Thiamine deficiency induces anorexia by inhibiting hypothalamic AMPK.


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BACKGROUND: Obesity and eating disorders are prevailing health concerns worldwide. It is important to understand the regulation of food intake and energy metabolism. Thiamine (vitamin B1) is an essential nutrient. Thiamine deficiency (TD) can cause a number of disorders in humans, such as Beriberi and Wernicke-Korsakoff syndrome.

OBJECTIVE: We demonstrated here that TD caused anorexia in C57BL/6 mice.

METHODS AND RESULTS: After feeding a TD diet for 16 days, the mice displayed a significant decrease in food intake and an increase in resting energy expenditure (REE), which resulted in a severe weight loss. At the 22nd day, the food intake was reduced by 69% and 74% for male and female mice, respectively in TD group. The REE increased by ninefolds in TD group. The loss of body weight (17-24%) was similar between male and female animals and mainly resulted from the reduction of fat mass (49% decrease). Re-supplementation of thiamine (benfotiamine) restored animal's appetite, leading to a total recovery of body weight. The hypothalamic adenosine monophosphate-activated protein kinase (AMPK) is a critical regulator of food intake. TD inhibited the phosphorylation of AMPK in the arcuate nucleus (ARN) and paraventricular nucleus (PVN) of the hypothalamus without affecting its expression. TD-induced inhibition of AMPK phosphorylation was reversed once thiamine was re-supplemented. In contrast, TD increased AMPK phosphorylation in the skeletal muscle and upregulated the uncoupling protein (UCP)-1 in brown adipose tissues which was consistent with increased basal energy expenditure. Re-administration of thiamine stabilized AMPK phosphorylation in the skeletal muscle as well as energy expenditure.

CONCLUSION: Taken together, TD may induce anorexia by inhibiting hypothalamic AMPK activity. With a simultaneous increase in energy expenditure, TD caused an overall body weight loss. The results suggest that the status of thiamine levels in the body may affect food intake and body weight.

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