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SHORT COMMUNICATION

Recent data on obesity research: β-aminoisobutyric acid

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Abstract: The world-wide epidemic of obesity is now affecting up to a third of the adult population. Research attempting to contribute to management of this health scourge has been recently refocused on the essential role of physical activity. Muscle activity induces a dramatic increase in transcription of the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α). This protein is a regulator of mitochondrial biogenesis and function. Very recently, in 2014 it was revealed that the mediator of this metabolic process is a low molecular myokine, the beta- aminoisobutyric acid (BAIBA). This compound with a simple molecular structure has a key metabolic role: it converts the cells of white adipose tissue into brown fat. The brown adipocytes contain a protein thermogenin. This substance turns off the energy stores, among others the adenosine triphosphate (ATP), thereby accelerating the breakdown of lipids into heat, water and CO_2. We may be at the threshold of new and effective management of obesity. The world eagerly expects to see how the BAIBA will compare with other recently reported agents to fight the overweight *(Fig. 2, Ref. 6)*. Text in PDF *www.elis.sk*.
Key words: obesity, prevalence, exercise, proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), beta-aminoisobutyric acid (BAIBA), brown adipocytes, fat degradation.

The increasing prevalence of obesity and its comorbidities represent a major threat to human health globally. Obesity contributes to the metabolic sybdrome with the accompanying risk of atherosclerosis, diabetes type 2 and degenerative bone disease. The most frequently used measure of obesity is based on the body mass index (BMI = weight in kg/height in m^2). The most recent data on adult prevalence of obesity by FAO (Food and Agriculture Organization) (1) indicate that obesity in Mexico is now even higher than in the USA. In Europe the population in the Czech Republic has the unenviable priority in excessive body mass.

It has been confirmed beyond doubt that physical activity is essential in controlling the body mass. Yet, specific metabolic pathways controlling adipose tissue metabolism have been largely undefined. About ten years ago it was revealed that exercise induces a dramatic transient increase in transcription of the peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) (2). This protein is a regulator of mitochondrial biogenesis and function. It is assumed that the combination of elevated muscle PGC-1α which regulates the metabolic genes in skeletal muscle, with exercise indicates potential therapeutic approach for efficient long-term control of body weight and for the treatment of the metabolic syndrome (3).

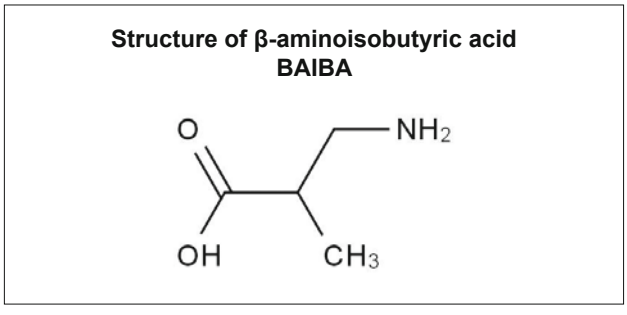

Fig. 1. Chemical structure of β-aminoisobutyric acid (BAIBA).

In January 2014 a research report appeared that may carry far reaching implications (4). The authors employed a metabolomic approach to examine metabolites secreted from myocytes with forced expression of PGC-1α, and identified β-aminoisobutyric acid (BAIBA) as a small molecule myokine (Fig. 1).

BAIBA increases the expression of brown adipocyte-specific genes in white adipocytes. It also increases β-oxidation in hepatocytes, both in vitro and in vivo and improves glucose homeostasis in mice. In humans, plasma BAIBA concentrations are increased with exercise and inversely associated with metabolic risk factors.

This amino acid with a simple molecular structure does not participate in protein biosynthesis. Its specific role is to convert the adipocytes in white adipose tissue into brown fat cells. Brown adipocytes contain a specific protein, thermogenin which turns off the activity of energy reserves (for example adenosin triphosphate, ATP). This results in a more efficient breakdown of lipids into heat, H_2O and CO_2 (5). BAIBA may thus contribute to exercise-induced protection from fat accumulation (Fig. 2).

Recently (6) attempts were reported to modify the metabolic syndrome in a genetic model of human adiposity, in the Prader – Willi syndrome. These genetically affected individuals manifest excessive appetite and extreme obesity. Agents have been tried to intervene in metabolic faults of this syndrome, with the assump-

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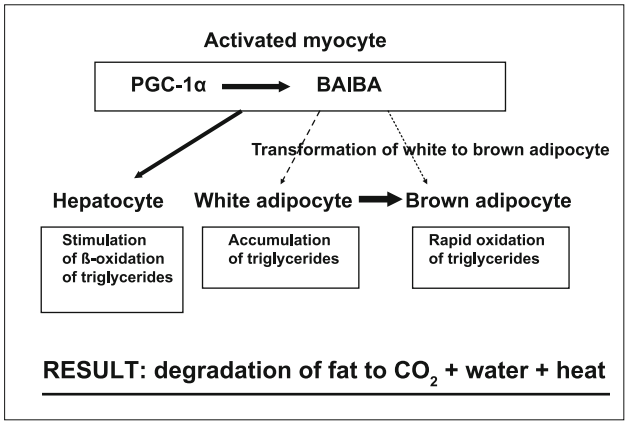

Fig. 2. Role of β-aminoisobutyric acid in fat degradation.

tion they would act similarly on the garden variety of obesity that affects the world population. It was reported that beloranib (Zafgen) may reduce lipid synthesis and accelerate fat metabolism in Prader-Willi subjects, by inhibiting the enzyme methionine aminopeptidase 2. This trial was performed in a very small sample of subjects. Ferring company is testing an oxytocin analog Carbetocin as an anti obesity medication.

The road to medical management of obesity seems to be long and complicated. Metabolic control of appetite and of body mass is subjected to multiple and complex mediators. Prader- Willi subjects may not be an ideal model for medication testing: appetite controlling role of hormones ghrelin and leptin may be different in genetic versus environmental type of obesity.

Conclusion

We will certainly witness in the near future an intensive pharmacological research, related to management of obesity, including testing of BAIBA. The scientific community and world public wait for strictly controlled studies in experimental animals and in human volunteers. Successful outcome would bring relief in human suffering caused by obesity but it would also offer vast economic gains to the pharmaceutical establishment. We may be, at last, at the threshold of new effective management of obesity.

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