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Research report

L-Ornithine intake affects sympathetic nerve outflows and reduces body weight and food intake in rats

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ABSTRACT

Ingesting the amino acid L-ornithine effectively improves lipid metabolism in humans, although it is unknown whether it affects the activities of autonomic nerves that supply the peripheral organs related to lipid metabolism, such as adipose tissues. Thus, we investigated the effects of L-ornithine ingestion on autonomic nerves that innervate adipose tissues and the feeding behaviors of rats. Intragastric injection of L-ornithine (2.5%) in urethane-anesthetized rats activated sympathetic nerve activity to white adipose tissue (WAT-SNA), and stimulated sympathetic nerve activity to brown adipose tissue (BAT-SNA). In addition, WAT-SNA responses to L-ornithine were abolished in rats with ablated abdominal vagal nerves. L-ornithine ingestion for 9 weeks also significantly reduced rats' body weight, food intake, and abdominal fat weight. Proopiomelanocortin (POMC) levels in the hypothalamus and uncoupling protein 1 (UCP1) levels in brown adipose tissue were significantly increased in rats that ingested 2.5% L-ornithine for 9 weeks. These results suggested that ingested L-ornithine was taken up in the gastrointestinal organs and stimulated afferent vagal nerves and activated the central nervous system. Subsequently, increased hypothalamic POMC activated sympathetic neurotransmission to adipose tissues and accelerated energy expenditure.

1. Introduction

Obesity is a common public health problem worldwide and one of the risk factors for metabolic syndrome. We previously investigated whether some factors in beverages had any preventative effects on diet-induced obesity in rats, and found that long term ingestion of flavangenol or *Lactobacillus paracasei* ST11 reduced the body weight and body fat of rats that were fed a high-fat diet (Tanida et al., 2008, 2009). It was also recently found that long-term ingestion of the amino acid salt monosodium glutamate also suppressed body weight gain in rats (Kondoh and Torii, 2008). Furthermore, intragastric (IG) injection of monosodium glutamate stimulated sympathetic nerve activity to white adipose tissue (WAT-SNA) and brown adipose tissue (BAT-SNA) (Tanida and Satomi, 2011). These results are consistent with an anti-obese effect of glutamate because sympathoexcitation in these tissues accelerates triglyceride degradation in white adipose tissue (WAT) and thermogenesis in brown adipose tissue (BAT) (Richard and Picard, 2011). Thus, these results suggest that some components in foods and beverages are both nutrients, such amino acids, and might have effective actions on metabolic syndrome through the autonomic nervous system.

L-ornithine is a free amino acid that was recently found to have multiple actions, including improved hepatic function (Briggs and Freedland, 1976) and increased growth hormone synthesis in the brain (Tujioka et al., 2012). This suggested that L-ornithine supplementation might be effective for central and peripheral organs for regulating their homeostatic functions. However, it has not been investigated whether L-ornithine affects feeding behavior or body weight regulation through autonomic neurotransmission. Thus, in

Abbreviations: IG, intragastric; BAT-SNA, brown adipose tissue-sympathetic nerve activity; BAT, brown adipose tissue; WAT-SNA, white adipose tissue-sympathetic nerve activity; WAT, white adipose tissue; POMC, Proopiomelanocortin.

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this study, we investigated the effects of L-ornithine taken up into gastrointestinal organs on sympathetic nerve outflows to WAT and the BAT in anesthetized rats and the effects of prolonged ingestion of L-ornithine on rats' body weight and food intake.

2. Materials and methods

2.1. Animals

We used male Wistar rats (weighing 235–292 g) in the present experiment. Animals were housed in a temperature-controlled room with a 12-hour light–dark cycle (07:00–19:00 h). Food and water were freely available. Animals were adapted to the experimental environment for at least 1 week prior to the experiment. All animal care and handling procedures were approved by the Institutional Animal Care and Use Committee of Ritsumeikan University.

2.2. Electrophysiological recording

On the day of the experiment, food was removed 3–4 h prior to surgery. Under anesthesia induced by intraperitoneal injection of 1.2 g/kg urethane (when it was insufficient, 0.2–0.3 g/kg of urethane was added), a polyethylene catheter was inserted into the femoral vein for intravenous injection. The rat was then cannulated through the trachea and fixed in a stereotaxic apparatus. Body temperature was maintained at 36.5–37.0 °C using a heating pad and monitored with a thermometer inserted into the rectum. To maintain constant depth of anesthesia, we checked whether rapid variations of mean blood pressure (±5 mmHg) would be caused by paw pinch

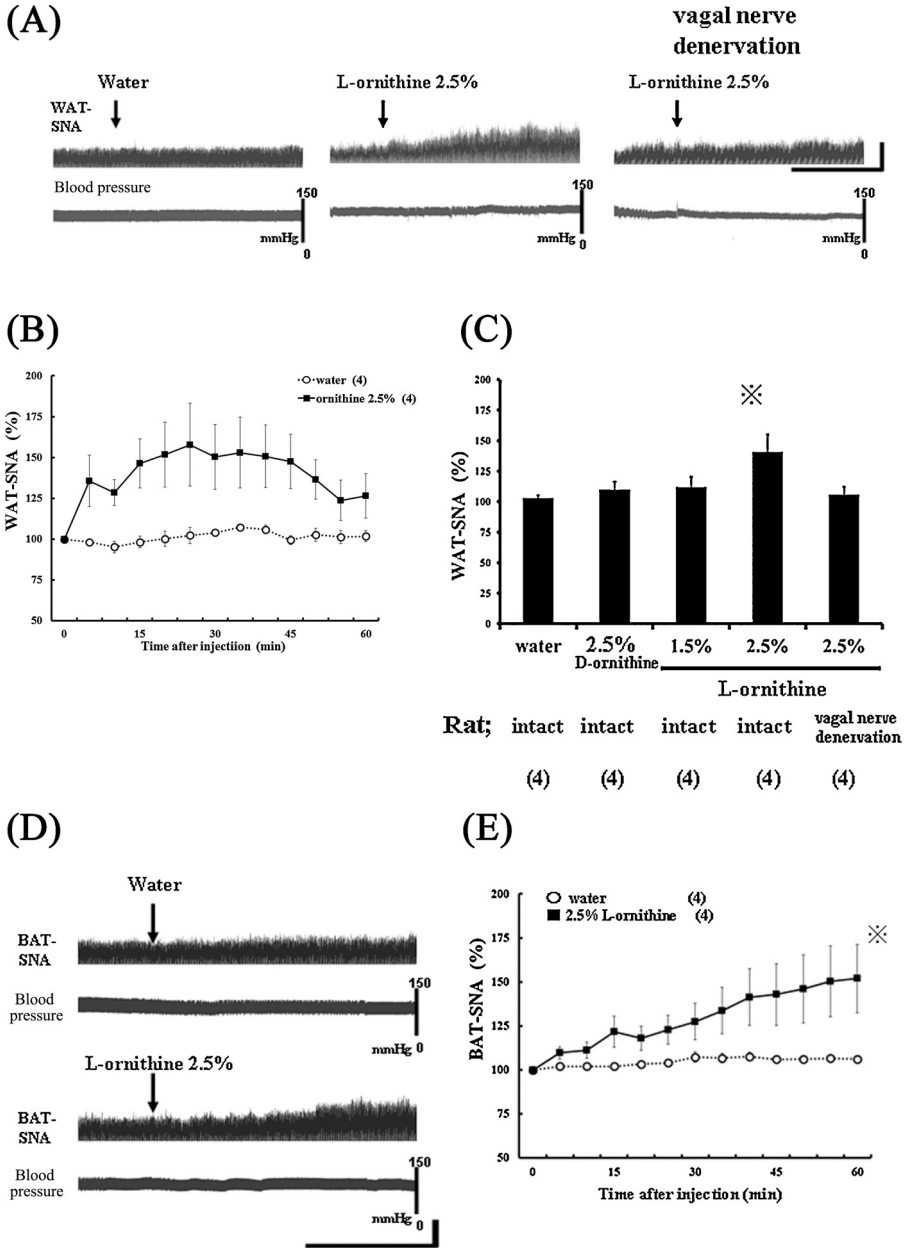

Fig. 1. Effects of IG injection of L-ornithine on neural activities of sympathetic nerves supplying to the WAT or BAT in urethane-anesthetized rats.
Raw tracing data of WAT-SNA (A) and BAT-SNA(D) before and after IG injection of water or 2.5% L-ornithine (Vertical bars; 100 impulses/5 s, Horizontal bars; 30 min). Time-course data of responses of WAT-SNA (B) and BAT-SNA (E) to water or 2.5% L-ornithine. Dose responses of WAT-SNA to L-ornithine (1.5%, 2.5%) in intact rats and response of WAT-SNA to 2.5% L-ornithine in rats treated vagal nerve denervation were described as bar graph (C). Values were expressed as means ± SEM. The numbers of animals used were shown in parentheses. Significant difference between values of groups after injection was analyzed by ANOVA. * $P < 0.05$ vs. water group.