www.kosmospublishers.com
contact@kosmospublishers.com

Mini Review | Advances in Nutrition and Food Science | ANAFS-231
ISSN: 2641-6816

# Branched Chain Amino Acids in Human Nutrition

**Marina Papaianni, Domenico Iannelli*, Rosanna Capparelli***

*Department of Agriculture, University of Naples Federico II, 80055 Naples, Italy*

**Received Date:** May 10, 2022; **Accepted Date:** May 19, 2022; **Published Date:** May 27, 2022

***Corresponding authors:** Domenico Iannelli and Rosanna Capparelli, Department of Agriculture, University of Naples Federico II, 80055 Naples, Italy. Email: domenico.iannelli1935@gmail.com; capparel@unina.it

## Abstract

Branched chain amino acids (BCAAs) cannot be synthesized from mammalian cells and must therefore, be derived from the diet. BCAAs are present in multiple pathways and have essential roles in vital processes, such as glucose metabolism and insulin secretion. The anabolic property of BCAAs deserves to find application in the clinical practice. However, at present, the therapeutic use of BCAAs is still controversial, in view of the low reproducibility of results. Techniques are being developed (in particular, metabolomics and transcriptomics), which can dissect the multiple factors (diet, gut microbiome, and physical activity), which alter BCAAs metabolism. The control of sarcopenia in aged people via BCAAs supplementation seems promising interesting results.

**Keywords**: Branched-chain amino acids; Diet; Neuro transmitters; Sarcopenia

## Introduction

The branched chain amino acids (BCAAs) are leucine, isoleucine, and valine; all three are essential amino acids. This means that they cannot be synthesized by mammalian cells and must be obtained from the diet **[1]**. However, there is evidence that BCAAs can also be derived from the microbiota **[2]** and that certain forms of cancer can obtain essential as well as non-essential amino acids from scavenging proteins **[3]**. BCAAs are catabolized by enzymes active on all three BCAAs, which display similar properties and metabolism. BCAAs represent an essential source of nutrients. Leucine is the most abundant component of proteins. This feature may explain why leucine activates mTORC1, the gene controlling the metabolism. Isoleucine and valine are the main source of carbon for the synthesis of glucose. BCAAs provide also the nitrogen for the synthesis of nucleotides and alert about the nutritional state of cells **[4]**. The catabolism of BCAAs involves the enzymes BCAT1 (active in the cytosol) and BCAT2 (active in the mitochondria). These enzymes rapidly transfer nitrogen from glutamate to branched chain keto acids (BCKAs) and finally to BCAAs. This procedure permits the rapid exchange of nitrogen between glutamate, BCAAs, and BCKA, even when the catabolism of BCAAs is reduced **[5]**. With the exception of BCAAs, amino acids are catabolized in the liver. Since BCAT is not expressed in the liver, BCAAs reach the circulation directly from the gut. At the end, the level of BCAAs in the blood closely reflects that of the organism. This inter organ cycle **(Figure 1)** monitors the level of BCAAs in the organism and reduces the damage in case of loss of these essential amino acids: this is one more function of BCAAs. Mice with the mitochondrial BCAT2 gene deleted demonstrate that accumulation of BCAAs alters protein circulation and glucose homeostasis **[6]**. Whole body analysis of BCAAs metabolism has shown that BCAAs metabolism varies between tissues, with BCAAs oxidation occurring prevalently in skeletal muscle **[7]**.

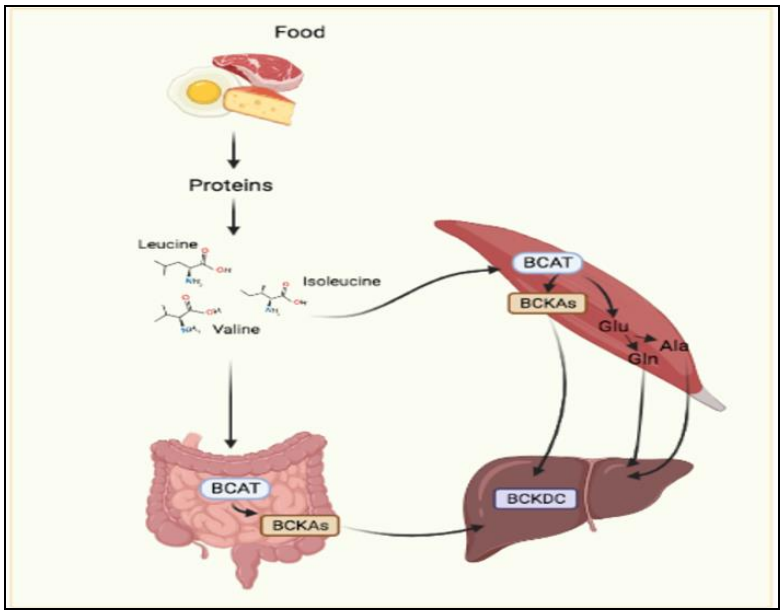


**Figure 1: BCAAs catabolism.** Ingested BCAAs are released in the peripheral blood, directly from the gut. In skeletal muscle BCAAs are catabolized by BCAT (Branched Chain Amino Transferase), producing BCKAs (Branched Chain KetoAcids) and glutamate. BCKAs are then oxidized in the liver by BCKDC (Branched Chain Ketoacid Dehydrogenase complex).

## Disorders of neurotransmission and glucose metabolism due to BCAAs

BCAAs and aromatic amino acids (AAA; phenylalanine, tyrosine, and tryptophan) are transported into the brain by the same protein. High levels of BCAAs in the blood may obstacle the passage of AAAs across the blood brain barrier and consequently the synthesis of neurotransmitters, particularly of dopamine, and serotonin. This condition explains why BCAAs supplementation is recommended for patients with liver cirrhosis to prevent hepatic encephalopathy **[8]**. BCAAs also control the production of serotonin during exercise. Some recent studies suggest that BCAAs may induce insulin resistance through mTOR activation **[9]**. However, other studies reached the opposed conclusion (of BCAAs improving glucose utilization) **[10]**.

## Disorders associated with a low- or high- protein diets

Feeding rats a diet devoid of proteins, but adequate in caloric content, lowers the plasma levels of BCAAs below basal levels. Low levels of amino acids and the low activity of muscles and liver of protein-depleted rats reflects the attempt of the body to save BCAAs **[11]**. BCAAs supplementation is recommended when a low-protein diet is prescribed to patients with chronic renal failure.

High-protein diets reduce protein break down and rise the fat-free mass. Protein supplementation is recommended to athletes to build muscles; to patients with severe diseases to reduce muscle wasting; or to obese patients to lose fat. High-protein diets are associated with high BCAAs concentrations in the peripheral blood and muscles, which can be explained reminding that a significant portion of ingested BCAAs escapes hepatic uptake and appears in the peripheral circulation.

## Disorders associated with decreased BCAAs levels or with BCAAs supplementation

BCAAs deficiency impairs mRNA translation, growth and protein wasting. Further, decreased BCAAs levels may interfere with the synthesis of neurotransmitters and with the brain function. BCAAs supplementation is thus recommended in case of diseases characterized by decreased BCAAs levels, such as liver cirrhosis, or chronic renal insufficiency. BCAAs are also recommended to correct cachexia or low ratio of BCAAs to AAAs, as observed in the hepatic encephalopathy. Unfortunately, the results from clinical trials do not provide strong evidence of beneficial effects of these therapies **[12]**.

## Role of leucinein reduction of sarcopenia in old people

Leucine has a major role in the synthesis of muscles proteins and plays a role also in controlling sarcopenia: the loss of muscle mass associated with aging. In aged people, the protein synthesis in the muscles is sensibly reduced. Studies carried out both on rats and men showed that leucine restores protein synthesis in old muscles. The dose of 6.7 g of BCAAs (of which 26% leucine) increases protein synthesis in young, but not in old people. When the content of leucine is increased to 41%, the degree of protein synthesis in the muscles increases equally, both in young and old people. At present, there is not an established daily recommended dose of BCAAs, but a ratio of leucine: isoleucine: valine, in proportion of 2:1:1. Some studies report effective the daily dose of BCAAs at the minimum dose of 5 g **[13]**. Supplementation of BCAAs is safe. Animal studies have shown that doses exceeding 10 g/kg body weight are not toxic **[14]**.

## Conclusion

The positive effects of BCAAs as a supplement to the diet of athletes (to stimulate muscle growth) and aged people (to prevent sarcopenia) are generally recognized. At the same time, it is worth noting that Western diets contain high levels of BCAAs (up to 20%), which contribute to very common diseases, such as type 2 diabetes, obesity, insulin resistance, and cardiovascular disorders. Methods that can dissect the multiple factors (diet, gut microbiome, and physical activity) influencing BCAAs metabolism are being developed, which will help to better understand metabolism. Diseases such as hypervalinemia **[15]** suggest that BCAAs may not all be transaminated by the same aminotransferase.

## References


1. Reeds PJ (2000) Dispensable and indispensable amino acids for humans. J Nutr 130: 1835S-40S.
2. Gojda J, Cahova M (2021) Gut Microbiota as the Link between Elevated BCAA Serum Levels and Insulin Resistance. Biomolecules 11: 1414.
3. Finicle BT, Jayashankar V, Edinger AL (2018) Nutrient scavenging in cancer. Nat Rev Cancer 18: 619-633.
4. Ananieva EA, Wilkinson AC (2018) Branched-chain amino acid metabolism in cancer. CurrOpin Clin NutrMetab Care 21: 64-70.
5. Harper AE, Miller RH, Block KP (1984) Branched-chain amino acid metabolism. Annu Rev Nutr 4: 409-454.
6. She P, Reid TM, Bronson SK, Vary TC, Hajnal A, et al. Disruption of BCATm in mice leads to increased energy expenditure associated with the activation of a futile protein turnover cycle. Cell Metab 6: 181-194.
7. Neinast MD, Jang C, Hui S, Murashige DS, Chu Q, et al. Quantitative Analysis of the Whole-Body Metabolic Fate of Branched-Chain Amino Acids. Cell Metab 29: 417-429.e4.
8. Fischer JE, Funovics JM, Aguirre A, James JH, Keane JM, et al. (1975) The role of plasma amino acids in hepatic encephalopathy. Surgery 78: 276-290.
9. White PJ, Lapworth AL, An J, Wang L, McGarrah RW, et al. Branched-chain amino acid restriction in Zucker-fatty rats improves muscle insulin sensitivity by enhancing efficiency of fatty acid oxidation and acyl-glycine export. Mol Metab 5: 538-551.
10. Nishitani S, Takehana K, Fujitani S, Sonaka I (2005) Branched-chain amino acids improve glucose metabolism in rats with liver cirrhosis. Am J PhysiolGastrointest Liver Physiol 288: G1292-1300.
11. Reeds PJ (1974) The catabolism of valine in the malnourished rat. Studies in vivo and in vitro with different labelled forms of valine. Br J Nutr 31: 259-270.
12. Als-Nielsen B, Koretz RL, Kjaergard LL, Gluud C (2003) Branched-chain amino acids for hepatic encephalopathy. Cochrane Database Syst Rev: CD001939.
13. Shimomura Y, Murakami T, Nakai N, Nagasaki M, et al. (2004) Exercise promotes BCAA catabolism: effects of BCAA supplementation on skeletal muscle during exercise. J Nutr 134: 1583S-1587S.
14. Okazaki S, Hatakeyama K, Tamura K, Tsufuhisa S,Shiotani S (1989) Acute and subacute toxicity study of BCAA-G in rats (inJapanese). Clinical Reports 23: 1843–1862.
15. Dancis J, Hutzler J, Tada K, Wada Y, Morikawa T, et al. (1967) A defect in valine transamination. Pediatrics 39: 813-817.


***Citation:*** *Papaianni M, Iannelli D, Capparelli R (2022) Branched Chain Amino Acids in Human Nutrition. Adv in Nutri and Food Sci: ANAFS-231.*