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| **Supplemental Table 1. Overview of studies examining the effects of branched-chain amino acids on muscle protein synthesis, muscle protein breakdown, and/or associated molecular signalling responses in humans.** | | | | | | | |
| **Study** | **Sample size, participant characteristics** | **Study design** | **Additional study details** | **BCAA intervention** | **Control/comparator intervention(s)** | **Relevant outcome measure(s)** | **Main finding(s)** |
| Apro et al. (2010)(1) | n=9 (4 men/5 women) healthy recreationally active young males (age: 27 ± 1 years; mean ± SE) and females (age: 24 ± 2 years; mean ± SE) | Randomized, double-blind, 2-arm crossover design | Oral beverage administration at rest prior to warm-up, following warm-up and before performing unilateral RE, during unilateral RE at 20 min, immediately following unilateral RE, and 15 and 45 min after unilateral RE | 85 mg/kg bodyweight BCAA (45% leucine, 30% valine, 25% isoleucine) | Citrus flavored water | Protein phosphorylation status at baseline, immediately post, and 1 h post RE in rested and exercised leg for: Akt(Ser473)  mTOR(Ser2448) p70S6K(Thr389) rpS6(Ser235/Ser236) p90RSK(Thr573) AMPK(Thr172) PDK1(Ser241)  eEF2(Thr56) | No difference in Akt(Ser473), mTOR(Ser2448), p90RSK(Thr573), AMPK(Thr 172), PDK1(Ser241), or eEF2(Thr56) phosphorylation between treatment beverages  Phosphorylation of p70S6K(Thr389) was increased in both the rested and exercised leg immediately and 1 h post RE vs. baseline only with BCAA. The increase in p70S6K(Thr389) phosphorylation immediately and 1 h post RE was greater with BCAA vs. Placebo  Phosphorylation of rpS6(Ser235/Ser236) was increased in both the rested and exercised leg immediately and 1 h post RE vs. baseline, but with a more pronounced increase for the exercised leg and for the BCAA supplement |
| Borgenvik et al. (2012)(2) | n=7 young healthy males and females (5/2) (age: 27 ± 2 years; mean ± SE) | Double-blind, randomized 2-arm crossover design | Oral beverage administration in the 10.5 h overnight fasted state at rest prior to unilateral RE warm-up, directly before beginning unilateral RE, during and immediately after unilateral RE, and 15 and 45 min after unilateral RE | 85 mg BCAA/kg bodyweight BCAA (45% leucine, 25% isoleucine, and 30% valine) | Flavored water | Protein phosphorylation status immediately post RE, and at 1 h and 3 h post RE in both rested and exercised legs for: Akt(Ser473)  mTOR(Ser2448)  p70S6K1(Thr389)  4E-BP1(Thr 36/37)  Total protein content at baseline and 3 h post RE in both rested and exercised legs for: MAFbx and MuRF-1  mRNA expression at baseline and 3 h post RE in both rested and exercised legs for: MuRF-1  MAFbx  Rheb  hVps34  REDD1  REDD2 | No difference in Akt(Ser473), mTOR(Ser2448), or 4E-BP1(Thr 36/37) phosphorylation between treatments  Phosphorylation of p70S6K1(Thr389) was increased in both legs at 1 h and 3 h post RE, and was further increased in both legs at 1 h post RE with BCAA vs. Placebo  No difference in total MAFbx protein between treatments  Total protein content of MuRF-1 increased at 3 h post RE in both legs in Placebo, but remained unchanged for BCAA  No difference in MuRF-1, Rheb, hVps34, REDD1, or REDD2 mRNA expression between treatments  MAFbx mRNA expression was lower with BCAA vs. Placebo |
| Churchward-Venne et al. (2014)(3) | n=40 healthy young males (age: 21 ± 1 years; mean ± SEM); W6 (n=8), W6+Low-Leu (n=8), W25 (n=8), W6+BCAA (n=8), and W6+High-Leu (n=8) | Randomized, double-blind, 5-arm parallel group design | Oral beverage administration in the overnight fasted state following unilateral RE. All treatments were iso-caloric. | 6.25 g whey protein + BCAA (W6+BCAA: 5.0 g leucine, 1.35 g isoleucine, 1.38 g valine) co-ingested with 35 g CHO and 5.68 g fat. | 1. 25 g whey protein (W25: 3.0 g leucine 1.35 g isoleucine, 1.38 g valine)  2. 6.25 g whey protein (W6: 0.75 g leucine, 0.34 g isoleucine, 0.35 g valine)  3. 6.25 g whey protein + lower dose of leucine (W6+Low-Leu: 3.0 g leucine, 0.34 g isoleucine, 0.35 g valine)  4. 6.25 g whey protein + higher dose of leucine (W6+High-Leu: 5.0 g leucine, 0.34 g isoleucine, 0.35 g valine) | Myofibrillar protein fractional synthesis (MyoPS) rate (FSR: %/h) in the fasted state, and over 0-1.5 h, 1.5-4.5 h, and 0-4.5 h in the fed and post RE fed state using L-[*ring*-13C6]-phenylalanine  Protein phosphorylation status at baseline, 1.5 h, and 4.5 h post RE in the fed and post RE fed state for:  Akt(Ser473)  mTOR(Ser2448)  p70S6K1(Thr389)  4E-BP1(Thr37/46)  rpS6(Ser240/244)  eEF2(Thr56) | All treatments significantly increased early (0-1.5 h) postprandial MyoPS rates (%/h) above basal rates, with no difference between treatments. Late (1.5-4.5 h) postprandial MyoPS rates (%/h) remained elevated above basal rates in all treatments; however, W25 and W6+High-Leu treatments were greater than W6+Low-Leu, W6+BCAA, and W6  Postprandial MyoPS rates (%/h) over 0-4.5 h were increased above basal rates for all treatments, but were greater for W25 and W6+High-Leu vs. W6  +Low-Leu, W6+BCAA, and W6  Phosphorylation of Akt (Ser473) in W6 at 4.5 h was greater in RE fed vs. fed. Phosphorylation of Akt(Ser473)  in W6+Low-Leu at 1.5 h was greater vs. W6 and W6+BCAA in the fed leg, and greater vs. W6 and W6+High-Leu in the RE fed leg. At 4.5 h, phosphorylation of Akt(Ser473) in W6+Low-Leu was greater vs. W6, W6+BCAA, and W6+High-Leu in the fed leg. Phosphorylation of Akt(Ser473) in W25 at 1.5 h was greater vs. W6 in the RE fed leg.  Phosphorylation of mTOR(Ser2448) was increased above basal at 1.5 h only after W6+Low-Leu, W25, and W6+High-Leu  treatments. At 4.5 h, phosphorylation of mTOR (Ser2448) remained increased only after W6+High-Leu    No difference in p70S6K1(Thr389),  4E-BP1(Thr 37/46), rpS6(Ser240/244), or eEF2(Thr56)  phosphorylation between treatment beverages |
| Everman et al. (2016)(4) | n=14 young healthy males and females; BCAA: 4 males/3 females (age: 19 ± 1 years; mean ± SE); Control: 6 males/1 female (age 23±2 years; mean ± SE) | 2-arm parallel group design | Intravenous infusion at rest in the ~10 h overnight fasted state | 3 h intravenous BCAA infusion of equimolar amounts of leucine, isoleucine, and valine (prime: 15.0 μmol·kg−1·min−1 during the first 30 min; constant infusion: 5.0 μmol·kg−1·min−1) in the absence or presence of intravenous insulin infusion | Intravenous saline infusion in the absence and presence of intravenous insulin infusion | Mixed muscle protein fractional synthesis (MPS) rate (FSR: %/h) using L-[*ring*-2H5]-phenylalanine  Whole-body phenylalanine rate of appearance (Ra) | MPS (%/h) was unaffected by BCAA infusion in the absence and presence of intravenous insulin infusion  Total phenylalanine Ra decreased in BCAA and control during the insulin infusion period. The change in whole- body phenylalanine Ra between the basal and insulin infusion periods was not different in BCAA vs. control |
| Ferrando et al. (1995)(5) | n=6 young healthy males (age: 33.7 ± 1 years; mean ± SD) | Mixed design (2 of the 6 participants received both treatments) | Oral beverage administration at rest in the 12 h overnight fasted state | 11 g BCAA (5.2 g leucine; 2.6 g isoleucine; 3.2 g valine) co-ingested with 50 g carbohydrate | 11 g EAA (4.0 g threonine; 3.8 g histidine; 3.2 g methionine) co-ingested with 50 g carbohydrate | Basal and postprandial (0-3 h) MPS rate (FSR: %/h) using L-[*ring*-13C6] phenylalanine  Basal and postprandial leg tracer phenylalanine kinetics (net balance, leg protein synthesis (Rd), leg protein breakdown (Ra)) by arterio-venous balance  Basal and postprandial whole-body phenyl-alanine flux (Ra) | Postprandial MPS (%/h) did not change vs. basal after either beverage  Net leg phenylalanine balance was unaffected by either beverage. There was no change in leg protein synthesis (Rd) or leg protein breakdown (Ra) in response to the BCAA beverage. The EAA beverage caused a 43% increase in leg protein synthesis (Rd), and a 36% increase in leg protein breakdown (Ra)  Whole-body phenylalanine flux (Ra) was suppressed by 27% for the BCAA beverage, and by 15% for EAA beverage |
| Ferreira et al. (2014)(6) | n=27 active males (age: 20.85 ± 0.51 years; mean ± SD); CHO (n=9), CHO + BCAA (n=8), and PLC (n=10) | Randomized, double-blind, 3-arm parallel group design | Oral beverage administration with 1/3 of assigned supplement dose at each of the following time points: 45 min pre-RE, 10 min pre-RE, and 5 min after RE | 120 mg/kg bodyweight BCAA (50% leucine, 25% isoleucine, 25% valine) co-ingested with 1.5 g/kg bodyweight carbohydrate | 1. CHO: 1.5 g/kg bodyweight CHO  2. PLC: energy-free flavored solution | Protein phosphorylation status at baseline, 0.5 h, 2 h, and 6 h post RE for: mTOR(Ser2448)  4E-BP1(Thr46)  IRS-1(Ser636/Ser639)  Akt(Ser473)  p70S6K1(Thr421/Ser424) | No difference in Akt(Ser473), mTOR(Ser2448), p70S6K1(Thr421/Ser424), or 4E-BP1(Thr46) phosphorylation between treatment beverages  IRS-1(Ser636/Ser639) phosphorylation was increased vs. baseline at 0.5 h and 2 h post RE for CHO and BCAA, but not PLC treatments.  IRS-1(Ser636/Ser639) phosphorylation was greater at 0.5 h and 2 h post RE for CHO and BCAA vs. PLC treatments |
| Fuchs et al. (2019)(7) | n=45 older healthy males (age: 71 ± 1 years; mean ± SEM) | Double-blind randomized 3-arm parallel group design | Oral beverage administration at rest in the overnight fasted state | 6 g BCAA (3 g leucine; 1.5 g isoleucine; 1.5 g valine) | 1. 30 g milk protein (containing 6 g BCAA, 2.64 g leucine)  2. 6 g branched-chain ketoacids (BCKA) (containing 3 g (keto-) leucine; 1.5 g (keto-) isoleucine; 1.5 g (keto-) valine | Basal and postprandial (0-2 h, 2-5, and 0-5 h) MyoPS rate (%/h) using L-[*ring*-13C6]-phenylalanine | All treatments significantly increased early (0-2 h) postprandial MyoPS rates (%/h) above basal rates, with no difference between treatments  During the late postprandial phase (2-5 h), MyoPS rates (%/h) remained elevated for the 30 g of milk protein treatment, but returned to basal rates following both BCAA and BCKA ingestion  Postprandial MyoPS rates (%/h) over 0-5 h were increased above basal rates for all treatments but were greater for 30 g of milk protein vs. both BCAA and BCKA |
| Jackman et al. (2017)(8) | n=10 young healthy resistance-trained males (age: 20.1 ± 1.3 years; mean ± SEM) | Randomized, counterbalanced, blinded 2-arm crossover design | Oral beverage administration immediately after an acute session of unilateral RE performed 3 h following a standardized breakfast (7 ± 1 kcal/kg body mass) with 30 ± 1% total energy provided by protein | 5.6 g BCAA (2.6 g leucine; 1.4 g isoleucine; 1.6 g valine) | Iso-caloric CHO beverage (4.6 g CHO) | Postprandial MyoPS rate (%/h) during recovery from RE (0-4 h) using L-[*ring*-13C6]-phenylalanine  Postprandial whole-body phenylalanine flux (Ra)  Protein phosphorylation status immediately pre (0 h), 1 h, and 4 h post-ingestion of BCAA or control following RE for: Akt(Ser473)  PRAS40(Thr246) p70S6K1(Thr389)  4E-BP1(Thr37/45) | MyoPS rates (%/h) were 22% higher in BCAA vs. control over the 4 h postprandial period after RE  Total AUC of phenylalanine Ra over the 4 h postprandial period after RE was ∼6% lower in BCAA vs. control  Phosphorylation of Akt(Ser473), PRAS40(Thr246), and p70S6K1(Thr389) was increased at 1 h vs. 0 h with the BCCA treatment, but not the control treatment. Phosphorylation of  4E-BP1(Thr37/45) was unchanged with either treatment |
| Jackman et al. (2023)(9) | n=10 young healthy resistance-trained males (age 21 ± 1 years; mean ± SD) | Randomized double-blind 2-arm counterbalanced crossover design | Oral beverage administration immediately after an acute session of unilateral RE performed 3 h following a standardized breakfast (30 kJ/kg body mass) with 30% total energy provided by protein. | 6.1 g BCAA (2.8 g leucine; 1.4 g isoleucine; 1.9 g valine) co-ingested with 30.6 g of CHO | Iso-caloric CHO beverage (34.7 g CHO) | Postprandial MyoPS rate (%/h) during recovery from unilateral RE (0-4 h) using L-[*ring*-13C6]-phenylalanine  Postprandial whole-body phenylalanine flux (Ra) | MyoPS rates (%/h) were ∼15% higher in BCAA vs. control over the 4 h postprandial period after RE  Total AUC of phenylalanine Ra over the 4 h postprandial period after RE was ∼7% lower in BCAA vs. control |
| Karlsson et al. (2004)(10) | n=7 healthy recreationally active young males (age: 25 ± 1 years; mean ± SE) | Randomized, double-blind, 2-arm crossover design | Oral beverage administration in the overnight fasted state before warm-up exercise, immediately before RE, during RE at 15 min, and at 15, 30, 60, and 90 min after RE. | 100 mg/kg bodyweight BCAA (45% leucine, 25% isoleucine, 30% valine) | Citrus flavored water | Protein phosphorylation status at rest, and immediately, 1 h, and 2 h post RE for: p70S6K1(Ser424/Thr421) ERK1/2(p44/p42)  MAPK(Thr202/Tyr204)  p38 MAPK(Thr180/Tyr182)  rpS6(Ser235/Ser236) p70S6K1(Thr389) | Phosphorylation of p70S6K(Ser424/Thr421) was increased above rest immediately and 2 h post RE in Placebo, and immediately, 1 h, and 2 h post RE in BCAA. The increase at 1 h and 2 h post RE was greater in BCAA vs. Placebo  Phosphorylation of p70S6K(Thr389) was unaltered directly after RE in Placebo, but was increased above rest and was greater for BCAA vs. Placebo at 1 h and 2 h post RE  Phosphorylation of rpS6(Ser235/Ser236) was unaltered directly after RE in Placebo, but was increased above rest and was greater for BCAA vs. Placebo at 1 h and 2 h post RE  No difference in ERK1/2(p44/p42), MAPK(Thr202/Tyr204), or  p38 MAPK(Thr180/Tyr182)  phosphorylation between treatment beverages |
| Liu et al. (2001)(11) | n=7 young (age 22.6 ± 1.5 years; mean ± SEM) males and females (5/2) | Randomized, 2-arm crossover design | Intravenous infusion at rest in the 12 h overnight fasted state | 6 h systemic intravenous infusion of BCAA (an equimolar mixture of leucine, isoleucine, and valine infused at a rate of 1.66 μmol·min−1·kg−1). For the first 30 min a faster infusion rate (5.0 μmol·min−1·kg−1) was used | Same as the BCAA intervention except that participants received 2 mg oral administration of dexamethasone every 6 h, for 3 days, prior to the study | Basal and post treatment infusion (3 h and 6 h) forearm tracer phenylalanine kinetics (net balance, protein synthesis (Rd), protein breakdown (Ra)) by arterio-venous balance based on L-[*ring*-2,6-3H]-phenylalanine  Basal and post-treatment infusion whole-body phenylalanine flux (Ra)  Protein phosphorylation status of eIF4E-BP1 and p70S6K under basal conditions and following BCAA infusion | Net forearm phenylalanine balance was improved at 6 h vs. basal in response to BCAA infusion only in the absence of dexamethasone  Forearm protein synthesis (phenylalanine Rd) was unchanged vs. basal in response to BCAA infusion at 3h and 6 h both with and without dexamethasone treatment  Forearm protein breakdown (phenylalanine Ra) was unchanged vs. basal in response to BCAA infusion at 3h and 6 h both with and without dexamethasone treatment  Whole-body phenylalanine flux (Ra) decreased with BCAA infusion vs. basal both with and without dexamethasone treatment  Phosphorylation of eIF4E-BP1 was increased vs. basal in response to BCAA infusion both with and without dexamethasone treatment  Phosphorylation of p70S6K was increased vs. basal in response to BCAA infusion only without dexamethasone treatment |
| Louard et al. (1990)(12) | n=20 young healthy males and females (age: 18-34 years; mean ± SEM); BCAA: 7 males/3 females; Control: 8 males/2 females | 2-arm parallel group design | Intravenous infusion at rest, in the postabsorptive overnight fasted state | 3 h systemic intravenous infusion of BCAA (an equimolar mixture of leucine, isoleucine, and valine infused at a rate of 1.66 μmol·min−1·kg−1). For the first 30 min a faster infusion rate (5.0 μmol·min−1·kg−1) was used | 3 h systemic intravenous infusion of saline (150 mmol/l NaCl) | Basal and post treatment infusion forearm tracer phenylalanine and leucine kinetics (net balance, protein synthesis (Rd), protein breakdown (Ra)) by arterio-venous balance based on L-[*ring*-2,6-3H]-phenylalanine and L-[l-14C]-leucine  Basal and post treatment infusion whole-body phenylalanine flux (Ra)  Basal and post treatment infusion whole-body leucine total flux, endogenous flux, oxidation, and non-oxidative disposal | Net forearm phenylalanine balance was unchanged vs. basal in response to both BCAA infusion and saline control infusion. The change from basal was not different between BCAA infusion vs. saline control infusion  Forearm protein synthesis (phenylalanine Rd) was reduced vs. basal in response to BCAA infusion but not saline control infusion. The change from basal was not different between BCAA infusion vs. saline control infusion  Forearm protein breakdown (phenylalanine Ra) was reduced vs. basal in response to BCAA infusion but not saline control infusion. The change from basal was greater for BCAA infusion vs. saline control infusion  Net forearm leucine balance was increased vs. basal in response to BCAA infusion, but not saline control infusion. The change from basal was greater for BCAA infusion vs. saline control infusion  Forearm protein synthesis (leucine Rd) was increased vs. basal in response to BCAA infusion but not saline control infusion. The change from basal was greater for BCAA infusion vs. saline control infusion  Forearm protein breakdown (leucine Ra) was unchanged vs. basal in response to both BCAA infusion and saline control infusion. The change from basal was not different between BCAA infusion vs. saline control infusion  Whole-body phenylalanine flux (Ra) decreased more with BCAA infusion (22%) vs. saline control infusion (6%)  Whole-body leucine total flux, leucine oxidation, and non-oxidative leucine disposal were increased with BCAA infusion vs. saline control infusion. However, endogenous leucine flux remained unchanged |
| Louard et al. (1995)(13) | n=18 young healthy males and females (age: 23 ± 1; mean ± SEM); BCAA: 5 females/3 males; Control: 2 females/8 males | 2-arm parallel group design | Intravenous infusion at rest, in the 12 h postabsorptive overnight fasted state | 16 h overnight systemic intravenous infusion of BCAA (an equimolar mixture of leucine, isoleucine, and valine infused at a rate of 1.66 μmol·min−1·kg−1) | 4 h systemic intravenous infusion of saline | Post treatment infusion forearm tracer phenylalanine and leucine kinetics (net balance, protein synthesis (Rd), protein breakdown (Ra)) by arterio-venous balance based on L-[*ring*-2,6-3H]-phenylalanine and L-[l-14C]-leucine  Post treatment infusion whole-body phenylalanine flux (Ra)  Post treatment infusion whole-body leucine total flux, endogenous flux, oxidation, and non-oxidative disposal | Net forearm phenylalanine balance was less negative with BCAA infusion vs. saline control infusion  Forearm protein synthesis (phenylalanine Rd) was not different between BCAA infusion vs. saline control infusion  Forearm protein breakdown (phenylalanine Ra) was reduced with BCAA infusion vs. saline control infusion  Net forearm leucine balance was greater with BCAA infusion vs. saline control infusion  Forearm protein synthesis (leucine Rd) was greater with BCAA infusion vs. saline control infusion  Forearm protein breakdown (leucine Ra) was not different between BCAA infusion vs. saline control infusion  Whole-body phenylalanine flux (Ra) was reduced with BCAA infusion (37%) vs. saline control infusion  Whole-body leucine total flux, leucine oxidation, and non-oxidative leucine disposal were increased with BCAA infusion vs. saline control infusion. However, endogenous leucine flux was not different between BCAA infusion vs. saline control infusion |
| Lysenko et al. (2018)(14) | n=9 young (age: 18-30 years) amateur endurance-trained athletes | Randomized, 2-arm crossover design | Oral administration in capsule form immediately and 5 h after acute endurance exercise | 0.1 g/kg body mass of BCAA (leucine, isoleucine, and valine [ratio: 2:1:1]) | No supplement provided | Total protein, protein phosphorylation status, and/or mRNA abundance of genes related to the regulation of proteolysis at baseline, 40 min, 5 h, and 22 h post-endurance exercise for:  Total FOXO1 protein  FOXO1(Ser256)  MuRF-1 mRNA  Atrogin-1 mRNA  CTSL mRNA  BNIP3 mRNA  Myostatin mRNA  Total protein, protein phosphorylation status, and/or mRNA abundance of genes related to the regulation of protein synthesis at baseline, 40 min, 5 h, and 22 h post-endurance exercise for:  Total p70S6K1 protein  p70S6K1(Thr389)  total eEF2 protein  eEF2(Thr56)  IGF1-Ea mRNA  IGF1-Ec mRNA  DDIT4 (REDD1) mRNA  \*Note: The authors measured other proteins and genes related to the regulation of mitochondrial biogenesis, but those are not reported here | No difference in total FOXO1 protein, CTSL mRNA, or BNIP3 mRNA between treatments  Phosphorylation of FOXO1(Ser256) was unchanged at 40 min, 5 h, and 22 h post-endurance exercise vs. baseline with BCAA. Phosphorylation of FOXO1(Ser256) was reduced at 40 min, 5 h, and 22 h post-endurance exercise vs. baseline with no supplement  MuRF-1 mRNA expression was increased vs. baseline at 40 min post-endurance exercise with no supplement. The increase at 40 min was greater with no supplement vs. BCAA  Atrogin-1 mRNA expression was decreased at 5 h post-endurance exercise vs. baseline only with BCAA  Myostatin mRNA expression was decreased at 5 h post-endurance exercise vs. baseline in both trials; however, this decrease was maintained at 22 h only for the no supplement trial  No difference in total p70S6K1 protein, p70S6K1(Thr389), total eEF2 protein, eEF2(Thr56), IGF1-Ea mRNA, or IGF1-Ec mRNA  DDIT4 (REDD1) mRNA expression was decreased at 5 h post-endurance exercise vs. baseline for BCAA only. DDIT4 (REDD1) mRNA expression was increased at 40 min with no supplement vs. BCAA |
| Moberg et al. (2016)(15) | n=8 young healthy resistance-trained males (age: 27 ± 2 years; mean ± SE) | Double-blind counterbalanced 4-arm crossover design | Oral beverage administration in the overnight fasted state immediately before and after RE warm-up sets, following sets 4 and 8 of RE, and 15, 30, 60, 90, and 120 min after RE | 110 mg/kg bodyweight BCAA (45% l-leucine, 25% l-isoleucine, and 30% l-valine) | 1. Placebo (flavored water)  2. 50 mg/kg bodyweight leucine  3. 290 mg/kg body-weight EAA (containing 50 mg/kg leucine) | Postprandial MPS and MyoPS rate (FSR: %/h) using L-[*ring*-13C6]-phenylalanine over 0-3 h post RE recovery    Protein phosphorylation status pre, immediately post, 90 min, and 180 min post RE for:  Akt(Ser473)  mTOR(Ser2448)  eEF2(Thr56)  S6K1(Thr389)  4E-BP1(Thr 37/46)  4E-BP1 Thr46)  4E-BP1(Ser65)  eIF4E:4E-BP1 protein interaction  S6K1 kinase activity at pre, immediately post, 90 min, and 180 min post RE | No difference in MPS or MyoPS rate (%/h) between beverages after RE  No difference in Akt(Ser473), eEF2(Thr56), or 4E-BP1(Thr 37/46)  phosphorylation between treatment beverages  mTOR(Ser2448) phosphorylation increased in all treatments immediately post RE. At 90 min post RE, phosphorylation remained elevated in Placebo, but increased more with the other treatment beverages. BCAA and EAA beverages led to greater phosphorylation than Leucine and Placebo groups at 180 min  S6K1 kinase activity was increased at 90 min post RE with all treatments but Placebo < Leucine < BCAA < EAA. At 180 min post RE, kinase activity remained elevated but was greater with BCAA and EAA than Placebo and Leucine treatments.  S6K1(Thr389) phosphorylation correlated with S6K1 kinase activity  Phosphorylation of  4E-BP1(Thr46) decreased post RE in all treatments. Phosphorylation returned to baseline at 90 min post RE in Placebo and Leucine but was elevated with BCAA and EAA. At 180 min post RE, the increase in phosphorylation above pre remained only for BCAA and EAA treatments  Phosphorylation of  4E-BP1(Ser65) was increased above pre, Placebo, and Leucine at 90 min post RE for BCAA and EAA and was increased with EAA vs. BCAA. At 180 min post RE, phosphorylation remained higher than pre, Placebo, and Leucine with no difference between BCAA and EAA  The amount of 4E-BP1  that immunoprecipitated with eIF4E was increased immediately post RE for all treatments. At 90 min post RE this amount  was reduced with Leucine, BCAA, and EAA vs. pre, but was unaltered with Placebo. At 180 min post RE, this amount was reduced vs. pre in all treatments, and to a  greater extent with EAA vs. Placebo and Leucine |
| Monteyne et al. (2020)(16) | n=19 recreationally active healthy young males (age: 22 ± 1 years; means ± SEM) | Randomized, double-blind, 2-arm parallel group design | Oral administration in the 10 h overnight fasted state following unilateral RE | 35 g mycoprotein (18.7 g total protein) enriched with free BCAA (ENR: 2.5 g leucine, 1.5 g isoleucine, and 1.9 g valine) | 70 g mycoprotein (31.5 g total protein) containing (MYCO: 2.5 g leucine, 1.5 g isoleucine, and 1.9 g valine) | MPS rate (%/h) in the rested fasted state, exercise fasted state, and over 0-4 h in the fed and post RE fed state using L-[*ring*-2H5]-phenylalanine | MPS (%/h) increased with protein ingestion, but to a greater extent following 70 g mycoprotein (MYCO) vs. 35 g mycoprotein enriched with BCAA (ENR) in both rested muscle and exercised muscle |
| RE, resistance exercise; BCAA, branched-chain amino acids; Akt, protein kinase B; mTOR, mechanistic target of rapamycin; p70S6K, ribosomal protein S6 kinase beta-1; rpS6, ribosomal protein S6; p90RSK, p90 ribosomal S6 kinase; AMPK, AMP-activated protein kinase; PDK1, phosphoinositide-dependent protein kinase; eEF2, eukaryotic elongation factor 2; 4E-BP1, eIF4E-binding protein-1; MAFbx, muscle atrophy F-box; MuRF-1, muscle RING-finger 1; Rheb, ras-homolog enriched in brain; hVps34, human vacuolar protein sorting-34; REDD1, regulated in development and DNA damage response-1; REDD2, regulated in development and DNA damage response-2; W6, 6.25 g whey protein; W6+Low-Leu, 6.25 g whey protein supplemented with leucine to 3.0 g total leucine; W25, 25 g whey protein; W6+BCAA, 6.25 g whey protein  supplemented with leucine, isoleucine, and valine to 5.0 g total leucine; W6+High-Leu, 6.25 g whey protein supplemented with leucine to 5.0 g total leucine; MyoPS, myofibrillar protein fractional synthesis; FSR, fractional synthesis rate; MPS, mixed muscle protein fractional synthesis; Ra, rate of appearance; EAA, essential amino acids; Rd, rate of disappearance; CHO, carbohydrate; CHO + BCAA, carbohydrate + branched-chain amino acids; PLC, placebo; IRS-1, insulin receptor substrate 1; BCKA, branched-chain ketoacids; PRAS40, proline-rich Akt substrate of 40 kDa; AUC, area under the curve; ERK1/2, extracellular signal-regulated kinase; MAPK, mitogen-activated protein kinase; NaCl, sodium chloride; FOXO1, Forkhead box protein O1; CTSL, cathepsin L; BNIP3, BCL2/adenovirus E1B 19 kDa interacting protein 3; IGF-1, insulin-like growth factor-1; DDIT4/REDD1, DNA damage inducible transcript 4/Regulated in development and DNA damage response 1; eIF4E, eukaryotic translation initiation factor 4E; ENR, 35 g mycoprotein (18.7 g total protein) enriched with free BCAA; MYCO, 70 g mycoprotein (31.5 g total protein). | | | | | | | |

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