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The association of serum leptin with the reduction of food intake and body weight during electroacupuncture in rats

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Abstract

Previous studies indicate that acupuncture or electroacupuncture (EA) treatment reduces body weight and food intake in rats by increasing the level of anoretic peptides and decreasing that of orexigenic peptides in the hypothalamus. Considering a well-established role of leptin as a major regulator for feeding behavior in the hypothalamus, we hypothesized that EA might exert its effect via increasing serum leptin levels. In this study, we tested our hypothesis by evaluating the effects of EA on food intake and body weight, as well as on serum leptin levels in rats. Rats were randomly divided into 3 groups: AL (fed ad libitum with no treatments), Holder (fed ad libitum with daily holder restraint) and EA (fed ad libitum with daily holder restraint and 100 Hz EA stimulation) groups. During the four-week experimental period, daily food intake and body weight were measured. At the end of the experiment, levels of serum leptin and corticosterone, and plasma epinephrine (Epi) and norepinephrine (NE) were determined. Here we demonstrate that EA treatment indeed led to reduction of food intake and body weight, and to an increase of serum leptin levels. The level of Epi, NE, and corticosterone increased in the Holder group, but such increase in the level of aforementioned stress hormones was not observed in the EA group. Overall, our results suggest that EA treatment reduces food intake and body weight in rats possibly through increasing leptin levels, and that this effect of EA is not due to the stress caused by the daily holder restraint.

Keywords: Electroacupuncture; Food intake; Body weight; Leptin; Rat

1. Introduction

The body weight control systems appear to respond more sensitively to weight loss rather than weight gain. This notion has been reflected in human evolutionary history, in which food scarcity, not overabundance, was the major danger. However, most people in developed and developing countries now have access to an abundance of food and tend to become more sedentary (Friedman, 2003; Marx, 2003; Pi-Sunyer, 2003). Obesity, which is considered a major risk factor for life-threatening diseases including type II diabetes, heart attack, stroke, and some types of cancer, has been increasing at an alarming rate in recent years, becoming now a worldwide public health problem (Friedman, 2000; Marx, 2003; Lazar, 2005). Increases in adult prevalence of obesity are reflected by a striking increase in childhood and adolescent weight. The early onset of obesity leads to an increased likelihood of obesity in later life as well as an increased prevalence of obesity-related diseases (Dietz, 1994; Kotani et al., 1997; Kopleman, 2000; Lazar, 2005). Therefore, proper regulation of food intake and body weight before adulthood is required.

Acupuncture has long been used in Eastern countries for the treatment of various diseases, generating few side effects, and is recently considered a new alternative method of medicine in Western countries (NIH Consensus Conference, 1998; Kaptchuk, 2002; Lacey et al., 2003). Previous studies have shown that acupuncture treatment increases the activity of the ventromedial

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hypothalamus (VMH, "satiety" center) in obese rats (Zhao et al., 2000) and decreases neuropeptide Y (NPY) expression in the arcuate nucleus of diabetic rats (Lee et al., 2004). Electroacupuncture (EA) is a modified technique of acupuncture using electrical stimulation and was found to have beneficial effects on obesity in children (Gadzhiev et al., 1993). Recently, it has been reported that low and high frequency EA significantly decreased food intake and body weight, and up-regulated the expression of α-melanocyte-stimulating hormone (α-MSH) and cocaine- and amphetamine-regulated transcript (CART) in the hypothalamic arcuate nucleus of obese rats (Tian et al., 2003, 2005).

The hormone leptin, released into the bloodstream by adipocytes, regulates feeding behavior by acting directly on neurons of the hypothalamus. A decrease in body fat leads to a decreased level of leptin, which in turn stimulates food intake by increasing NPY and agouti-related protein (AgRP) in the arcuate nucleus. On the other hand, increased body fat is associated with increased leptin levels, which act to reduce food intake by increasing α-MSH and CART in the arcuate nucleus (Schwartz et al., 2000; Bear et al., 2001; Ahima and Osei, 2004).

Based on the similarity between the physiological results of leptin action and the central effects of EA on food intake and body weight, we hypothesized that EA might reduce food intake and body weight by increasing the serum leptin levels. To explore our hypothesis, we examined the effects of EA on food intake and body weight, and on serum leptin in young male Sprague–Dawley (SD) rats.

2. Materials and methods

2.1. Experimental animals

Young male SD rats (Sam:TacN(SD)BR, 190–210 g, 7 weeks) were housed in groups of four, with water and food available ad libitum. The room was maintained with a 12-h light/dark cycle (08:00–20:00 light, 20:00–08:00 dark) and kept at 23 ± 2 °C. After 5-day acclimation in this laboratory environment, rats were randomly divided into 3 groups: AL group (fed ad libitum with no treatments, $n = 8$, 4 rats/cage), Holder group (fed ad libitum with daily holder restraint for 4 weeks, $n = 8$, 4 rats/cage) and EA group (fed ad libitum with daily holder restraint and high frequency EA stimulation at Zusanli (ST36) acupoint for 4 weeks, $n = 8$, 4 rats/cage). Daily food intake and body weight were measured at 14:00 every day during the 4-week experimental period. The study was approved by the Institutional Animal Care and Use Committee of Kyung-Hee University and all procedures were conducted in accordance with the NIH guidelines.

2.2. EA stimulation

Rats of the Holder and EA groups were restrained in a plastic holder (5.3 × 15, 5.6 × 17, 6.0 × 24 cm in diameter × length). Two stainless-steel needles of 0.25 mm in diameter and 4 cm in length were inserted into the Zusanli (ST36) acupoint which is located at the anterior tibial muscle and about 10 mm below the knee joint (Fig. 1). This point is known to reduce body weight and food intake in rats (Tian et al., 2003, 2005). For EA stimulation, train-pulses (100 Hz, 0.3 ms pulse width, 0.2–0.3 mA) were applied to the inserted needle for 30 min. The other needle (anode) was inserted into the anterior tibial muscle 5 mm distal to the first one. Anodal and cathodal leads from an electrical stimulator were connected to the two acupuncture needles. The rat in the Holder group was restrained for 30 min without EA stimulation. The EA stimulation and holder restraint experiment were performed between 14:00 and 15:00.

2.3. Measurement of serum leptin and corticosterone, and plasma catecholamines

On the final day of the experiments, cardiac blood was collected under CO_2 asphyxiation. Serum and plasma were separated, respectively, and stored at −70 °C until the day of the analysis. Serum leptin levels were determined with commercially available $[I]^{125}$-labelled rat leptin RIA kits (Linco Research, Inc., USA). The measurement of serum corticosterone was performed with a commercial rat corticosterone EIA kits (DSL, USA). Plasma Epi and NE were assayed using HPLC with electrochemical detection.

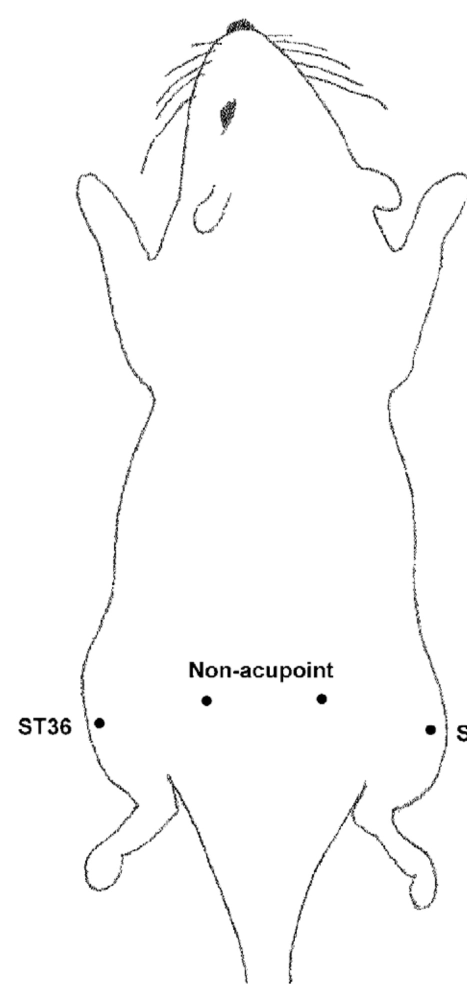

Fig. 1. Location of the acupoint ST36 and non-acupoint in the rat. ST36 = Zusanli acupoint which is located at the anterior tibial muscle and about 10 mm below the knee joint. Non-acupoint = located midway between the coccyx and hip joints.