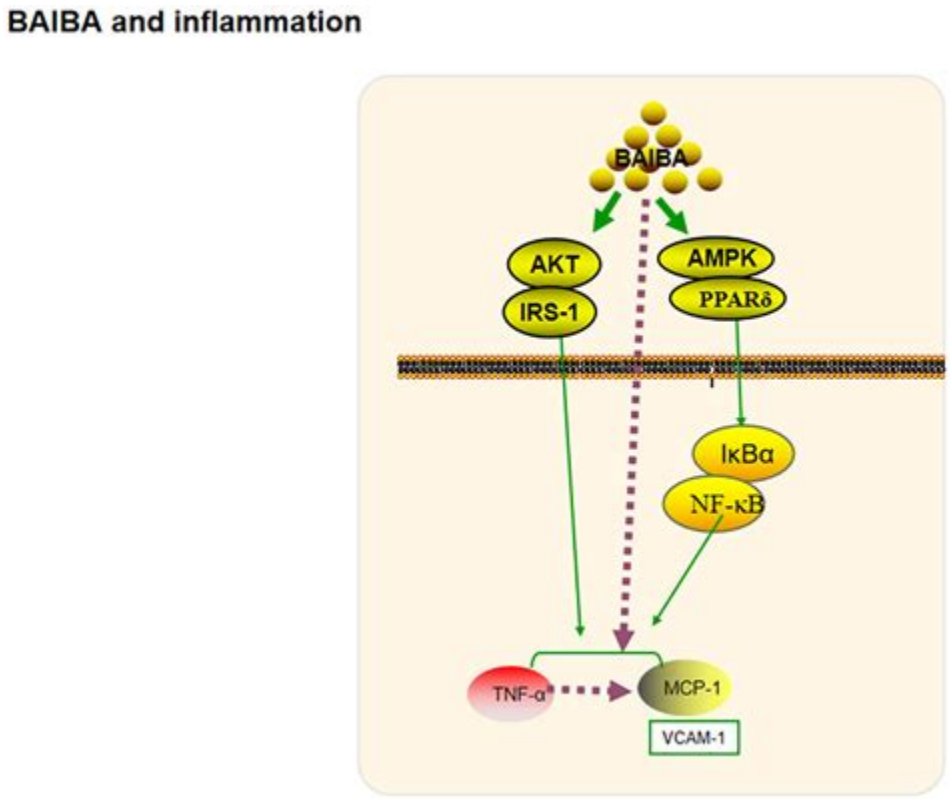
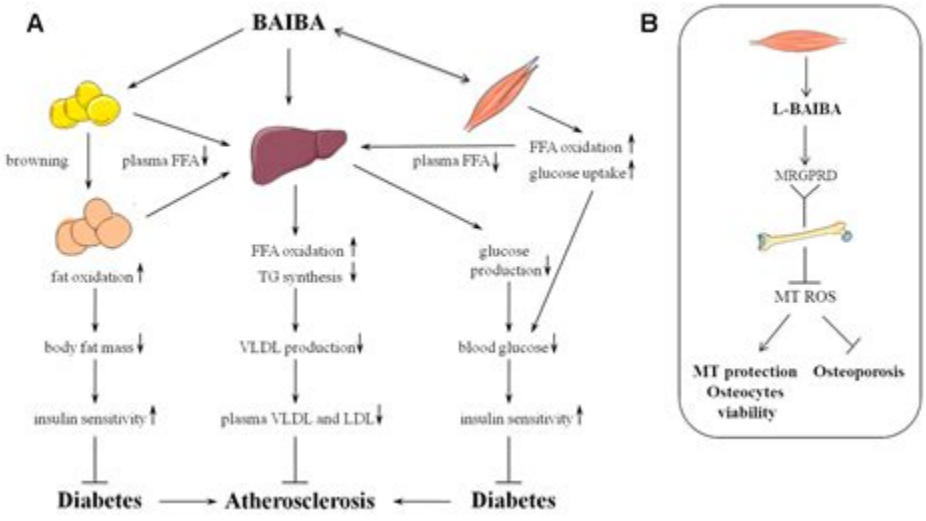
On the other hand, the inhibitory effects of L-BAIBA on oxidative stress-induced apoptosis were abolished by the inhibition of both AMPK and PI3K/Akt. In conclusion, we demonstrated that L-BAIBA confers protection against oxidative stress in PC12 cells by activating the AMPK and PI3K/Akt pathways.

Signaling metabolite β-aminoisobutyric acid as a metabolic regulator .



β-aminoisobutyric acid (BAIBA) is produced in skeletal muscle during exercise and has beneficial effects on obesity-related metabolic disorders such as diabetes and non-alcoholic fatty liver disease. Thus, it is supposed to prevent high fat diet (HFD)-induced inflammation and insulin resistance in adipose tissue though anti-inflammatory effects in obesity.

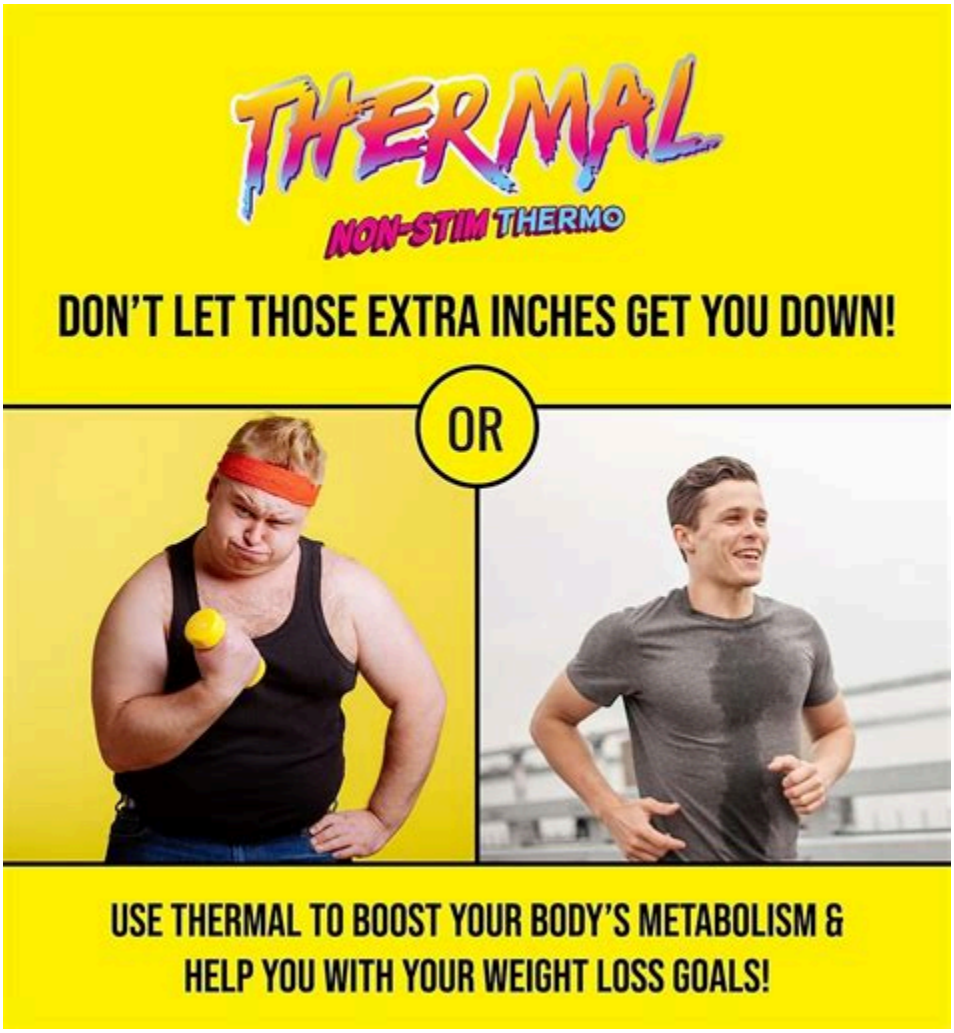
β-Aminoisobutyric acid (L-BAIBA) is a novel regulator of . - Nature



One of the newest things that are investigated in recent time are the effects of ß-aminoisobutyric acid

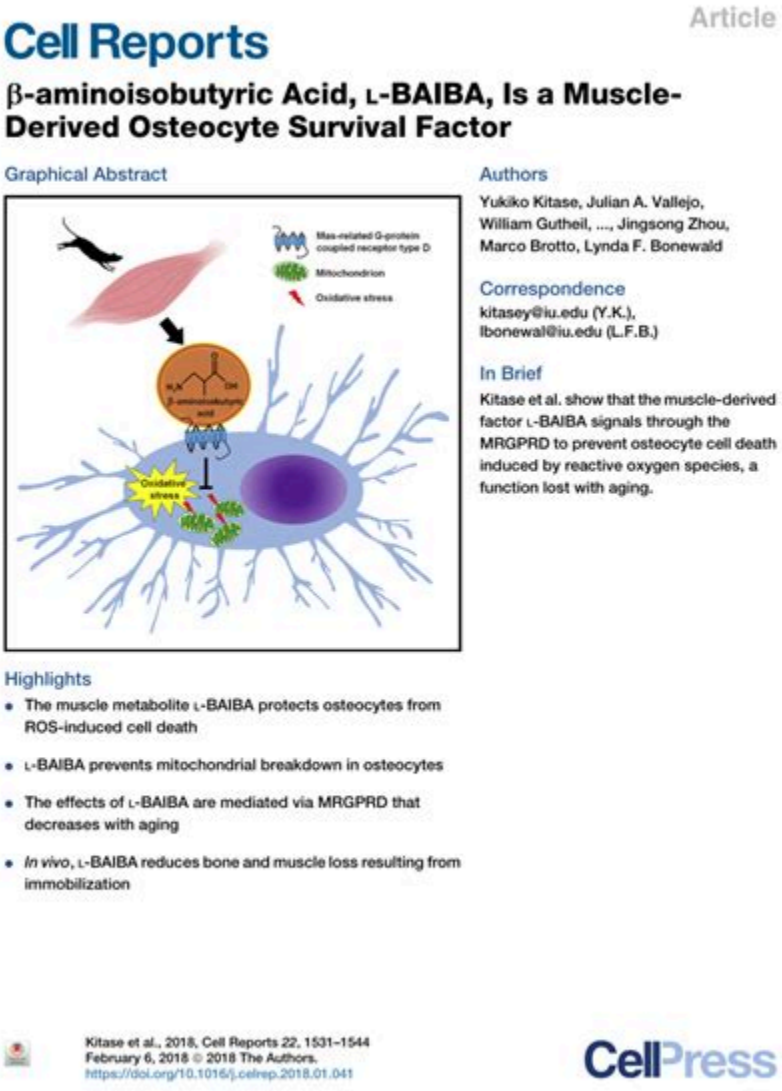
(BAIBA) on the process of browning and therefore its role in treatment of obesity and associated diseases. Roberts et al. (2014) first showed that BAIBA could be a new small molecular myokine. This group of scientists proved that BAIBA is .

Lose Body Fat with MitoBurn BAIBA | MUSCLE INSIDER



There are no currently known side effects at the above doses, but because it is a new ingredient with limited human research, caution is suggested. In 2019, safety data was conducted on mice and showed L-BAIBA's LD50 (lethal dose for 50% of animals) was well over 2,000mg/kg of body weight, which means we're very comfortable with the suggested dose.

β-aminoisobutyric Acid, l -BAIBA, Is a Muscle-Derived Osteocyte .



Article

Cell Reports

β-aminoisobutyric Acid, L-BAIBA, Is a Muscle-Derived Osteocyte Survival Factor

Graphical Abstract

Authors

Yukiko Kitase, Julian A. Vallejo, William Gutheil, ..., Jingsong Zhou, Marco Brotto, Lynda F. Bonewald

Correspondence

kitasey@iu.edu (Y.K.), lbonewal@iu.edu (L.F.B.)

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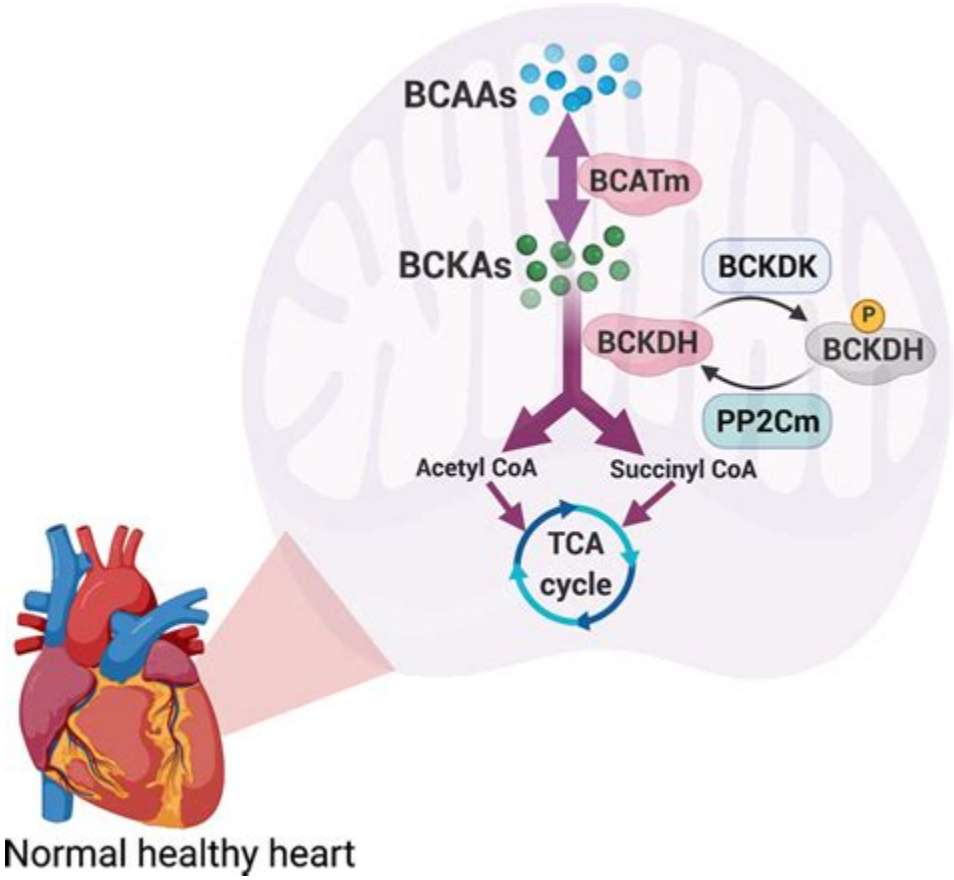
Kitase et al., 2018, Cell Reports 22, 1531–1544
February 6, 2018
https://doi.org/10.1016/j.celrep.2018.01.041

CellPress

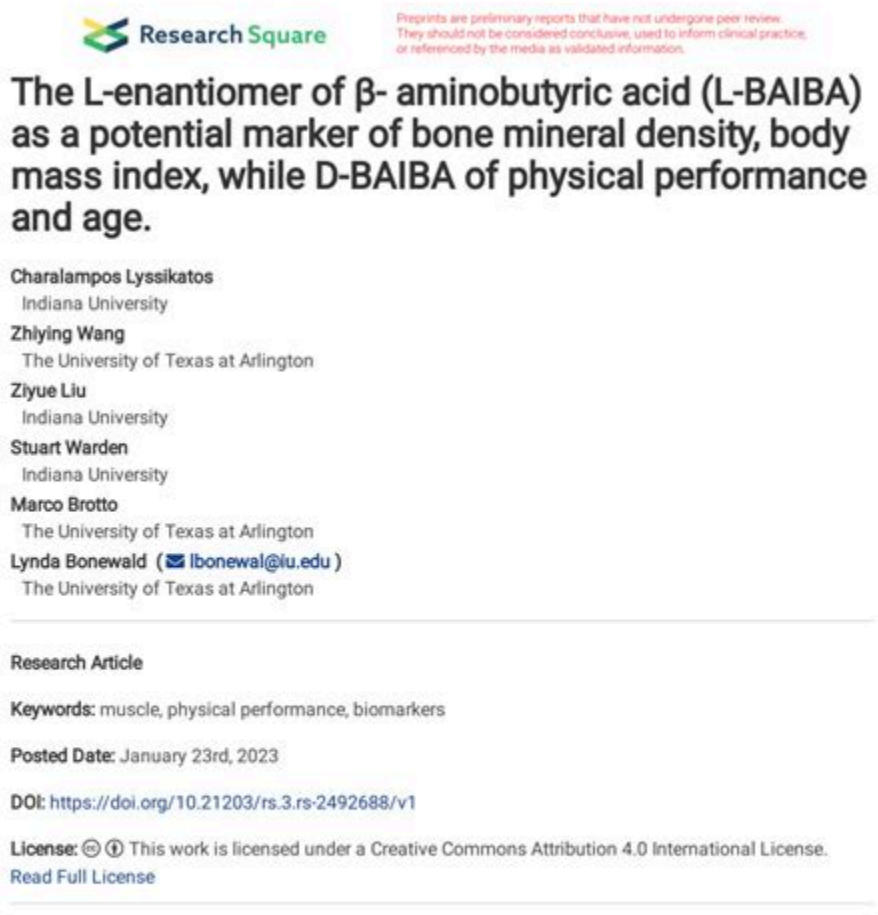
To determine the effects of L-BAIBA on prefrontal extracellular dopamine level, the perfusion medium was switched from MRS containing with or without . In left side histograms, ordinate: .

β-aminoisobutyrics acid, a metabolite of BCAA, activates the AMPK/Nrf-2 .



L-BAIBA Protects Osteocytes from Cell Death Induced by Oxidative Stress (A) Cell death assay using the osteocyte cell line MLO-Y4. L-BAIBA as well as L/D-BAIBA, but not D-BAIBA, showed highly significant protective effects on MLO-Y4 cell death induced by oxidative stress. ***p < 0. 001 versus H 2 O 2. (B) Comparison of potency between L-BAIBA and well-known antioxidants β-estradiol and N .

l-β-aminoisobutyric acid, L-BAIBA, a marker of bone mineral density and .



The L-enantiomer of β- aminobutyric acid (L-BAIBA) as a potential marker of bone mineral density, body mass index, while D-BAIBA of physical performance and age.

Charalampos Lyssikatos
Indiana University
Zhiying Wang
The University of Texas at Arlington
Ziyue Liu
Indiana University
Stuart Warden
Indiana University
Marco Brotto
The University of Texas at Arlington
Lynda Bonewald (lbonewal@iu.edu)
The University of Texas at Arlington

Research Article

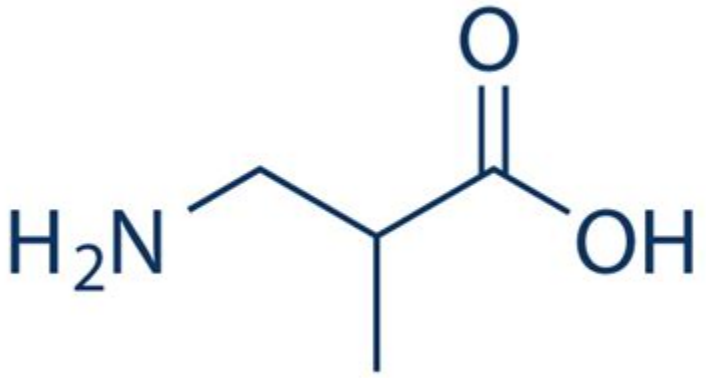
Keywords: muscle, physical performance, biomarkers

Posted Date: January 23rd, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2492688/v1

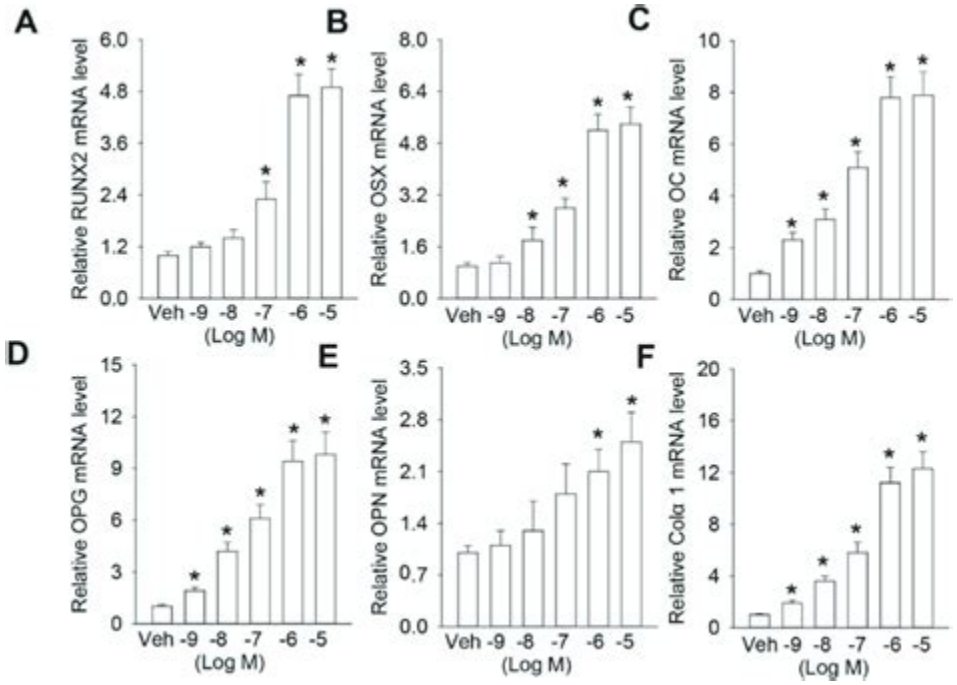
Mitochondrial dysfunction often accompanies podocyte damage and is associated with an increase in oxidative stress and apoptosis. β-Aminoisobutyric acid (BAIBA) belongs to natural β-amino acids and is known to exert anti-inflammatory and antioxidant effects.

3-Aminoisobutyric acid - Wikipedia



One of the major limitations in our understanding of the physiological effects of D-BAIBA and L-BAIBA is that most of the supplementation studies in animal models were performed with the D,L-BAIBA racemate, which makes it impossible to determine which of the BAIBA enantiomers were responsible for the observed effects. 3. Metabolic Effects of BAIBA

l-β-aminoisobutyric acid, L-BAIBA, a marker of bone mineral . - Nature



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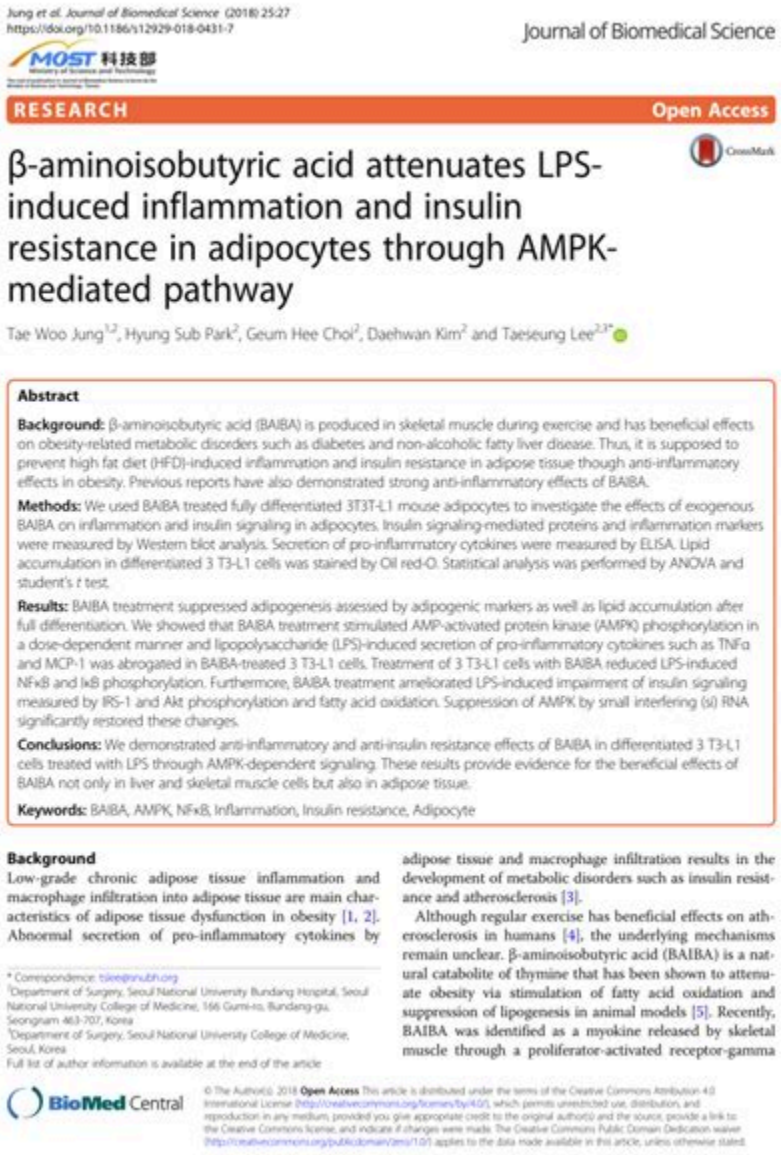

Jung et al. Journal of Biomedical Science (2018) 25:27
https://doi.org/10.1186/s12929-018-0431-7

Journal of Biomedical Science

RESEARCH Open Access

β-aminoisobutyric acid attenuates LPS-induced inflammation and insulin resistance in adipocytes through AMPK-mediated pathway

Tae Woo Jung[1,2], Hyung Sub Park[2], Geum Hee Choi[2], Daehwan Kim[2] and Taeseung Lee[2,3*]

Abstract

Background: β-aminoisobutyric acid (BAIBA) is produced in skeletal muscle during exercise and has beneficial effects on obesity-related metabolic disorders such as diabetes and non-alcoholic fatty liver disease. Thus, it is supposed to prevent high fat diet (HFD)-induced inflammation and insulin resistance in adipose tissue though anti-inflammatory effects in obesity. Previous reports have also demonstrated strong anti-inflammatory effects of BAIBA.

Methods: We used BAIBA treated fully differentiated 3T3T-L1 mouse adipocytes to investigate the effects of exogenous BAIBA on inflammation and insulin signaling in adipocytes. Insulin signaling-mediated proteins and inflammation markers were measured by Western blot analysis. Secretion of pro-inflammatory cytokines were measured by ELISA. Lipid accumulation in differentiated 3 T3-L1 cells was stained by Oil red-O. Statistical analysis was performed by ANOVA and student's *t* test.

Results: BAIBA treatment suppressed adipogenesis assessed by adipogenic markers as well as lipid accumulation after full differentiation. We showed that BAIBA treatment stimulated AMP-activated protein kinase (AMPK) phosphorylation in a dose-dependent manner and lipopolysaccharide (LPS)-induced secretion of pro-inflammatory cytokines such as TNFα and MCP-1 was abrogated in BAIBA-treated 3 T3-L1 cells. Treatment of 3 T3-L1 cells with BAIBA reduced LPS-induced NFκB and IκB phosphorylation. Furthermore, BAIBA treatment ameliorated LPS-induced impairment of insulin signaling measured by IRS-1 and Akt phosphorylation and fatty acid oxidation. Suppression of AMPK by small interfering (si) RNA significantly restored these changes.

Conclusions: We demonstrated anti-inflammatory and anti-insulin resistance effects of BAIBA in differentiated 3 T3-L1 cells treated with LPS through AMPK-dependent signaling. These results provide evidence for the beneficial effects of BAIBA not only in liver and skeletal muscle cells but also in adipose tissue.

Keywords: BAIBA, AMPK, NFκB, Inflammation, Insulin resistance, Adipocyte

Background

Low-grade chronic adipose tissue inflammation and macrophage infiltration into adipose tissue are main characteristics of adipose tissue dysfunction in obesity [1, 2]. Abnormal secretion of pro-inflammatory cytokines by adipose tissue and macrophage infiltration results in the development of metabolic disorders such as insulin resistance and atherosclerosis [3].

Although regular exercise has beneficial effects on atherosclerosis in humans [4], the underlying mechanisms remain unclear. β-aminoisobutyric acid (BAIBA) is a natural catabolite of thymine that has been shown to attenuate obesity via stimulation of fatty acid oxidation and suppression of lipogenesis in animal models [5]. Recently, BAIBA was identified as a myokine released by skeletal muscle through a proliferator-activated receptor-gamma

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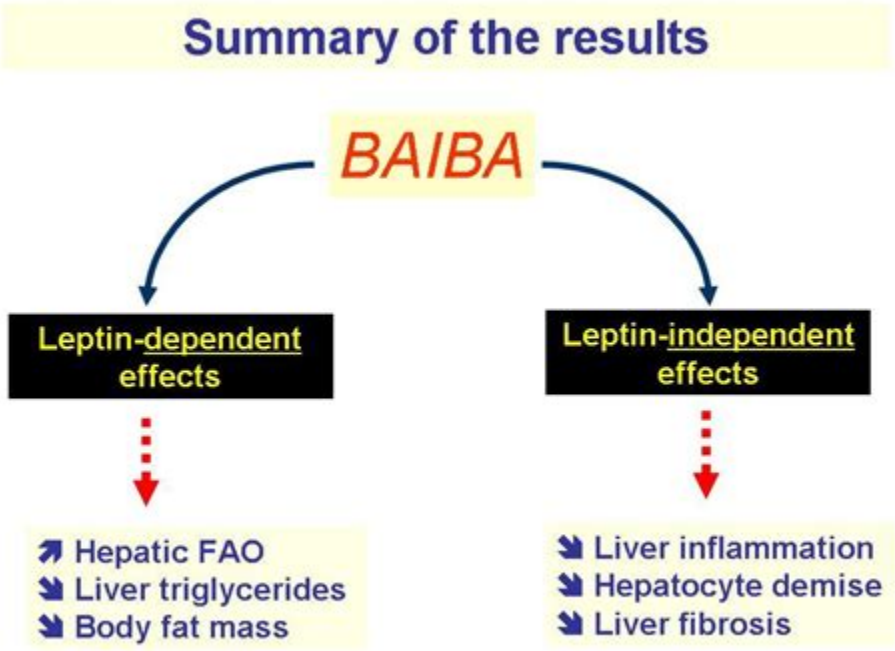
Full list of author information is available at the end of the article

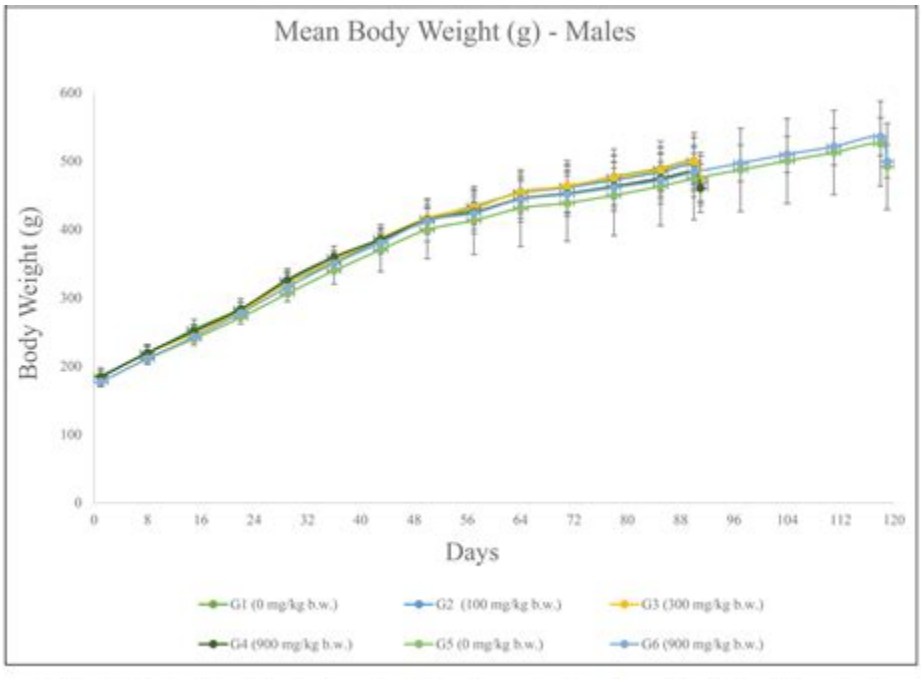
Published: 11 October 2023 l -β-aminoisobutyric acid, L-BAIBA, a marker of bone mineral density and body mass index, and D-BAIBA of physical performance and age Charalampos Lyssikatos,.

L-Baiba (Beta-aminoisobutyric acid): Risks and Benefits — Evolve Further



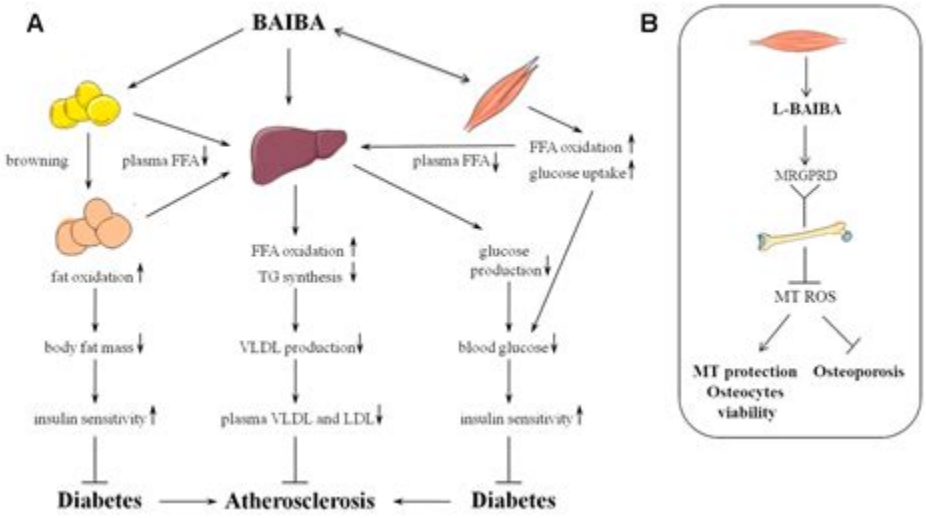
BAIBA is a myokine that is generated in response to exercise stimulus. Once researchers saw that BAIBA levels increased during exercise, they began connecting the dots, noting that it's actually more of a signal in the body, and initiates an incredible chain reaction of thermogenic, fat-releasing mechanisms. [1,4] BAIBA's presence is inversely co.

Safety Assessment of L-β-Aminoisobutyric Acid (L-BAIBA): Subchronic .



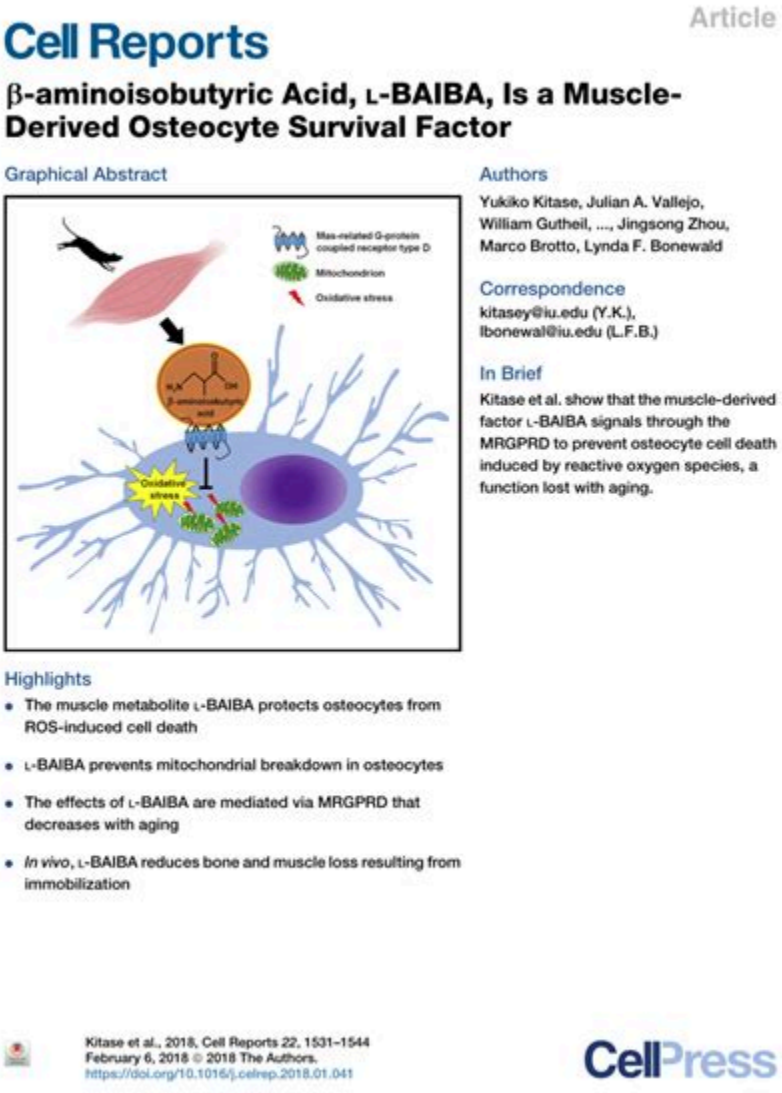
In summary, aerobic exercise produces PGC-1alpha generating BAIBA release into the body's circulation. BAIBA then acts on white adipose tissue to transform it into brown fat via PPARalpha. Brown fat generates heat from fat, essentially burning calories and raising the body's metabolism. BAIBA also stimulates hepatocytes (liver cells) to .

β-Aminoisobutyric acid (L-BAIBA) is a novel regulator of . - PubMed



3-Aminoisobutyric acid 3-Aminoisobutyric acid (also known as β-aminoisobutyric acid or BAIBA) is a product formed by the catabolism of thymine . During exercise, the increase of PGC-1α protein triggers the secretion of BAIBA from exercising muscles to blood (concentration 2 to 3 μM in human serum).

β-aminoisobutyric Acid, L-BAIBA, Is a Muscle-Derived Osteocyte Survival .



Article

Cell Reports

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Graphical Abstract

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Kitase et al., 2018, Cell Reports 22, 1531–1544
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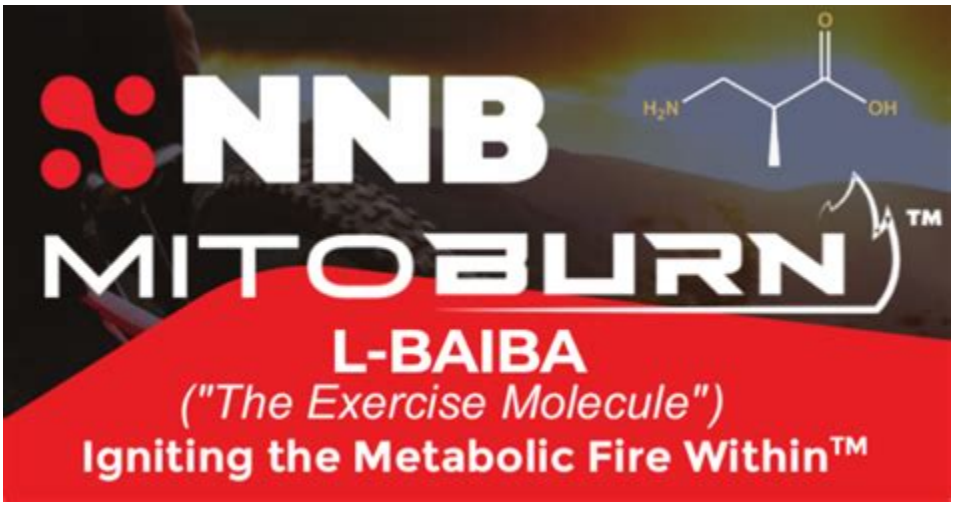
https://doi.org/10.1016/j.celrep.2018.01.041

CellPress

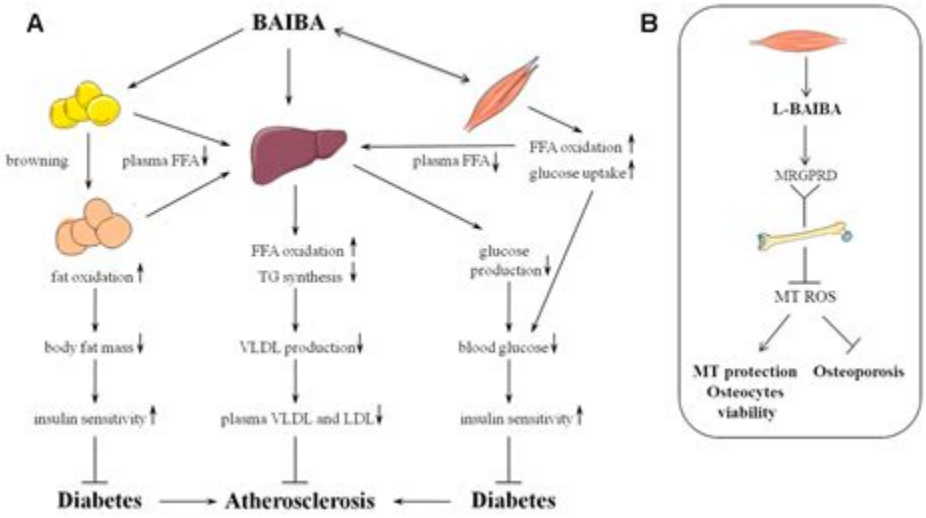
However, no toxicological effects of L-BAIBA in animals or humans have been established. The present study was designed to evaluate the safety and toxic potentials of this compound, where L-BAIBA was administered orally to Sprague Dawley rats at 100, 300, and 900 mg/kg/day for 90 days. . All animals were observed for cage side clinical signs .

MitoBurn: β-Aminoisobutyric Acid (L-BAIBA) from NNB Nutrition



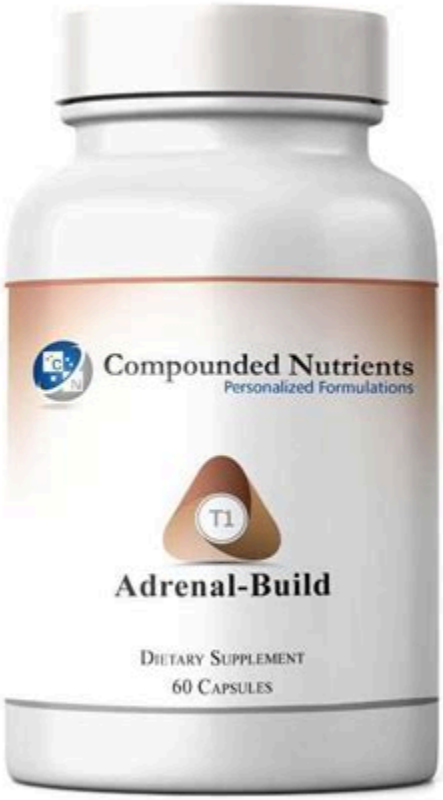
The effects of l- BAIBA are mediated via MRGPRD that decreases with aging • In vivo, l- BAIBA reduces bone and muscle loss resulting from immobilization Summary Exercise has beneficial effects on metabolism and on tissues.

Beta-Aminoisobutyric Acid as a Novel Regulator of Carbohydrate and .



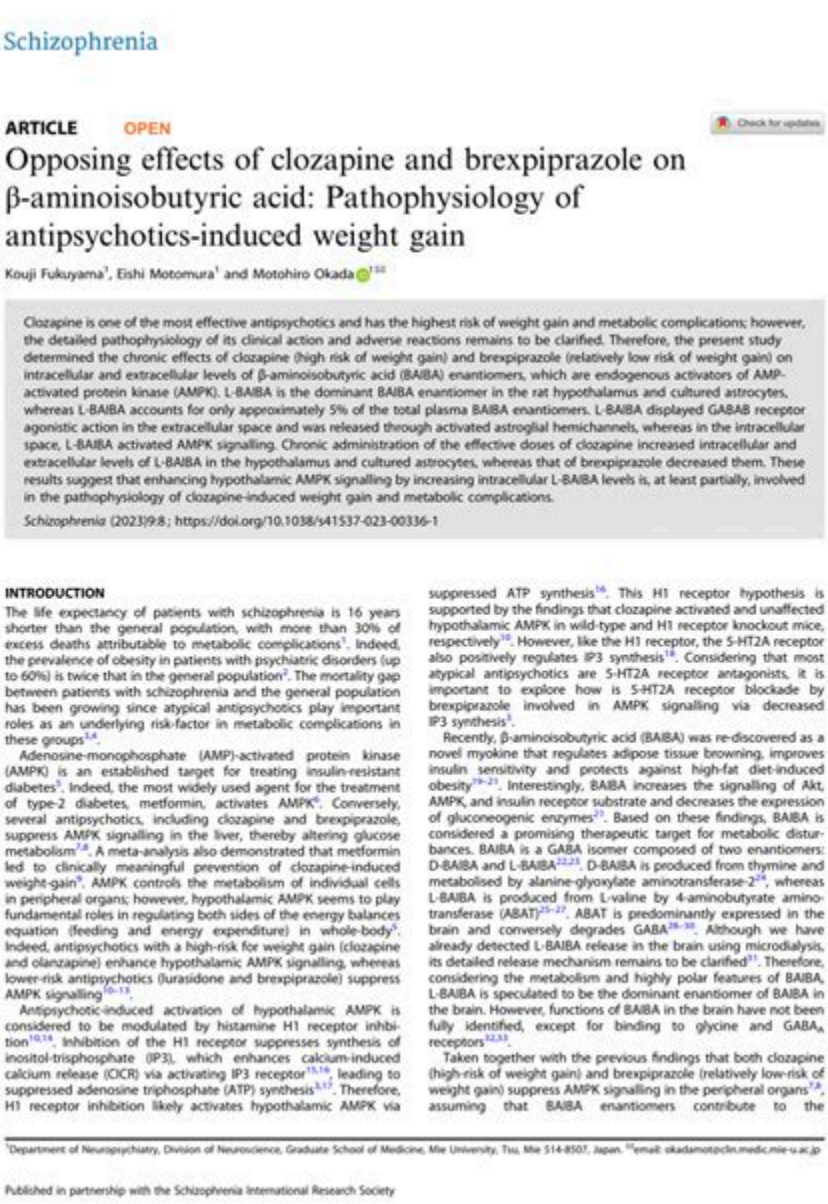
Here we identify b-aminoisobutyric acid (BAIBA) as a major osteocyte-protective factor. In 2014, BAIBA was described as a small (103. 6-Da) molecule produced by skeletal muscle during exercise (Roberts et al. , 2014), and it was shown to signal the beneficial effect of exercise from skeletal muscle to other tissues and organs in an endocrine manner.

Nutrients | Free Full-Text | Beta-Aminoisobutyric Acid as a Novel .



L-BAIBA is converted to D-BAIBA and vice versa through the stereoisomerization pathway between L-MMS and D-MMS (24, 27). MMSDH has been less reported in organs and seems to be concentrated in the liver. . it is important to achieve drug efficacy without toxic side effects. A toxicological study showed that L-BAIBA can be delivered without .

Opposing effects of clozapine and brexpiprazole on β . - Nature



Schizophrenia

ARTICLE OPEN

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Opposing effects of clozapine and brexpiprazole on β-aminoisobutyric acid: Pathophysiology of antipsychotics-induced weight gain

Kouji Fukuyama[1], Eishi Motomura[1] and Motohiro Okada[1]✉

Clozapine is one of the most effective antipsychotics and has the highest risk of weight gain and metabolic complications; however, the detailed pathophysiology of its clinical action and adverse reactions remains to be clarified. Therefore, the present study determined the chronic effects of clozapine (high risk of weight gain) and brexpiprazole (relatively low risk of weight gain) on intracellular and extracellular levels of β-aminoisobutyric acid (BAIBA) enantiomers, which are endogenous activators of AMP-activated protein kinase (AMPK). L-BAIBA is the dominant BAIBA enantiomer in the rat hypothalamus and cultured astrocytes, whereas L-BAIBA accounts for only approximately 5% of the total plasma BAIBA enantiomers. L-BAIBA displayed GABAB receptor agonistic action in the extracellular space and was released through activated astroglial hemichannels, whereas in the intracellular space, L-BAIBA activated AMPK signalling. Chronic administration of the effective doses of clozapine increased intracellular and extracellular levels of L-BAIBA in the hypothalamus and cultured astrocytes, whereas that of brexpiprazole decreased them. These results suggest that enhancing hypothalamic AMPK signalling by increasing intracellular L-BAIBA levels is, at least partially, involved in the pathophysiology of clozapine-induced weight gain and metabolic complications.

Schizophrenia (2023)9:8 ; https://doi.org/10.1038/s41537-023-00336-1

INTRODUCTION

The life expectancy of patients with schizophrenia is 16 years shorter than the general population, with more than 30% of excess deaths attributable to metabolic complications[1]. Indeed, the prevalence of obesity in patients with psychiatric disorders (up to 60%) is twice that in the general population[2]. The mortality gap between patients with schizophrenia and the general population has been growing since atypical antipsychotics play important roles as an underlying risk-factor in metabolic complications in these groups[3,4].

Adenosine-monophosphate (AMP)-activated protein kinase (AMPK) is an established target for treating insulin-resistant diabetes[5]. Indeed, the most widely used agent for the treatment of type-2 diabetes, metformin, activates AMPK[6]. Conversely, several antipsychotics, including clozapine and brexpiprazole, suppress AMPK signalling in the liver, thereby altering glucose metabolism[7,8]. A meta-analysis also demonstrated that metformin led to clinically meaningful prevention of clozapine-induced weight-gain[9]. AMPK controls the metabolism of individual cells in peripheral organs; however, hypothalamic AMPK seems to play fundamental roles in regulating both sides of the energy balances equation (feeding and energy expenditure) in whole-body[5]. Indeed, antipsychotics with a high-risk for weight gain (clozapine and olanzapine) enhance hypothalamic AMPK signalling, whereas lower-risk antipsychotics (lurasidone and brexpiprazole) suppress AMPK signalling[10–13].

Antipsychotic-induced activation of hypothalamic AMPK is considered to be modulated by histamine H1 receptor inhibition[10,14]. Inhibition of the H1 receptor suppresses synthesis of inositol-trisphosphate (IP3), which enhances calcium-induced calcium release (CICR) via activating IP3 receptor[15,16], leading to suppressed adenosine triphosphate (ATP) synthesis[3,17]. Therefore, H1 receptor inhibition likely activates hypothalamic AMPK via suppressed ATP synthesis[16]. This H1 receptor hypothesis is supported by the findings that clozapine activated and unaffected hypothalamic AMPK in wild-type and H1 receptor knockout mice, respectively[10]. However, like the H1 receptor, the 5-HT2A receptor also positively regulates IP3 synthesis[18]. Considering that most atypical antipsychotics are 5-HT2A receptor antagonists, it is important to explore how is 5-HT2A receptor blockade by brexpiprazole involved in AMPK signalling via decreased IP3 synthesis[3].

Recently, β-aminoisobutyric acid (BAIBA) was re-discovered as a novel myokine that regulates adipose tissue browning, improves insulin sensitivity and protects against high-fat diet-induced obesity[19–21]. Interestingly, BAIBA increases the signalling of Akt, AMPK, and insulin receptor substrate and decreases the expression of gluconeogenic enzymes[21]. Based on these findings, BAIBA is considered a promising therapeutic target for metabolic disturbances. BAIBA is a GABA isomer composed of two enantiomers: D-BAIBA and L-BAIBA[22,23]. D-BAIBA is produced from thymine and metabolised by alanine-glyoxylate aminotransferase-2[24], whereas L-BAIBA is produced from L-valine by 4-aminobutyrate aminotransferase (ABAT)[25–27]. ABAT is predominantly expressed in the brain and conversely degrades GABA[28–30]. Although we have already detected L-BAIBA release in the brain using microdialysis, its detailed release mechanism remains to be clarified[31]. Therefore, considering the metabolism and highly polar features of BAIBA, L-BAIBA is speculated to be the dominant enantiomer of BAIBA in the brain. However, functions of BAIBA in the brain have not been fully identified, except for binding to glycine and $GABA_A$ receptors[32,33].

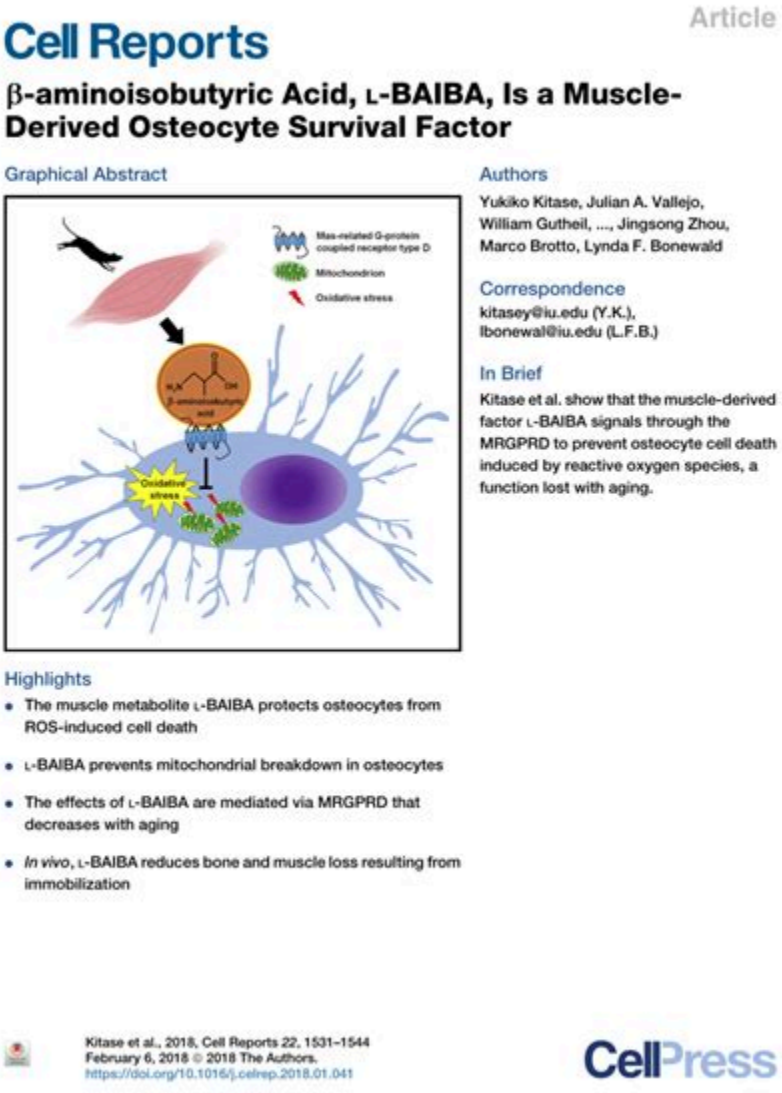
Taken together with the previous findings that both clozapine (high-risk of weight gain) and brexpiprazole (relatively low-risk of weight gain) suppress AMPK signalling in the peripheral organs[7,8], assuming that BAIBA enantiomers contribute to the

[1]Department of Neuropsychiatry, Division of Neuroscience, Graduate School of Medicine, Mie University, Tsu, Mie 514-8507, Japan. ✉email: okadamotoclin.medic.mie-u.ac.jp

Published in partnership with the Schizophrenia International Research Society

Introduction. β-aminoisobutyric acid (BAIBA) is an aminobutyric acid (ABA) first discovered in 1951 1. BAIBA has been shown to be involved in various metabolic processes such as the browning of white fat and hepatic β-oxidation 2, improvement of glucose homeostasis through reducing insulin resistance in skeletal muscle 3, prevention of diet induced obesity 4, and protection against metabolic .

β-aminoisobutyric Acid, l-BAIBA, Is a Muscle-Derived . - PubMed



Article

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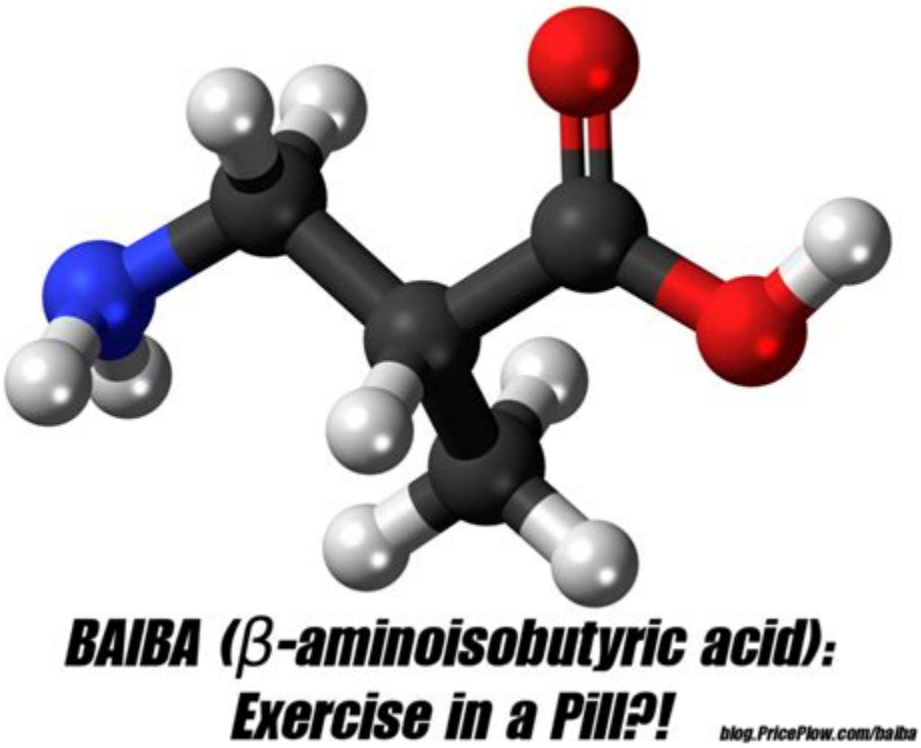
CellPress

Lose Body Fat with MitoBurn BAIBA Fri, 2021-03-12 12:31 The supplement industry is always looking for its next magic bullet: a pill that can result in massive effects with little work or effort.

BAIBA: Weight Loss Ingredient Coined "The Exercise Molecule"



Diabetic nephropathy is one of the most frequent complications of type 2 diabetes, characterized by the progressive damage of renal tissue and impairments in glomerular filtration, clinically.

PDF β-aminoisobutyric Acid, l-BAIBA, Is a Muscle-Derived Osteocyte Survival .

Article

Cell Reports

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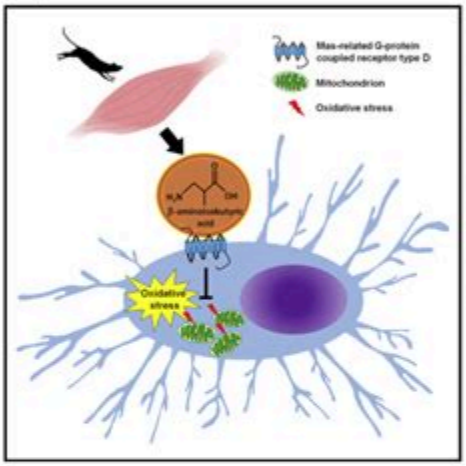

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https://doi.org/10.1016/j.celrep.2018.01.041

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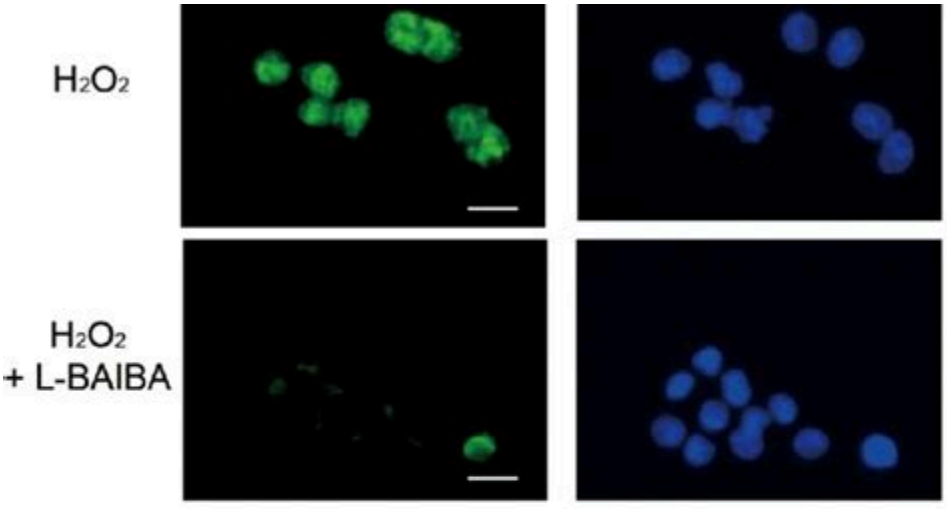
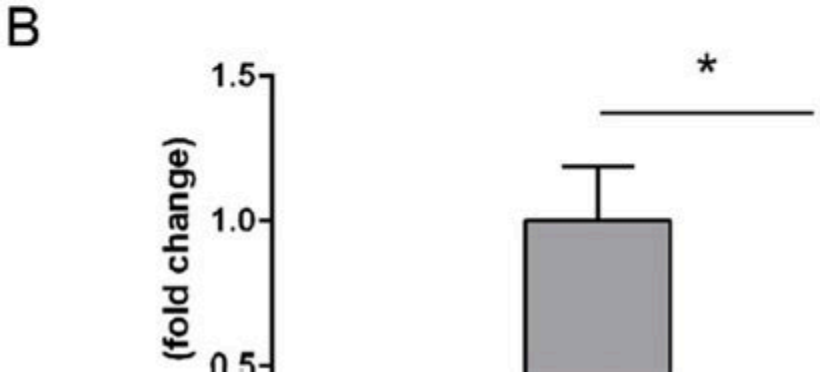
Results We found that L-BAIBA can protect the lung from I/R injury by inhibiting ferroptosis, which depends on the up-regulation of the expressions of GPX4 and SLC7A11 in C57BL/6 mice. Additionally, we demonstrated that the Nrf-2 signaling pathway is key to the inhibitory effect of L-BAIBA on ferroptosis in A549 and BEAS-2B cells.

L-Baiba - Does This Have The Same Effects As Exercise?

L-Baiba (Beta-aminoisobutyric acid): Risks and Benefits. Evolve Further. June 30, 2023. Body. L-Baiba (Beta-aminoisobutyric acid): Risks and Benefits.

β-Aminoisobutyric acid, L-BAIBA, protects PC12 cells from hydrogen .





Exercise has beneficial effects on metabolism and on tissues. The exercise-induced muscle factor β-aminoisobutyric acid (BAIBA) plays a critical role in the browning of white fat and in insulin resistance. Here we show another function for BAIBA, that of a bone-protective factor that prevents osteoc …

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