Received: 18 March 2022 | Accepted: 19 March 2022

DOI: 10.1002/oby.23433

Obesity A Research Journal | THE OBESITY SOCIETY | WILEY

COMMENTARY

Obesity, exercise training, and BCAA supplementation: All that glitters (may not be) gold

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Obesity remains a key global health concern intimately linked with cardiometabolic disease. Although the molecular underpinnings connecting obesity and type 2 diabetes are multifaceted, adiposity-induced effects can dysregulate beta cell function and multiorgan insulin sensitivity (1). Weight loss can attenuate such adverse alterations; however, in weight-stable conditions, the benefits of aerobic exercise training on insulin sensitivity are transient, likely affected by the proximity to the latest bout (2). Even so, continued interest persists in seeking alternatives, including dietary supplementation, to enhance the potency of exercise for optimal improvement in both performance and cardiometabolic health.

Branched-chain amino acids (BCAAs), for instance, feature unique properties that historically have made them attractive candidates to enhance the benefits of exercise, particularly resistance training. However, circulating BCAAs are associated with obesity and type 2 diabetes (3), with implications that the strength of this relationship may be predictive of type 2 diabetes incidence. Further reports indicate that increased levels of BCAAs in plasma are positively associated with hemoglobin A_{1c} levels in women with type 2 diabetes and overweight/obesity (4). These findings contradict the (generally) perceived benefits of BCAA supplementation to enhance exercise-induced adaptations (e.g., stimulate muscle protein synthesis) and skeletal muscle recovery. Admittedly, multiple factors, including habitual diet, exercise mode, the presence or absence of exercise training, and timing of ingestion, can influence the practical utility of BCAA supplementation.

Recently, Zhang and colleagues (5) employed a factorial design to examine the mechanistic basis concerning exercise training with and without BCAA supplementation in lean and obese C57BL/6 mice. At 8 weeks of age, mice were fed either a high-fat diet to induce obesity or standard chow for 12 weeks. Treadmill running was subsequently initiated wherein diets were supplemented with BCAAs (1.6 g/kg/d) or not for a further 12 weeks. Separate groups of lean and obese mice were then divided into the following groups: 1) control (no exercise; no BCAAs), 2) exercise (no BCAAs), 3) BCAAs (no exercise), or 4) a combination of exercise and BCAA supplementation. Following 12 weeks of treadmill running, mice were euthanized for tissue collection and analyses.

Results showed that exercise training significantly reduced plasma levels of BCAAs among obese mice with or without BCAA supplementation. Exercise training also reduced BCAA accumulation in subcutaneous white adipose tissue induced by supplementation; however, this was not observed in the exercise-only group. Whereas exercise training improved insulin tolerance in obese mice, BCAA supplementation eradicated this benefit. More specifically, exercise training with BCAAs significantly decreased phosphorylation of protein kinase B (AKT) (Ser473 and Ser474) in subcutaneous white adipose tissue among obese mice, suggesting dysregulated insulin signaling related to supplementation. Further results revealed that exercise training with BCAAs in obese mice upregulated fatty acid synthase, suggesting heightened potential for lipogenesis, possibly linked to an inhibitory effect of BCAAs on the activated AKT signaling via exercise. Such metabolic aberrations were not observed in lean mice.

Although the benefits of exercise training are well defined, instances in which adaptations may be weakened represent a practical dilemma. Indeed, it remains unclear whether the results of Zhang et al. (5) can be recapitulated or if they translate to humans with obesity. Nevertheless, the findings from this investigation permit researchers with an intriguing opportunity to determine whether

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BCAA supplementation may differentially undermine the acute effects of exercise on insulin sensitivity in individuals with and without obesity. Future work should ensure that participants remain in energy balance during insulin sensitivity assessments to properly delineate exercise-related effects from energy imbalance on biomarkers involving glucose control and lipogenesis.

FUNDING INFORMATION

This publication was made possible, in part, by support from the Indiana Clinical and Translational Sciences Institute funded by grant number UL1TR002529 from the National Institutes of Health, National Center for Advancing Translational Sciences, Clinical and Translational Sciences Award.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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