Isolated Leucine and Branched-Chain Amino Acid Supplementation for Enhancing Muscular Strength and Hypertrophy: A Narrative Review

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Branched-chain amino acids (BCAA) are one of the most popular sports supplements, marketed under the premise that they enhance muscular adaptations. Despite their prevalent consumption among athletes and the general public, the efficacy of BCAA has been an ongoing source of controversy in the sports nutrition field. Early support for BCAA supplementation was derived from extrapolation of mechanistic data on their role in muscle protein metabolism. Of the three BCAA, leucine has received the most attention because of its ability to stimulate the initial acute anabolic response. However, a substantial body of both acute and longitudinal research has now accumulated on the topic, affording the ability to scrutinize the effects of BCAA and leucine from a practical standpoint. This article aims to critically review the current literature and draw evidence-based conclusions about the putative benefits of BCAA or leucine supplementation on muscle strength and hypertrophy as well as illuminate gaps in the literature that warrant future study.

Keywords: anabolism, BCAA, muscular adaptations, muscle mass

Of the 20 amino acids recognized to compose the building blocks of human protein, only three possess a branched side chain: leucine, isoleucine, and valine. Numerous supplements are sold consisting of these three amino acids, collectively known as the branched-chain amino acids (BCAA), with claims that they enhance muscular adaptations. The validity of these claims has been an ongoing source of controversy in the sports nutrition field despite the immense popularity of BCAA among athletes and the general public.

Branched-chain amino acids have many important physiological roles and characteristics. The BCAA comprise three of nine amino acids that are considered to be essential amino acids (EAA) given that they cannot be synthesized endogenously and, thus, must be acquired via diet to sustain human health (Wu et al., 2013). The BCAA contain an aliphatic side chain with a branch that carries a carbon atom attached to three or more carbon atoms. The BCAA are among the most hydrophobic of amino acids, allowing them to be particularly effective in maintaining the stability of folded proteins and carrying out functions for globular proteins (Brosnan & Brosnan, 2006). Due to their amphipathic helices, BCAA also specifically interact with both lipid acyl chains and head groups (Brosnan & Brosnan, 2006).

The unique properties of BCAA make them of integral importance for skeletal muscle metabolism. Thus, BCAA have long been viewed as potential candidates for supplementation. The BCAA facilitate the ability of muscle fibers to absorb blood sugar and modulate insulin signaling (Yoon, 2016). Most notably, BCAA are important regulators of muscle protein metabolism where they function in many capacities and are unique in that they largely bypass first-pass metabolism in the liver (Brosnan & Brosnan, 2006). Of the three BCAA, leucine is most notably a key regulator of muscle protein synthesis (MPS), exerting modulating effects even in the presence of hyperaminoacidemia (Rieu et al., 2006).

Much of the early data on BCAA supplementation came from rodent studies. These studies suggested that BCAA in rats may be rate limiting for MPS, and thus, supplementation could have a hypertrophic benefit (Buse, 1981; Garlick & Grant, 1988). However, such findings have questionable generalizability to humans. In particular, rats possess a much smaller percentage of skeletal muscle mass compared with humans. Moreover, processes involved with regulating MPS differ from that in humans at both the initiation and translation stages (Wolfe, 2017). For these reasons, this review will focus on human data.

Branched-chain amino acids, and leucine in particular, play an integral role in muscle protein metabolism (Matthews, 2005). However, the context in which supplementation occurs must be taken into account when evaluating the efficacy of BCAA and/or leucine supplementation for muscle hypertrophy and strength. There are many important factors that may influence findings on this topic, including diet (total macronutrient and energy intake), the presence or lack of a resistance training (RT) component, timing of ingestion, whether other amino acids were consumed, population demographics, measurement protocols, and other considerations. These factors and their lack of standardization between

studies make it difficult to form strong conclusions about BCAA supplementation. That said, scrutiny of the available data allows us to draw important inferences from a practical standpoint. The purpose of this article will be to review the current literature and draw evidence-based conclusions about the putative benefits of BCAA supplementation on muscle strength and hypertrophy as well as to point out gaps in the literature that warrant future study.

BCAA and Net Muscle Protein Balance

A net positive addition of muscle proteins involves an increase in MPS and/or suppression of muscle protein breakdown (MPB; Glynn et al., 2010). Accretion of muscle proteins results from periods of positive net muscle protein balance (MPS > MPB) that exceed negative balance. However, the available evidence indicates that MPS is the main modulator of net muscle protein balance and, thus, protein accretion (Tipton et al., 2018). Biolo et al. (1997) observed that an amino acid infusion increased MPS, leading to positive net muscle protein balance with little change in MPB either at rest or after exercise. Muscle hypertrophy results from increased myofibrillar proteins (e.g., actin, myosin, troponin, etc.), in particular, and synthesis rates of these proteins are increased by resistance exercise and protein ingestion (Joanisse et al., 2020). Currently, the effect of nutrition and exercise on the breakdown of any individual muscle protein remains undetermined. It is also likely that some degree of increased MPB following exercise is an important factor in the synthesis of new proteins, although the specifics of this hypothesis remain undetermined. Given the greater relative importance of MPS and measurement difficulties with MPB, the focus of this section will be mainly on MPS and related anabolic signaling.

Protein synthesis is regulated by a network of intracellular signaling cascades that modulate mRNA translation at initiation and elongation. The major player in this regulatory network is mechanistic target of rapamycin (mTOR), or more specifically, mTOR Complex 1, the primary regulator of protein synthesis (Caron et al., 2010; Laplante & Sabatini, 2012). Energy and protein intake are the main nutritional effectors of mTOR Complex 1, which acts as a "nutrient sensor" and, thus, is permissive for MPS. In particular, the BCAA, largely modulated by leucine, activate signaling pathways that converge at mTOR Complex 1 (Blomstrand et al., 2006). Activated mTOR phosphorylates ribosomal protein s6 kinase 1 and eukaryotic initiation factor 4E-Binding protein-1, each of which uniquely allows for ribosomal binding (Showkat et al., 2014). Although it is clear the BCAA, and leucine in particular, stimulate mTOR and MPS (Kimball & Jefferson, 2006), evidence indicates that beyond a certain threshold of leucine and total protein intake, there is no further benefit to the MPS response (Breen & Phillips, 2012; Witard et al., 2014). Leucine is of particular interest here as the "leucine trigger" hypothesis asserts that MPS will be maximized at a threshold value below which maximal stimulation fails to occur (Breen & Phillips, 2012). The value most commonly referenced as the "threshold" for leucine is 2–3 g (Witard et al., 2016); however, further work is need to better elucidate how leucine needs differ depending on context. Most notably, threshold values in older adults are yet to be clearly established. The anabolic effects of total protein also are context dependent, but the optimal dose of high-quality protein for stimulating muscle protein accretion is likely between 20 and 40 g (Macnaughton et al., 2016) and would be dependent on factors such as training status, RT program, energy status, bodyweight, and potentially level of muscularity (Schoenfeld & Aragon, 2018). Thus, although it seems clear that BCAA are important, there is a threshold at which their effects become redundant. What that point is, and how best to reach it, has been investigated in different contexts with different nutrient and amino acid formulations.

Resistance training participation is an important consideration when assessing the potential efficacy of BCAA in optimizing the MPS response. A bout of resistance exercise has a well-documented role as a potent stimulator of the mTOR and MPS (Burd et al., 2010). Investigations have found that to maximize the MPS response, those engaging in resistance exercise have a higher need for EAA than those who do not. Churchward-Venne et al. (2012) compared the MPS responses during rest versus postresistance exercise by providing groups with either a 25 g dose of whey protein or a suboptimal dose of whey (6.25 g) matched for leucine content. Researchers found no significant between-group differences in the initial 1.5 hr period following the exercise bout; however, a significant difference in the MPS response favoring the 25 g dose of whey was noted at 3–4 hr postexercise. This finding suggests that sufficient EAA quantity as provided by the 25 g of whey protein is important for maximizing the MPS response when there is a higher need for amino acid building blocks, such as during the post-RT period.

Whereas the addition of BCAA to inadequate intact, isolated protein intake does not seem to elicit an MPS response equivalent to adequate postexercise protein intake, there may be situations in which MPS may be stimulated with a combination of inadequate protein and BCAA. Tipton et al. (2009) found that untrained participants who consumed 16.6 g of whey protein with 3.4 g of leucine had the same net protein balance as those who ingested 20 g of whey protein alone following a bout of resistance exercise. Similarly, Atherton et al. (2017) observed that in older and young adults ingesting a supplement that contained free leucine, 10 g protein, and 24 g carbohydrate, the response of MPS was enhanced following resistance exercise compared with 10 g of protein alone. Moreover, Churchward-Venne et al. (2012) demonstrated that ingestion of additional leucine with a suboptimal isolated protein source does not "rescue" the anabolic response to that of an adequate amount of protein. However, supplementation of leucine to an inadequate dose of whey protein in combination with carbohydrate coingestion was effective to stimulate MPS to the level of sufficient (25 g) protein (Churchward-Venne et al., 2014). The food matrix also seems to influence the anabolic response to protein and BCAA ingestion (Burd et al., 2019). Collectively, these studies suggest that MPS is maximized with adequate consumption of high-quality protein. However, in situations where there is not a whole protein source or sufficient EAA availability, a higher dose of leucine or the presence of other nutrients can "rescue" the MPS response.

Due to the effects of age-related anabolic resistance, higher doses of leucine are required in older adults to maximize the MPS response (Breen & Phillips, 2011). Although the exact etiology of anabolic resistance is yet to be fully elucidated, it is likely resultant to a convergence of many factors at the level of the muscle, nervous, and other interacting systems (Breen & Phillips, 2011; Wilkinson et al., 2018). Factors such as a reduction of motoneurons, anabolic hormones, blood flow, and higher chronic inflammation all likely contribute to a reduced sensitivity to anabolic stimuli. Although some functional decline is inevitable, the evidence does converge on an almost complete attenuation of anabolic resistance in older individuals who have maintained physical function, partake in RT, and consume higher doses of protein/leucine (Breen & Phillips, 2011). Katsanos et al. (2006) observed that 1.7 g of leucine given to older adults within an EAA mixture was inadequate to

match the MPS response in younger adults; however, 2.8 g of leucine proved sufficient for this purpose. Thus, older adults can maximize MPS by ingesting extra leucine to equal ~3 g or ingesting doses of high-quality protein (~30–35 g) that reach leucine thresholds (Koopman et al., 2009; Pennings et al., 2012; Symons et al., 2009).

Although we know that adequate leucine augments the anabolic response acutely in older individuals, it may also sensitize the anabolic response on a more chronic basis. To investigate this, Casperson et al. (2012) measured the anabolic response to the same meal before and after 2 weeks of leucine supplementation. The results showed that supplementing 4 g of leucine on a chronic basis produced higher rates of MPS with ingestion of the same meal that was administered preintervention. These results suggest that older individuals might be able to achieve an "anabolic sensitization" effect over time with higher levels of leucine intake.

What emerges when assessing the available evidence is that a hierarchy exists to the requisite amino acid building blocks that would ensure the most robust anabolic response. Whole intact proteins > EAA > BCAA > leucine alone represents the hierarchy of anabolic stimulation provided that sufficient leucine is present in each condition (Moberg et al., 2016). Leucine alone may stimulate the translational pathways, but without sufficient EAA building blocks to sustain MPS, the response is limited (Churchward-Venne et al., 2012). Although BCAA contain two additional building blocks that have their own unique contribution to the MPS response, other EAA are still limited (Jackman et al., 2017). Moreover, isoleucine and valine may compete with leucine for transport into the muscle cell, thus further limiting the effectiveness of BCAA alone (Churchward-Venne et al., 2014). High-quality intact proteins provide the full complement of EAA and, if contained in a food matrix, will be ingested with other constituents that could potentially enhance hypertrophic adaptations (Burd et al., 2019; Mobley, Mumford, et al., 2017; van Vliet et al., 2017). We have likely only scratched the surface in identifying components in whole food sources that have the potential to induce an anabolic response. Some examples include dairy exosomes seen in whey protein (Mobley, Mumford, et al., 2017), fat contained in whole milk (Elliot et al., 2006), and undetermined properties in whole eggs (Bagheri et al., 2020; van Vliet et al., 2017). It is also noteworthy that most studies employ a dose of approximately 20–25 g of protein as the treatment because this dose is thought to maximally stimulate MPS and ensure that leucine is at or above threshold values (Churchward-Venne et al., 2012). In contrast, Macnaughton et al. (2016) compared 20 g versus 40 g whey protein ingested after a high-volume session totaling 20 sets of full-body training and found that a 40 g dose elicited a ~20% greater MPS response. Thus, it remains possible that consumption of more protein and sufficient EAA is of greater consequence when intensive resistance exercise involves a large amount of muscle mass. Recently, Park et al. (2020) reported that a 70 g dose of protein elicited a greater MPS response than 35 g. This breach of previously assumed limits of protein dosing to maximize the acute anabolic response might be explained by the use of older subjects and a slowly digested protein source (beef patties) within a mixed-macronutrient meal. Whereas it is clear that sufficient EAA is requisite for maximizing MPS, the amount that is sufficient changes with context.

BCAA and Muscle Hypertrophy

Although acute data offer important mechanistic insights, scrutiny of longitudinal research is needed to fully elucidate the effects of BCAA supplementation on hypertrophic adaptations (see Table 1).

In this regard, findings largely show that young and middle-aged individuals consuming adequate protein receive no additional benefit from BCAA supplementation. Spillane et al. (2012) observed no significant changes in lean-body mass in participants who ingested 9 g/day of BCAA compared with placebo. Evidence with larger leucine doses also showed no added benefit when adequate protein (≥ 1.6 g$\cdot$kg$^{-1}\cdot$day^{-1}) was consumed (Aguiar et al., 2017; DE Andrade et al., 2020). Mobley, Mumford, et al. (2017) reported no hypertrophic differences between supplementation with placebo, 3 g of leucine alone, or 25 g of whey protein (standardized for leucine content) during 12 weeks of RT. All participants in the study reported ingesting ~1.8 g$\cdot$kg$^{-1}\cdot$day^{-1} of protein, after which supplementation conferred no additional benefits to muscle protein accretion. Interestingly, the group that consumed whey protein alone had a higher satellite cell number, suggesting an increased potential for long-term/subsequent growth. Similarly, DE Andrade et al. (2020) showed that supplementation with 10 g/day leucine did not enhance gains in muscle mass or strength when compared with an isonitrogenous control during 12 weeks of RT. Overall, the evidence appears clear that in the presence of adequate daily protein provision, there is no further benefit to additional leucine or BCAA supplementation on measures of muscle hypertrophy.

Although it seems clear that BCAA supplementation has little or no efficacy for enhancing gains in muscle mass during RT with sufficient energy and protein intake, there is some evidence that muscle loss may be minimized by BCAA during energy restriction. Dudgeon et al. (2016) reported that trained, college-aged males better maintained lean body mass with RT in a hypocaloric condition while being supplemented with BCAA. However, Dieter et al. (2016) noted that this study had significant issues, including the inappropriate use of statistical testing that may have unduly biased results. Unsupervised training sessions, lack of supervised supplement administration, lack of any diet reporting or monitoring, a small sample size, and other issues further call into question the validity of these findings. In particular, the BCAA group did not lose fat mass during the intervention, suggesting a lack of adherence to the low energy diet. Future work should investigate the potential efficacy of BCAA in hypocaloric conditions as this area remains understudied. Moreover, it is clear that increased protein intake leads to maintenance of muscle during RT with energy restriction (Mettler et al., 2010). Thus, it is questionable whether BCAA supplementation would further enhance the response of muscle during energy restriction. Since direct and kinetic evidence supports the general superiority of intact, high-quality protein over BCAA alone in other contexts, a logical rationale is lacking for ingestion of BCAA over a more complete protein source regardless of energy status.

There is evidence of the potential hypertrophic benefits of BCAA, leucine in particular, in older individuals. However, it must be interpreted from the lens of a lack of standardization and generally low protein intakes in the studies available. A meta-analysis by Komar et al. (2015) aimed to synthesize the literature relating to leucine supplementation and its effects on anthropometric parameters such as lean body mass (LBM), body mass index, and body weight in older individuals and those prone to sarcopenia. Supplementation increased body weight, LBM, and body mass index. The authors concluded that supplementation of various protein products containing at least 2 g/day of leucine independent of training exerted beneficial effects on body composition measures in those prone to sarcopenia. However, only one study meeting inclusion criteria matched participants for protein intake ~0.99 g/kg (Verhoeven et al., 2009). The intervention arm in

Table 1 Longitudinal Studies With BCAA/Leucine and an RT Component

Study	Population	Duration/RT	Dietary reporting	Supplement	Supplement timing	Outcome measures	Between-group strength results	Between-group body composition results
Spillane et al. (2012)	19 untrained males (18–35 years old) BCAA: $n = 10$ PLA: $n = 9$	8 weeks: 4 days/week Upper lower Supervised	Average protein intake reported: ~1.14 g/kg of body mass for both groups. No significant differences reported between groups.	BCAA: 9 g BCAA (2:1:1, leucine: isoleucine: valine).	Training days (4×/week): Half dose pre- and postexercise within 30 min.	Strength: 1RM bench press and leg press. Body composition: Percentage body fat, fat mass, and fat-free mass were determined using DXA.	No significant differences between groups.	No significant differences between groups.
Dudgeon et al. (2016)	17 resistance-trained males (21–28 years old) BCAA: $n = 9$ CHO/PLA: $n = 8$	8 weeks: 4 days/week Bodybuilding split Unsupervised	Subjects were prescribed hypocaloric diet, but there was no dietary reporting.	BCAA: 14 g (2:1:1)	Training days (4×/week): 7 g pre- and postworkout for a total of 14 g.	Strength: 1RM Bench press and back squat. Followed by repetitions to failure at 80% 1RM. Body composition: Percentage body fat, fat mass, and fat-free mass were determined using hydrostatic weighing.	BCAA group bench 1RM increased (7.1 ± 1.6 kg; $p < .05$), CHO group bench 1RM decreased (-3.7 ± 2.3 kg; $p < .05$), which was a significant difference between groups ($p < .01$). The CHO group exhibited an increase in repetitions to fatigue (5.3 ± 0.2; $p < .05$) in the squat with no changes observed in the BCAA group.	Body mass did not change in the BCAA group, but the CHO group had a significant ($p < .05$) reduction in body mass (-2.3 ± 0.7 kg). There was a significant ($p < .05$) loss in lean mass (-0.90 ± 0.06 kg) and a nonsignificant loss in fat mass 1.4 kg ($p > .05$). BCAA group showed no change in lean mass. However, the BCAA group exhibited a significant ($p < .05$) decrease in fat mass (-0.05 ± 0.08 kg). When looking at the raw values, doubt is cast on the magnitude of the deficit in the BCAA group with oddities in the statistical findings (i.e., CHO lost a lot more fat mass and BCAA group lost very little).
Mobley, Haun, et al. (2017)	75 untrained college age males (20–22 years old) PLA: $n = 15$ LEU: $n = 14$ WPC: $n = 17$ WPH: $n = 14$ SPC: $n = 15$	12 weeks: 3×/week Full-body DUP Supervised	All groups reported consuming at least ~1.3 g/kg body mass per day. There were some significant Group × Time interactions for protein intake at different time points and groups. Refer to "Table 4" of Mobley (2017).	Supplement contained other nutrients (see "Table 2" of Mobley 2017) Protein: PLA: 0.4 g LEU: 2.3 g WPC: 26.3 g WPH: 25.4 g SPC: 39.2 g Matched for ~3.0 g leucine.	Training days (3×/week): Given prior to training and instructed to consume 30 min prior to sleep. Nontraining days: Instructed to consume between a meal and before sleep.	Strength: 3RM squat and bench press, isometric mid-thigh pull. Body composition: Percentage body fat, fat mass, and fat-free mass were determined using DXA. Leg muscle thickness was assessed using ultrasound.	No significant differences between groups.	No significant differences between groups.

(continued)

Table 1 (continued)

Study	Population	Duration/RT	Dietary reporting	Supplement	Supplement timing	Outcome measures	Between-group strength results	Between-group body composition results
Aguiar et al. (2017)	20 healthy young participants assigned to two groups: PLA ($n = 10$) LEU ($n = 10$)	8 weeks: 2×/week Lower body Supervised	Groups reported consuming ~1.7 g/ kg of body mass per day. No significant differences reported between groups.	3 g/day leucine	Postworkout	Strength: Training load adjusted and monitored during RT program. Body composition: mCSA of the VL and RF via ultrasound.	No significant differences between groups.	No significant difference between groups.
De Andrade et al. (2020)	25 resistance-trained men randomly assigned to two groups: PLA ($n = 13$) LEU ($n = 12$)	12 weeks: 2×/week lower body supervised. Continued upper body training not supervised.	Participants had a protein intake of 1.8 ± 0.4 g protein·kg⁻¹·day⁻¹. No significant differences reported between groups.	10 g/day leucine	Two separate 5-g doses (5 g at ~8:00 AM and 5 g immediately postworkout ~6:00 PM).	Strength: Leg press 1RM Body composition: mCSA of the VL via ultrasound.	No significant differences between groups.	No significant differences between groups.
Kim et al. (2012)	A total of 155 women aged 75+ years defined as sarcopenic assigned to four groups: Exercise + AA supplementation ($n = 38$) Exercise ($n = 39$) AA supplementation ($n = 39$) HE ($n = 39$)	12 weeks: Each session had a 5-minute warm up, 30 minutes strengthening exercise, 20 minutes of balance and gait training, and a 5-minute cool down.	Not reported	3 g EAA packets (42% leucine, 10.5% valine, and 10.5% isoleucine) taken twice daily (6 g total) for 3 months.	3 g twice daily; participants recorded intake on what time of day and the amount taken daily, but no specific timing mentioned.	Strength/function: Pre and post physical fitness test (usual and maximum walking speeds, knee extension strength). Body composition accessed via BIA.	Significant Group × Time interaction for usual and maximum walking speeds (exercise + AA and exercise > HE). Knee extension strength was only significantly greater in the exercise + AA group compared with HE, but no significant differences were found between exercise and exercise + AA supplementation.	Significant Group × Time interaction for leg muscle mass (exercise + AA > HE). No significant differences between exercise and exercise + AA supplementation.
Bagheri et al. (2020)	30 untrained, sedentary, postmenopausal women (≥50 years and ≤60 years) BCAA: $n = 10$ PLA: $n = 10$ CON: $n = 10$	8 weeks: 3 days/week Full body Supervised	Average protein intake reported: PLA: 0.75 g/kg BCAA: 0.71 g/kg No significant differences reported between groups.	BCAA: 9 g (2:1:1)	Training days (3×/week): half dose pre- and postexercise within 30 min.	Strength: Isometric knee extension, isometric handgrip strength, and predicted 1RM (leg press and bench press) based on <10RM. Body composition: BMI, body fat percentage, and muscle mass were determined using a multifrequency BIA device.	No significant differences between groups.	No significant differences between groups.

Abbreviations: AA = amino acids; BCAA = branched-chain amino acids; DXA, dual-energy X-ray absorptiometry; CHO = carbohydrates; EAA = essential amino acids; RT = resistance training; BMI = body mass index; mCSA = muscle cross-sectional area; VL = vastus lateralis; RF = rectus femoris; HE = Health Education; BIA = bioelectrical impedance analysis; 1RM = one-repetition maximum; PLA = placebo; CON = control; LEU = L-leucine; WPC = whey protein concentrate; WPH = whey protein hydrolysate; DUP = daily undulating periodization; SPC = soy protein concentrate.

this study was supplemented with 7.5 g/day of leucine; no hypertrophic benefits were observed above placebo. Less heterogenous data and more standardization would greatly strengthen conclusions on this topic.

Additional evidence is particularly needed in older individuals consuming leucine or BCAA in conjunction with an RT program. Komar et al. (2015) contained an RT arm and observed greater improvements in lean mass in women with sarcopenia who received an EAA supplement (Kim et al., 2012). As participants were provided with a full complement of EAA, this precludes the ability to draw conclusions about BCAA alone. Recently, Bagheri et al. (2020) investigated the utility of BCAA in conjunction with an RT program in postmenopausal women. The authors reported that although the intervention increased strength and hypertrophy, no differences were observed in the BCAA arm compared with placebo. These findings suggest that BCAA supplementation lacks efficacy even in older adults. Previous mechanistic underpinnings and practical considerations would suggest that a higher leucine threshold combined with a lower propensity for adequate calorie intake (Giezenaar et al., 2016) may enhance the efficacy of supplementation in this population. In particular, supplemental provisions that raise per meal leucine may be warranted to enhance hypertrophy in cases where it is not possible to consume sufficient per meal protein. However, even in the case of leucine, more randomized controlled trials are needed in older individuals with supplementation in conjunction with an RT intervention to make strong recommendations on potential benefits in different contexts.

Effects on Strength Performance

Consistent with evidence that BCAA supplementation lacks efficacy for promoting muscle hypertrophy, research generally fails to support a longitudinal benefit for improving strength-based performance as well (see Table 1). Spillane et al. (2012) found that participants who engaged in heavy RT 4 days/week × 8 weeks exhibited similar improvements in upper and lower body strength and endurance performance when ingesting BCAA compared with a control group. The addition of leucine to diets of adequate protein also confers no benefits to strength (Aguiar et al., 2017; DE Andrade et al., 2020). Although Dudgeon et al. (2016) concluded that supplementing a hypocaloric diet with BCAA helped to preserve dynamic muscular strength, the aforementioned statistical issues and study design flaws call into question the validity of these findings. Therefore, there is no clear benefit on strength performance with longitudinal BCAA supplementation.

Previous reviews investigating BCAA supplementation have suggested a potential benefit to muscle recovery. A meta-analysis by Rahimi et al. (2017) pooled data from eight studies that investigated the effects of BCAA on exercise-induced muscle damage in recovery from exercise. The analysis found that BCAA significantly reduced creatine kinase (CK) at both <24 hr and at 24 hr postexercise compared with placebo, but those effects were not significant at any follow-up times for muscle soreness and lactate dehydrogenase. In addition, a 2017 systematic review by Fouré and Bendahan (2017) concluded that BCAA may be efficacious on outcomes of exercise-induced muscle damage provided that muscle damage was low to moderate and that BCAA supplementation intake was higher than 200 mg·kg^{-1}·day^{-1} for an extended time period (>10 days).

Although data generally do seem to support the potential for attenuating markers of muscle damage with BCAA supplementation, it is unclear whether there is a meaningful relationship to acute performance outcomes. VanDusseldorp et al. (2018) investigated the effects of BCAA supplementation on the time course of recovery following eccentric exercise with assessed markers including CK, soreness, maximal voluntary isometric contraction, jump squat, and perceived soreness. There were no significant group by time interaction effects observed for CK, soreness, maximal voluntary isometric contraction, vertical jump, or jump squat. The CK concentrations increased in both groups following the 4, 24, 48, and 72 hr marks, but CK was lower in the BCAA group compared with placebo, and individuals supplementing with BCAA reported less soreness at the 48 and 72 hr time points. However, although BCAA had a positive effect on maximal voluntary isometric contraction, it did not improve jump squat performance. Given the findings, the authors noted that this finding holds questionable applicability to the majority of individuals who engage in dynamic movements and also questioned whether effects would hold true if individuals consumed a diet consisting of adequate protein. Waldron et al. (2017) similarly observed a preservation in isometric strength as well as a small benefit to preserving countermovement jump performance compared with placebo. Alternatively, Smith et al. (2018) found no improvements in upper body muscular strength involving bench press and rowing exercises among participants supplementing with BCAA. Kephart et al. (2016) also demonstrated that BCAA failed to directly improve performance via fatigue reduction. The investigators found that strength decrements under fatigued conditions were similar among participants ingesting a BCAA–carbohydrate supplement relative to those ingesting carbohydrate alone. Moreover, Estoche et al. (2019) found that BCAA did not improve countermovement jump and repetition performance at different time points after a bout of RT. Therefore, the current state of the literature, although equivocal, largely does not support the ability of BCAA supplementation to attenuate acute decrements in strength, particularly relative to tasks with higher ecological validity.

In older individuals, the BCAA and leucine data on strength and physical function are limited by inadequate total daily protein intake and/or dietary control. The aforementioned meta-analysis by Komar et al. (2015) found body composition benefits to various protein products containing 2 g of leucine but did not show a positive effect for enhancing muscle strength. The one study meeting inclusion criteria that matched participants for protein intake ~0.99 g/kg (Verhoeven et al., 2009) showed no benefit to augmenting muscle strength with 7.5 g of leucine supplementation per day. Importantly, this study and most of the others did not have an RT arm, which would be important in actualizing strength. A study by Rondanelli et al. (2011) provided older adult participants with 8 g of EAA (2.5 g leucine) daily and found improvements in muscle function, activities of daily living, and grip strength compared with the placebo group. In this study, participants were habitually eating at or below the recommended dietary allowance for protein intake (0.8 g/kg) and received EAA not BCAA. It should be noted that the recommended dietary allowance was derived from nitrogen balance studies on relatively sedentary subjects (National Research Council (US) Subcommittee, 1989) and fails to account for greater protein requirements for LBM preservation during hypoenergetic conditions (Carbone et al., 2019) as well as for maximizing LBM gain, which the collective evidence indicates is at least double the recommended dietary allowance (Morton et al., 2017). Similarly, Kim et al. (2012) observed larger increases in leg extension strength in sarcopenic women who supplemented with EAA. However, diet composition of participants was not prescribed or reported. Recently, Bagheri et al. (2020) found no benefit to strength with BCAA supple-

mentation in postmenopausal women. On aggregate, the data are equivocal on whether there is a strength-related benefit from the use of additional leucine or BCAA in older individuals that fail to meet sufficient protein intakes, although it would seem that EAA provision would be at least as beneficial and likely more so. More evidence is needed in this population to appropriately ascertain adequate protein needs and what, if any, role additional leucine/EAA/BCAA could play.

Practical Implications

Given the current evidence, the majority of the literature fails to support BCAA supplements as ergogenic aids in the context of strength and hypertrophy. Importantly, longitudinal studies largely fail to support the efficacy of BCAA supplementation provided sufficient daily protein is ingested. However, given preliminary evidence, more research is needed on the topic in older individuals. Leucine, in particular, may be efficacious in helping older individuals reach leucine threshold levels. The greater need for leucine and lower propensity for adequate calorie intake (Giezenaar et al., 2016) in this population raises the possibility that supplementing with leucine may be warranted in cases where it is not possible to consume sufficient high-quality daily protein, particularly in cases where higher per meal protein needs cannot be met. Provided that total protein intake requirements are met, there are no apparent benefits from consuming additional BCAA as building muscle requires a full complement of EAA. Therefore, individuals seeking to optimize strength-related performance and body composition should focus on ensuring that they consume adequate daily protein ($\geq$1.6 g·kg^{-1}·day^{-1}) replete in all nine EAA (Morton et al., 2017). Consuming high-protein meals that contain all EAA will maximally stimulate MPS. Thus, the ingestion of additional BCAA through supplementation would be superfluous for anabolism. Individuals should also be aware that BCAA yield an average of 4.65 kcal/g (May & Hill, 1990); thus, adding them to every serving of drinking water comes with additional calories, albeit arguably negligible. Perhaps more importantly, there is a clear and seemingly unnecessary monetary cost of the supplement.

In conclusion, the proposed benefits of BCAA used in the marketing of supplements appear to be at odds with the overall state of the current literature, which does not support the efficacy of supplementation on muscle strength and hypertrophy. Further research is warranted in older individuals to determine whether BCAA supplementation may confer specific benefits in this population.

Acknowledgments

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