Effects of Branch Chain Amino Acids (BCAAs)-induced insulin resistance on athletic performance

Hassan I. Osman [1,2,3], Ahmed A. Elgamel [3]

1 = Napata Research and Innovation Center (NRIC), Khartoum North, Khartoum, Sudan
2 = Osman Medical Research Services (OMRS), 6th of October City, Greater Cairo Governorate, Egypt
3 = Sudan Anti-Doping Agency (SADA), Khartoum, Khartoum, Sudan

Abstract

In this article, the authors explore BCAAs as a potential enhancement of athletic ability in professional athletes. However, a look into published evidence suggests no need to look into the ban of BCAA-based supplements as of this writing. This, however, does not negate the necessity of further research into the topic.

Article Type: Review Article

Keywords: BCAAs; Insulin Resistance; Athletes; Supplements; SADA; Doping; Anti-Doping

Introduction:

Carbohydrate intake monitoring, adaptation and optimization has historically been the major nutritional aspect of endurance training refinement (1,2).

It has been rather established that a considerable amount of ‘energy’ is consumed during exercise (3,4). The action of physical exercise results in an increase in concentrations of beta-aminoiso-butyric acid, which is brought about through the catabolism of valine (5). Long-term, organized, professional training is how the elite-level performance required by professional athletes comes to be; this occurs through a plethora of physiological adaptations (mainly strength and aerobic metabolic capacity) that manifest as a direct result of the aforementioned training (6,7).

In addition to the promotion of glucose uptake and the synthesis of skeletal muscle protein, branch chain amino acids (henceforth referred to as BCAAs) can also be oxidized to provide energy. (8–10).

BCAAs provide ‘energy’, help with the synthesis of muscle protein and aid glucose uptake - this, through piquing the interest of experts, has resulted in them being introduced as a nutritional supplement amongst athletes (8).

This has raised a question - given the hypothesized causation of insulin resistance through elevated BCAAs (elaborated below), why haven't there been reports of increased insulin resistance amongst said athletes?

Clinical overview:

The ongoing classification of diabetes mellitus (DM) (Type 1 and Type 2) was first articulated nearly 9 decades ago (11,12). However, more recent medical research has revealed that the anachronistic classification is in need of being revisited (11).
Projections indicate that around 1 billion people will be living with DM by the middle of this century (13). Type 2 Diabetes (T2D) is, and has been, manifesting itself as a developing international healthcare concern that carries high rates of morbidity and mortality (14). It is the most common presentation of DM (11). Published evidence leads to the hypothesis that the toxic products resulting from BCAA catabolic disorders play a role in the bringing about of type 2 diabetes and atherosclerosis (15).

BCAAs and Athletic Performance:

BCAAs, particularly leucine, have received immense research interest; the primary motivators behind this interest would be: a) leucine's stimulation of the acute synthetic response, b) function of leucine in the metabolism of protein, c) role of leucine in the homeostasis of energy, d) role of leucine in the regulation of fatigue, e) leucine stimulation of protein synthesis and f) role in mitigation of muscular breakdown following exercise sessions (16–24)
A 2026 study that observed the results of introducing leucine supplementation to endurance athletes reported enhancement in muscle strength as well as potential aerobic endurance as well as 'exercise-induced central fatigue' (25). It is important to note that the sample size in this study was twenty; indicating a need for more studies of similar nature.

BCAAs and Insulin Resistance:

As of a plethora of published data, it has been hypothesized that the potential for a relationship of undefined mechanisms between insulin resistance and BCAAs (elevated BCAAs may cause insulin resistance) (8,26). This is based on the following published data (26–32):

1) Plasma levels of BCAAs have been correlated with insulin resistance
2) Diabetic animals have been found to have elevated levels of BRCAAs
3) In obese rats fed BCAAs, 2 observations were made: a) Insulin signaling pathway of skeletal muscles was inhibited, b) insulin resistance in said skeletal muscles was enhanced
4) Akt phosphorylation was reduced, while glucose reuptake was increased
5) Correlation between increased BCAA levels and increased hepatic resistance to insulin (inhibition of pathways)
   a) Addition of BCKAs (the catabolic product of BCAAs) to the cerebral cortex or glial cells has been found to induce insulin resistance and dysfunction of the mitochondria

Additionally, a 2015 publication in which the authors divided rats into exercise and sedentary groups reported significantly decreased plasma BCAA levels in the exercise group (33).

How BCAAs promote insulin resistance:

Published evidence illustrates two mechanisms by which BCAAs promote insulin resistance (28), those being:

1. mTORC1 signaling pathway model
2. metabolic disorder model

A relationship can be reasonably hypothesized between insulin sensitivity/resistance, expression of catabolic genes in adipose tissue, and BCAA catabolism (8,34–38)

Evidence to the contrary - or is it?

Published evidence suggests that BCAA supplementation induces and helps improve insulin sensitivity (39). It has also been hypothesized, and with sufficient evidence, that BCAA supplementation aids in reduction of the blood glucose levels in people living with chronic liver disease as well as improvements in insulin resistance (40,41).
With that being said, however, it has been established that when the concentration of leucine/isoleucine is increased to 80-150%, it induces insulin resistance and inhibits uptake of glucose (42).
As of this writing, the quantity of published data is insufficient to deduce a definitive hypothesis. However, the amount of published data leans heavily towards BCAA and leucine supplementation not resulting in any significant improvements in athletic performance amongst either amateur or professional athletes (43,44).

Conclusion:
In conclusion, the argument being made here is whether or not the use of BCAA supplements should be permitted by authorities and regulatory bodies. As of this writing, BCAAs are not on the World Anti-Doping Agency's (WADA) list of prohibited substances (45). The following is a summary of the data at hand:

1. The use of BCAA supplements amongst athletes is a common occurrence (8)
2. In adipose tissues, glucose uptake is promoted by BCAAs (46)
3. In the hepatic system, liver glucose uptake is promoted by BCAAs (47)
4. In skeletal muscles, glucose uptake is promoted by BCAAs (48–53)
5. BCAA supplements play a major role in post-workout recovery and in workout (8)

The authors believe that the data published provides insufficient evidence to call for a ban of BCAA-supplement amongst athletes. However, the data published thus far justifies a need for the necessary discussion as well as potential re-assessment of current position as more evidence is unveiled. In agreement with our colleagues from Nigeria, we believe that responsible use is of the utmost importance in seeing to it that fair play is continuously observed and that results continue to be guaranteed to be based on merit (54).

COI:

The authors hereby declare no conflicts of interest.

References:

1. Alghannam A, Gonzalez J, Betts J. Restoration of Muscle Glycogen and Functional Capacity: Role of Post-Exercise Carbohydrate and Protein Co-Ingestion. Vol. 10. 2018;10(253).

2. Hawley J, Leckey J. Carbohydrate Dependence During Prolonged, Intense Endurance Exercise. Vol. 2015. 2015(45):S5–12.

3. Cobbold C. Battle of the sexes: Which is better for you, high or low intensity exercise? JSHS. 2018;7:429–32.

4. Shou J, Chen PJ, Xiao WH. The Effects of BCAAs on Insulin Resistance in Athletes. J Nutr Sci Vitaminol (Tokyo). 2019;65(5):383–9. doi:10.3177/jnsv.65.383

5. Roberts L, Bostrom P, O'Sullivan J, Schinzel R, Lewis G, Dejam A, et al. Beta-Aminoisobutyric acid induces browning of white fat and hepatic beta-oxidation and is inversely correlated with cardiometabolic risk factors. Vol. 19. 2014;19:96–108.

6. Alghannam A, Ghaith M, Alhussain M. Regulation of Energy Substrate Metabolism in Endurance Exercise. Vol. 18. 2021;18:4963.

7. Hawley J. Effect of increased fat availability on metabolism and exercise capacity. Vol. 34. 2002;34:1485–91.

8. Shou J, Chen PJ, Xiao WH. The Effects of BCAAs on Insulin Resistance in Athletes. J Nutr Sci Vitaminol (Tokyo). 2019;65(5):383–9. doi:10.3177/jnsv.65.383

9. Kawaguchi T, Izumi N, Charlton M, Sata M. Branched-chain amino acids as pharmacological nutrients in chronic liver disease. Vol. 54. 2011;54:1063–70.

10. Evans W, Fisher E, Hoerr R, Young V. Protein metabolism and endurance exercise. Vol. 37. 2007;37:337–40.

11. Franks PW, Rich SS, Linder B, Zaghloul NA, Cefalu WT. A Research Roadmap to Address the Heterogeneity of Diabetes and Advance Precision Medicine. J Clin Endocrinol Metab. 2025 Feb 18;110(3):601–10. doi:10.1210/clinem/dgae844

12. Himsworth H. Diabetes mellitus: its differentiation into insulinsensitive and insulin-insensitive types. Vol. 82. 2011;82(12):1440–4.

13. Sun H, Saeedi P, Karuranga S, et. al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Vol. 183. 2022;183:109119.

14. Luan X, Tian X, Zhang H, Huang R, Li N, Chen P, et al. Exercise as a prescription for patients with various diseases. Vol. 8. 2019;8:422–41.

15. Fiehn O, Garvey W, Newman J, Lok K, Hoppel C, Adams S. Plasma metabolomic profiles reflective of glucose homeostasis in non-diabetic and type 2 diabetic obese African-American women. Vol. 5. 2012;5:e15234.

16. Jahan-Mihan A, El Khoury D, Brewer G, Chapleau A. Current Perspectives on Protein Supplementation in Athletes: General Guidance and Special Considerations for Diabetes-A Narrative Review. Nutrients. Vol. 17. 2025;17:3528.

17. Jäger R, Kerksick C, Campbell B, Cribb P, Wells S, Skwiat T, et al. International Society of Sports Nutrition Position Stand: Protein and exercise. Vol. 14. 2017;14(20).

18. Neinast M, Murashige D, Arany Z. Branched Chain Amino Acids. Vol. 81. 2019;81:139–64.

19. Phillips S. The impact of protein quality on the promotion of resistance exercise-induced changes in muscle mass. Vol. 13. 2016;13(64).

20. Anthony J, Anthony T, Layman D. Leucine supplementation enhances skeletal muscle recovery in rats following exercise. Vol. 129. 1999;129:1102–6.

21. Higashida K, Inoue S, Nakai N. Iron deficiency attenuates protein synthesis stimulated by branched-chain amino acids and insulin in myotubes. Vol. 531. 2020;531:112–7.

22. Gawedzka A, Grandys M, Duda K, Zapart-Bukowska J, Zoladz J, Majerczak J. Plasma BCAA concentrations during exercise of varied intensities in young healthy men-the impact of endurance training. Vol. 8. 2020;8:e10491.

23. Bassit R, Sawada L, Bacurau R, Navarro F, Martins Jr E, Santos R, et al. Branched-chain amino acid supplementation and the immune response of long-distance athletes. Vol. 18. 2002;18:376–9.

24. Waskiw-Ford M, Hannaian S, Duncan J, Kato H, Abou Sawan S, Locke M, et al. Leucine-Enriched Essential Amino Acids Improve Recovery from Post-Exercise Muscle Damage Independent of Increases in Integrated Myofibrillar Protein Synthesis in Young Men. Vol. 12. 2020;12:1061.

25. Li T, Xu W, Chen J, Kan Z, Sui X, Zhao Z, et al. Effects of Leucine Supplementation on Athletic Performance, Central Fatigue, and Serum Metabolism in Endurance Athletes: A Randomized Controlled Trial and Targeted Metabolomics Study. Metabolites. 2026 Jan 27;16(2):94. doi:10.3390/metabo16020094

26. Badoud F, Lam K, Dibattista A, Perreault M, Zulyniak M, Cattrysse B, et al. Serum and adipose tissue amino acid homeostasis in the metabolically healthy obese. Vol. 13. 2014;13:3455–66.

27. Lackey D, Lynch C, Olson K, Mostaedi R, Ali M, Smith W, et al. Regulation of adipose branched-chain amino acid catabolism enzyme expression and cross-adipose amino acid flux in human obesity. Vol. 304. 2013;304:E1175-E1187.

28. Lynch C, Adams S. Branched-chain amino acids in metabolic signalling and insulin resistance. Vol. 10. 2014;10:723–36.

29. Newgard C, An J, Bain J, Muehlbauer M, Stevens R, Lien L, et al. A branched-chain amino acid-related metabolic signature that differentiates obese and lean humans and contributes to insulin resistance. Vol. 9. 2009;9:311–26.

30. Shah S, Bain J, Muehlbauer M, Stevens R, Crosslin D, Dungan J, et al. Association of a peripheral blood metabolic profile with coronary artery disease and risk of subsequent cardiovascular events. Vol. 3. 2010;3:207–14.

31. Newgard C. Interplay between lipids and branched-chain amino acids in development of insulin resistance. Vol. 15. 2012;15:606–14.

32. Amaral A, Leipnitz G, Fernandes C, Seminotti B, Schuck P, Wajner M. Alpha-ketoisocaproic acid and leucine provoke mitochondrial bioenergetic dysfunction in rat brain. Vol. 1324. 2010;1324:75–84.

33. Xiao W, Chen P, Liu X, Zhao L. The impaired function of macrophages induced by strenuous exercise could not be ameliorated by BCAA supplementation. Nutrients. 2015;7:8645–56.

34. Sunny N, Kalavalapalli S, Bril F, Garrett T, Nautiyal M, Mathew J, et al. Cross-talk between branched-chain amino acids and hepatic mitochondria is compromised in nonalcoholic fatty liver disease. Vol. 309. 2015;309:E311–9.

35. Shin A, Fasshauer M, Filatova N, Grundell L, Zielinski E, Zhou J, et al. Brain insulin lowers circulating BCAA levels by inducing hepatic BCAA catabolism. Vol. 20. 2014;20:898–909.

36. Suryawan A, Hawes J, Harris R, Shimomura Y, Jenkins A, Hutson S. A molecular model of human branched-chain amino acid metabolism. Vol. 68. 1998;68:72–81.

37. Sears D, Hsiao G, Hsiao A, Yu J, Courtney C, Ofrecio J, et al. Mechanisms of human insulin resistance and thiazolidinedione-mediated insulin sensitization. Vol. 106. 2009;106:18745–50.

38. She P, Van H, Reid T, Hutson S, Cooney R, Lynch C. Obesity-related elevations in plasma leucine are associated with alterations in enzymes involved in branched-chain amino acid metabolism. Vol. 293. 2007;293:1552–63.

39. Ikehara O, Kawasaki N, Maezono K, Komatsu M, Konishi A. Acute and chronic treatment of L-isoleucine ameliorates glucose metabolism in glucose-intolerant and diabetic mice. Vol. 31. 2008;31:469–72.

40. Korenaga K, Korenaga M, Uchida K, Yamasaki T, Sakaida I. Effects of a late evening snack combined with alpha-glucosidase inhibitor on liver cirrhosis. Vol. 38. 2010;38:1087–97.

41. Kawaguchi T, Nagao Y, Matsuoka H, Ide T, Sata M. Branched-chain amino acid-enriched supplementation improves insulin resistance in patients with chronic liver disease. Vol. 22. 2008;22:105–12.

42. Jang C, Oh S, Wada S, Rowe G, Liu L, Chan M, et al. A branched chain amino acid metabolite drives vascular fatty acid transport and causes insulin resistance. Vol. 22. 2016;22:421–6.

43. Del Guerra G, Ohannesian V, Semerdjian R, Silva R, Chagas E, Alves M, et al. Branched-chain amino acid supplementation and endurance performance: reporting guidelines and systematic review of biochemical vs clinical evidence. 2026;1–12. doi:https://doi.org/10.1080/00913847.2026.2627863

44. Chandra SZ, Simanungkalit SF, Sofianita NI. Factors Associated with Performance in Athletics and Football Athletes at SKO Ragunan, Jakarta, 2025. Z. 2025;9(1).

45. WORLD ANTI-DOPING CODE INTERNATIONAL STANDARD PROHIBITED LIST 2025.

46. Hinault C, Mothesatney I, Gautier N, Jr L, Van O. Amino acids and leucine allow insulin activation of the PKB/mTOR pathway in normal adipocytes treated with wortmannin and in adipocytes from db/db mice. Vol. 18. 2004;18:1894–6.

47. Higuchi N, Kato M, Miyazaki M, Tanaka M, Kohjima M, Ito T, et al. Potential role of branched-chain amino acids in glucose metabolism through the accelerated induction of the glucose-sensing apparatus in the liver. Vol. 112. 2011;112:30–8.

48. Nishitani S, Takehana K, Fujitani S, Sonaka I. Branched-chain amino acids improve glucose metabolism in rats with liver cirrhosis. Vol. 288. 2005;288:1292–300.

49. Nishitani S, Matsumura T, Fujitani S, Sonaka I, Miura Y, Yagasaki K. Leucine promotes glucose uptake in skeletal muscles of rats. Vol. 299. 2002;299:693–6.

50. Kimball S, Jefferson L. Signaling pathways and molecular mechanisms through which branched-chain amino acids mediate translational control of protein synthesis. Vol. 136. 2006;136:227S-231S.

51. Jackman S, Witard O, Philp A, Wallis G, Baar K, Tipton K. Branched-chain amino acid ingestion stimulates muscle myofibrillar protein synthesis following resistance exercise in humans. Vol. 8. 2017;8:390.

52. Crozier S, Kimball S, Emmert S, Anthony J, Jefferson L. Oral leucine administration stimulates protein synthesis in rat skeletal muscle. Vol. 135. 2005;135:376–82.

53. Moberg M, Apró W, Ekblom B, Van H, Holmberg H, Blomstrand E. Activation of mTORC1 by leucine is potentiated by branched-chain amino acids and even more so by essential amino acids following resistance exercise. Vol. 310. 2016;310:C874–84.

54. Ochor DC, Nwikiri B. The Role of Enzymatic Activity in Enhancing Athletic Performance: A Biochemical Evaluation of Nutritional Supplement Efficacy in Sport Science. Vol. 3. 2026;3(1):30–52.