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High- or low-salt diet from weaning to adulthood: Effect on body weight, food intake and energy balance in rats☆

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KEYWORDS
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Abstract *Objective:* To get some additional insight on the mechanisms of the effect of salt intake on body weight.
Design and methods: Rats were fed a low (LSD), normal (NSD), or high (HSD) salt diet. In a first set, body weight, tail-cuff blood pressure, fasting plasma thyroid-stimulating hormone, triiodothyronine, L-thyroxine, glucose, insulin, and angiotensin II were

Abbreviations: ANG II, angiotensin II; BAT, brown adipose tissue; BP, tail-cuff blood pressure; GLUTs, glucose transporters; HSD, high-salt diet; LO, locomotion frequencies; LSD, low-salt diet; NSD, normal-salt diet; RE, rearing frequencies; SNS, sympathetic nervous system; SGLTs, sodium-glucose transporters; T3, plasma triiodothyronine; T4, plasma L-thyroxine; TSH, thyroid-stimulating hormone; UCP1, uncoupling protein 1; WAT, white adipose tissue.

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Angiotensin II;
Blood pressure

measured. Angiotensin II content was determined in white and brown adipose tissues. Uncoupling protein 1 expression was measured in brown adipose tissue. In a second set, body weight, food intake, energy balance, and plasma leptin were determined. In a third set of rats, motor activity and body weight were evaluated.
Results: Blood pressure increased on HSD. Body weight was similar among groups at weaning, but during adulthood it was lower on HSD and higher on LSD. Food intake, L-thyroxine concentration, uncoupling protein 1 expression and energy expenditure were higher in HSD rats, while non-fasting leptin concentration was lower in these groups compared to NSD and LSD animals. Plasma thyroid-stimulating hormone decreased on both HSD and LSD while plasma glucose and insulin were elevated only on LSD. A decrease in plasma angiotensin II was observed in HSD rats. On LSD, an increase in brown adipose tissue angiotensin II content was associated to decreased uncoupling protein 1 expression and energy expenditure. In this group, a low angiotensin II content in white adipose tissue was also found. Motor activity was not influenced by the dietary salt content.
Conclusions: Chronic alteration in salt intake is associated with changes in body weight, food intake, hormonal profile, and energy expenditure and tissue angiotensin II content.

Introduction

Salt restriction is usually recommended as antihypertensive treatment [1]. However, effects on glucose and lipid metabolism [2—4] have been reported in response to severe sodium restriction. We have previously demonstrated that 12-week-old male Wistar rats receiving low-salt diet (LSD) from weaning to adulthood present lower blood pressure, kidney mass, and glucose uptake in isolated adipocytes [5]. Recently, we found that rats on chronic LSD have a higher body weight than rats on normal salt diet (NSD) and on high salt diet (HSD) [6]. A lower triacylglycerol-containing lipoprotein removal rate [7] and decreased insulin sensitivity [6] were also shown in rats on LSD.

A hypothesis for the higher body weight observed in response to salt restriction is an increase in food intake and/or a decrease in energy expenditure. Decreased energy expenditure may be due to hypoactive brown adipose tissue (BAT), low motor activity or a hormonal factor. So, in the present study, body weight, food intake and energy balance were evaluated after chronic salt restriction and overload. Parameters like plasma glucose, angiotensin II, insulin, leptin, thyroid-stimulating hormone (TSH), triiodothyronine (T3), and L-thyroxine (T4) were determined. Tissue angiotensin II content was measured in BAT and white adipose tissue (WAT), in which the uncoupling protein 1 (UCP1) expression was also evaluated. This study provides evidence that changes in hormonal profile, food intake, and energy balance are involved in body weight regulation disrupted by changes in salt intake.

Methods

All experiments reported herein are in accordance with the guidelines of the Ethics Committee of the University of São Paulo School of Medicine, São Paulo, Brazil.

Animals

Male Wistar rats from the Institutional Animal Facility were fed a LSD (0.06% Na, TD 92141-Harlan Teklad), NSD (0.5% Na, TD 92140), or HSD (3.12% Na, TD 92142), from weaning (3 weeks of age) to adulthood (12 weeks of age). The only difference between the three diets was their sodium content. Rats were housed in a controlled-temperature environment (25 °C), with a 12-h light/dark cycle and free access to chow and tap water.

Experimental protocol

Rats on LSD, NSD, and HSD were studied in three different and independent sets. In the first set, body weight was measured at weekly intervals, from weaning until 12 weeks of age. Tail-cuff blood pressure (BP), plasma glucose, insulin, angiotensin II, TSH, T3, T4 and hematocrit were measured before excision of the white and brown adipose tissues for determination of angiotensin II content and uncoupling protein 1 expression (only in the BAT), at 12 weeks of age. In a second set, body weight and food intake were determined. After overnight fasting, energy balance was determined by calorimetry, and blood samples were collected for leptin evaluation. Blood samples from some additional rats in non-fasted condition were also collected for leptin