acid pool, which appears to be constant, and the content of free BCAAs in the human skeletal muscle is only ~0.1 g (0.6–1.2 mmol)/kg muscle (2). This pool of free BCAAs is extremely small compared with the BCAA content of muscle proteins. The total concentration of BCAA in human blood (0.3–0.4 mM) is relatively high compared with that of the other amino acids (except glutamine) (5,6). However, the amount of BCAAs in human blood is also very small compared with that in muscle proteins. Recent studies have demonstrated that free BCAAs, especially leucine, play a very important role in protein metabolism; leucine promotes protein synthesis and inhibits protein degradation via mechanisms involving the mammalian target of rapamycin (7,8). These findings suggest that leucine is not only a building block of proteins but also a modulator of protein metabolism. From this background, it is interesting to consider the efficacy of BCAAs when these amino acids are ingested as a supplement. Here, we describe regulation of the BCAA catabolism during exercise and a nutraceutical effect of these amino acids on skeletal muscle in relation to exercise.

Regulation of BCAA catabolism

All of the steps of the BCAA catabolic pathway are located in mitochondria (1). The first two steps in the pathway are common to the three BCAAs (Fig. 1). The first reaction,
Branched-chain amino acids

**FIGURE 1** The first two steps in the BCAA catabolic pathway. KIV, α-ketoisovalerate; KMV, α-keto-β-methylvalerate; KIC, α-ketoisocaproat e; CoA-SH, coenzyme A, reduced form; IB-CoA, isovaleryl-CoA; MB-CoA, α-methylbutyryl-CoA; IV-CoA, isovaleryl-CoA; R-CoA, acyl-CoA; Pase, phosphatase. Adapted from Shimomura et al. (9).

### Exercise enhances BCAA catabolism

**Effects of BCAA supplementation on muscle soreness and muscle fatigue induced by squat exercise in humans: a preliminary study**

An oral BCAA supplement (77 mg/kg body weight) before exercise has been reported to increase intracellular and arterial BCAA levels during exercise, resulting in the suppression of endogenous muscle protein breakdown (25). Oral BCAA administration (12 g/d for 2 weeks and additionally 20 g each before and after the exercise test) also reportedly suppresses the rise in serum creatine kinase activity for several days after exercise (26). These findings suggest that BCAA supplementation might reduce muscle damage induced by exercise. Therefore, we conducted a preliminary human study to evaluate whether BCAA supplements might attenuate muscle soreness and muscle fatigue induced by exercise.

Young healthy female and male adults, who did not take regular exercise, were recruited, and 16 female and 14 male subjects aged 21–24 y old participated (BMI 21.6 ± 0.5 kg/m² for females and 22.2 ± 0.8 kg/m² for males). Squat exercise was used to induce delayed-onset muscle soreness (DOMS) and muscle fatigue. The composition of the test solutions used in
Muscle soreness in females was highest on the second and third days in the placebo trial, indicating that DOMS occurred following the squats exercise trials (Fig. 2A). However, although DOMS also occurred after the BCAA trial, peak soreness occurred only on the second day and was significantly lower than that which occurred following the placebo trial (Fig. 2A). DOMS on days 3–5 in females was also significantly lower in the BCAA trial than in the placebo (Fig. 2A). In male subjects, DOMS peaked on the second day and tended to be lower in the BCAA than in the placebo trial throughout the test period, although the differences did not attain statistical significance (Fig. 2B). However, the calculated area under the curve for muscle soreness over the 5-d period was lower in the BCAA trial than in the placebo trial in both sexes (data not shown). The suppression of DOMS by BCAA supplementation appeared to be slightly less in male subjects than in female subjects. The reason for the sex difference is not clear, though it may be related to the smaller BCAA dose ingested by males because of their greater body mass: male subjects ingested 77 ± 3 mg/kg body weight, whereas females consumed 92 ± 2 mg/kg body weight. Further study is required to clarify this point.

Muscle fatigue in female and male subjects was highest right after exercise and gradually decreased during the following 4 d in both the BCAA and placebo trials (data not shown). The fatigue reported during the 4 d after the exercise trial (from the second through fifth days) in both sexes tended to be lower in the BCAA trial than in the placebo trial.

The results obtained in this preliminary study indicate that the ingestion of 5 g of BCAAs before exercise can reduce DOMS and muscle fatigue for several days after exercise. The mechanisms that underlie these BCAA effects have not yet been examined. However, one possibility is that BCAA may attenuate exercise-induced protein breakdown, while leucine may stimulate muscle protein synthesis. If the finding is substantiated, the results could support the usefulness of BCAA in muscle recovery from exercise. Further studies are required to elucidate the mechanisms responsible for the effects of BCAA supplementation.

**LITERATURE CITED**


**FIGURE 2** Effect of the BCAA supplement on DOMS induced by squat exercise. (A) females; (B) males. Values are means ± SEM for 16 females and 14 males. *P < 0.05 to the corresponding placebo trial (Wilcoxon signed-rank test).


