Autonomic Responses

Sympathetic and Renin-Angiotensin Systems Contribute to Increased Blood Pressure in Sucrose-Fed Rats


Background: This study evaluated the effect of chronic sucrose feeding on hemodynamic parameters and renal sympathetic nervous activity. In addition, angiotensin I, II, and 1–7 levels were determined in plasma, heart, kidney, and the epididymal adipose tissue.

Methods: Male Wistar rats were treated for 30 days with 20% sucrose solution (n = 21) or tap water (n = 19) and food ad libitum. Blood pressure, cardiac output, and total peripheral resistance were recorded at the end of the 30-day treatment period. Sympathetic and angiotensinergic systems were evaluated by acute hexamethonium and captopril administration; plasma and tissue (heart, kidney, and epididymal adipose tissue) angiotensins were measured by high-performance liquid chromatography; and angiotensin-converting enzyme activity was determined by continuous fluorescent assay. Plasma renin activity and plasma levels of insulin and leptin were evaluated by radioimmunoassay.

Results: Chronic sucrose feeding was associated with increased blood pressure (BP) (129 ± 1 mmHg) and circulating insulin (171%) and leptin (356%) levels when compared with the control group. The sucrose group also showed a 27% higher renal sympathetic nervous activity. The depressor response to hexamethonium was similar in both groups, whereas captopril caused a more pronounced decrease in BP in the sucrose group than in controls (−40 ± 2 mmHg), possibly reflecting the higher plasma renin activity and plasma content of angiotensin II and renal angiotensin II in sucrose rats.


Key Words: Sympathetic nervous system, renin-angiotensin system, hypertension, sucrose feeding, leptin, insulin.

A stimulatory effect of dietary carbohydrates on the sympathetic nervous system (SNS) activity was first recognized 29 years ago. Sucrose-induced elevations of blood pressure (BP) have been attributed to increased SNS activity; however, the mechanisms linking carbohydrate intake and SNS activation have not been clearly identified. Oral fructose has proved to be as potent as glucose in stimulating the SNS in humans and rodents, causing hypertension, hyperinsulinemia, insulin resistance, and hypertriglyceridemia in rats.

The effect of dietary carbohydrates on renal sympathetic nerve activity (rSNA) is controversial. Although it is well known that nutrient intake can affect sodium handling by the kidney and sympathetic activity to nonrenal tissues, the effects of carbohydrates on rSNA remain to be determined. An earlier study showed a preferential SNS activation (indirectly evaluated using norepinephrine turnover) to the heart but not to the kidney after 4 days of sucrose feeding. The effects of a longer period of sucrose feeding on rSNA (directly measured by electrophysiologic activity), however, have not been evaluated.

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From the Departments of Physiology (RRdAF, BAC, CTB, RRC, MSD), Medicine, Division of Nephrology (DHC), and Biophysics (AKC), Universidade Federal de São Paulo; Department of Internal Medicine, Laboratory of Experimental Hypertension, University of São Paulo School of Medicine (KLL, LF, JCH), São Paulo, Brazil.

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Address correspondence and reprint requests to Dr. Miriam S. Dolnikoff, Disciplina de Fisiologia Cardiovascular e Respiratória, UNIFESP–EPM, Rua Botucatu, 862, 04023-060 São Paulo, SP Brazil; e-mail: miriamdolni@yahoo.com

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Although the exact mechanisms underlying the sugar-induced hypertension are unknown, alterations of the renin-angiotensin system (RAS) have also been suggested. In fact, angiotensin (Ang) II receptor and angiotensin-converting enzyme (ACE) blockade was shown to decrease the elevated BP induced by a high-sucrose diet.

Considering that rSNA leads to increased renin secretion and BP, we decided to investigate whether or not these mechanisms are correlated with the hypertension provoked by sucrose feeding. Therefore, the aims of the present study were to evaluate in chronic sucrose-fed rats: (1) rSNA and hemodynamic parameters (cardiac output and total peripheral resistance); sympathetic tonicity effect on BP was estimated by the acute ganglionic blockade; and (2) renal, cardiac, and adipose tissue RAS components (Ang I, II, and 1–7). The RAS tonicity effect on BP was evaluated by acute ACE inhibitor administration. Plasma ACE and renin (PRA) activities were also measured.

**Methods**

**Animals**

Animals were provided by the Animal Facility of the Universidade Federal de São Paulo. All animal procedures were conducted according to the “Guidelines for Ethical Care of Experimental Animals” and were approved by the institutional Ethics Committee (CEP 0758/05). Male Wistar rats (n = 45, 165 ± 2 g) were housed in plastic cages (four rats/cage), fed rat chow ad libitum, and maintained in a room with a constant temperature (23°C) on a 12-h light/dark cycle. The rats were randomly divided into a control (C, n = 24) and a sucrose-fed group (SC, n = 21). A known volume of tap water or 20% sucrose solution was offered each day, for 30 days, and the remaining volume was measured daily to calculate the drinking water.

**Experimental Procedure**

In the present study, rats were divided into four independent series of experiments. In the first series (n = 5 SC, 5 C), rats were individually housed in metabolic cages for 24-h urine collection for volume and sodium determinations. In sequence, the rats were used for hemodynamic measurements performed under conscious conditions. The effects of SNS blockade and ACE inhibition on BP and heart rate (HR) were evaluated in a second series (n = 5 SC, 5 C), also under conscious condition. A third series was used for recording the rSNA (n = 6 SC, 10 C) in anesthetized animals, and in the fourth series the animals were euthanized by decapitation for blood and tissue collection (n = 5 SC, 4 C). With the exception of the last series of experiments, at least 24 h before the experiments began, rats were anesthetized with halothane (2%) and instrumented with femoral venous and arterial catheters for drug injection and arterial pressure recording. The BP and HR were recorded in awake and freely moving rats. The mean arterial pressure (MAP) and HR signals were derived from the pulsatile arterial pressure curve and recorded on a computer-based data acquisition system (PowerLab system; AD Instruments, New South Wales, Australia).

In euthanized animals, kidney (KM), cardiac (CM), and left-ventricular (LVM) masses were determined. Adipose tissues were weighed and in epididymal adipose tissue, cell diameters, Ang I, Ang II, and Ang 1–7 were determined. The Ang I, II, and Ang 1–7 content was also determined in the kidney and left ventricle.

**Hemodynamic Measurements**

The rats were instrumented 3 days before the experiments under halothane anesthesia (2%). A catheter was inserted into the right atrium through the jugular vein, and a temperature sensor was positioned in the thoracic aorta through the right carotid artery. Catheters were externalized through the neck. In conscious rats, 3 days after surgery, when baseline values of the cardiovascular parameters were stable, cardiac output (CO) was estimated by a thermodilution technique using the Cardiomax III system (Columbus Instruments Inc., Columbus, OH). The total peripheral resistance (TPR) was calculated by dividing BP by CO.

**Hexamethonium and Captopril Administration**

In the second series of experiments, the effects of SNS blockade and ACE inhibition on BP and HR were evaluated in conscious rats, at least 24 h after surgical implantation of catheters. Hexamethonium (30 mg/kg) and captopril (10 mg/kg) were randomly administrated and the cardiovascular parameters were recorded during 30 min after each dosing.

**Renal Sympathetic Nerve Activity Recording**

In the third series of experiments, in urethane-anesthetized rats (1.2 g/kg, intravenously), the left renal sympathetic nerve was exposed, placed on bipolar silver recording electrodes, and covered with mineral oil. The signal from the renal nerve was displayed on an oscilloscope and the nerve activity was amplified (Neurolog, Digitimer, 10 to 20 K; Hertfordshire, England) and filtered by a band-pass filter (50 to 1000 Hz). After hexamethonium bromide (30 mg/kg, intravenously) administration, the baseline noise level of rSNA was determined. The neural activity was analyzed off-line using software (Spike Histogram, ADInstruments) and was expressed as spikes per second, subtracting the background noise. One methodologic limitation of this procedure is related to the comparison of multifiber recordings in rSNA between individuals. However, this method has been successfully used in animal models to compare sympathetic nerve discharges between normotensive and hypertensive animals.
Plasma Sodium, Plasma and Tissue Angiotensin Measurements

Plasma and urinary sodium were assayed by flame photometry. In the fourth series of experiments, Ang I and II were measured using reverse phase chromatography coupled with ultraviolet detection (214 nm). The Ang I, II, and 1–7 contents were expressed as nanograms per gram of tissue.

Plasma Renin and Angiotensin-Converting Enzyme Activities

Trunk blood was collected in cold tubes containing EDTA for PRA measurements by radioimmunoassay (Diagnostic Products Corp, Los Angeles, CA), and in tubes without anticoagulants for plasma ACE activity determination. Measurements using benzoylcarbonyl-L-phenylalanyl-histidyl-L-leucine (Z-Phe-His-Leu) as substrates were performed as described previously. For confirmation of the results, plasma ACE activity was also measured, using 2,4-dinitrophenyl) as substrate in a continuous fluorimetric assay.

Biochemical Determinations

Plasma glucose and triglycerides were quantified enzymatically using commercial kits from Labtest Diagnóstica (Lagoa Santa, Brazil). Plasma leptin and insulin levels were determined using a specific rat leptin and insulin radioimmunoassay kit (Linco Research, St. Charles, MO).

Adipocyte Isolation

Epididymal fat pads were minced and added to a flask containing 4.0 mL of EHB buffer (Earle’s salts, 25 mm HEPES, 4% bovine serum albumin [BSA]), 5 mmol/L of glucose, and 1.25 mg/mL of collagenase type II, pH 7.4, at 37°C. After incubation, the isolated adipocytes were washed three times with 25 mL of EHB (Earle’s salts, 20 mmol/L HEPES, 1% BSA, no glucose, 2 mmol/L sodium pyruvate, and 4.8 mmol/L NaHCO₃), pH 7.4, at 37°C and resuspended until a 5% lipocrit was reached and their size and number were determined.

Statistical Analysis

Values are expressed as mean ± SEM. Comparison between groups C and SC was performed using Student’s t-test for unpaired samples. The null hypothesis was rejected whenever \( P < 0.05 \).

Results

Effects of Sucrose Feeding on Body Weight, Water Intake, Tissue Mass, Plasma and Urinary Sodium, and Metabolic Parameters

Body weight gain was similar in groups C and SC after 30 days of sucrose feeding. As shown in Table 1, drinking and urinary volume were increased \( (P < 0.05) \) in SC compared with C rats. However, the amount of sodium excretion was not different between groups (Table 1). Plasma sodium as well as glucose concentration were similar in SC and C rats (Table 1). Chronic sucrose feeding for 30 days caused a marked \( (P < 0.05) \) increase in plasma insulin and leptin levels (171% and 356%, respectively), compared with C rats. Plasma triglycerides were 45% higher \( (P < 0.05) \) in the SC group than in the C group. The SC rats also displayed a 50% higher epididymal adipose tissue mass and a 30% increase in adipocyte diameter compared with the C group (Table 1). The KM, CM, and LVM did not differ between groups (Table 1).

| Table 1. Physiological, metabolic, and hormonal parameters in control (C) and sucrose-fed (SC) rats |
|----------------------------------------------------|------------------|------------------|
| Body weight (g)                                    | C     | SC    |
| Water intake (mL/24 h)                              | 26.0 ± 1.1 | 52.6 ± 5.0* |
| Urinary volume (mL/24 h)                            | 13 ± 0.8  | 30 ± 4.2*  |
| Plasma sodium (mEq/L)                              | 144.6 ± 1.8 | 144.8 ± 0.7 |
| Urinary sodium excretion (UNaV) (mEq/24 h)         | 5.2 ± 0.8  | 4.1 ± 0.3  |
| Plasma glucose (mmol/L)                            | 5.6 ± 0.1  | 5.7 ± 0.2  |
| Plasma insulin (pmol/L)                            | 171.6 ± 10.6 | 464.3 ± 21.7* |
| Plasma triglycerides (mmol/L)                       | 0.88 ± 0.05 | 1.28 ± 0.14*  |
| Plasma leptin (ng/mL)                              | 3.2 ± 0.4  | 14.6 ± 1.2*  |
| CM (g/100 g body weight)                            | 0.419 ± 0.03 | 0.435 ± 0.03  |
| KM (g/100 g body weight)                            | 1.07 ± 0.06 | 0.95 ± 0.06  |
| LVM (g/100 g body weight)                           | 0.25 ± 0.01 | 0.26 ± 0.004 |
| Adipocyte diameter (µm)                             | 72.7 ± 2.6  | 92.9 ± 0.8*  |
| Epididymal adipose tissue (g/100 g body weight)     | 0.8 ± 0.06  | 1.2 ± 0.06*  |
| Retroperitoneal adipose tissue (g/100 g body weight)| 0.73 ± 0.07 | 0.94 ± 0.05*  |

CM = cardiac mass; KM = kidney mass; LVM = left-ventricular mass; n = number of animals.

Data are presented as mean ± SEM.

* \( P < 0.05 \) vs. C.
\[\text{Table 2. Hemodynamic measurements in control (C) and sucrose-fed (SC) conscious rats}\]

<table>
<thead>
<tr>
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<th>C</th>
<th>n</th>
<th>SC</th>
<th>n</th>
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<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td>102.0 ± 3.1</td>
<td>5</td>
<td>129.0 ± 1.3*</td>
<td>5</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>410.7 ± 6.5</td>
<td>5</td>
<td>413.2 ± 10.7</td>
<td>5</td>
</tr>
<tr>
<td>TPR (mm Hg/mL/min)</td>
<td>0.93 ± 0.04</td>
<td>5</td>
<td>1.39 ± 0.03*</td>
<td>5</td>
</tr>
<tr>
<td>CO (mL/min)</td>
<td>104.1 ± 1.8</td>
<td>5</td>
<td>99.9 ± 2.3</td>
<td>5</td>
</tr>
<tr>
<td>SV (µL)</td>
<td>242.0 ± 5.1</td>
<td>5</td>
<td>217.6 ± 13.7</td>
<td>5</td>
</tr>
</tbody>
</table>

\(\text{CO} = \text{cardiac output}; \text{HR} = \text{heart rate}; \text{MAP} = \text{mean arterial pressure}; \text{SV} = \text{stroke volume}; \text{TPR} = \text{total peripheral resistance}.\)

Data are presented as mean ± SEM.

* \(P < .05\) vs C.

**Hemodynamic Parameters and Effects of Hexamethonium and Captopril Administration in Conscious Rats**

Compared with C, MAP increased (\(P < .05\)) 26.5% in SC rats, associated with a 49.5% increase in TPR (\(P < .05\)) (Table 2). There were no significant differences in HR, CO, and SV (Table 2). The contribution of SNS tonus to the MAP increase was evaluated by acute hexamethonium administration. The ganglionic blockade induced similar and significant (\(P < .05\)) reductions in MAP in both groups (SC = -54 ± 2, and C = -51 ± 3 mm Hg; Fig. 1) with no significant change in HR. As shown in Fig. 1, the participation of ACE in the BP control was evaluated by captopril administration, and a significant decrease (\(P < .05\)) of MAP was observed in SC (-39 ± 2 mm Hg) as compared with C rats (-12 ± 0.5 mm Hg), with no significant change in HR.

**Effects of Sucrose Feeding on Renal Sympathetic Nerve Activity in Anesthetized Rats**

Fig. 2A shows that rSNA was higher (\(P < .05\)) in SC than in C rats (SC = 147 ± 6.6 spikes/sec, C = 116 ± 6.6 spikes/sec). During rSNA recording, the MAP was also higher (\(P < .05\)) in SC (131 ± 5.4 mm Hg) compared with C (99.6 ± 2 mm Hg), as shown in Fig. 2B. Fig. 2C shows a representative trace of rSNA in both groups of animals.

**Plasma Renin and Angiotensin-Converting Enzyme Activities and Angiotensin Levels**

As shown in Table 3, PRA was 310% higher (\(P < .05\)) in the SC group than in the C group, whereas no changes in plasma ACE were observed despite using two different methods. Chronic sucrose feeding was also associated with a 58.5% decrease in plasma Ang I (\(P < .05\)), whereas plasma Ang II increased 40% (\(P < .05\)) (Table 3), indicating an elevation in Ang II generation. This result was confirmed by a 3.6-fold increase (\(P < .05\)) in the plasma Ang II/Ang I ratio.

**Tissue Angiotensins**

In SC rats, the cardiac Ang II content and the Ang II/Ang I ratio decreased (\(P < .05\)) 39.7% and 48%, respectively (Table 4). The cardiac Ang 1–7 content was similar in both groups. In the epididymal adipose tissue of SC rats, the content of both Ang I and Ang II decreased (\(P < .05\)), 45.3% and 24.7%, respectively, and the Ang II/Ang I ratio increased (\(P < .05\)) 1.3 times. In this tissue, a higher (\(P < .05\)) Ang I–7 content (72.5%) in SC rats was also observed (Table 4). In the kidney, no change was observed in Ang I content, but an increase (\(P < .05\)) of 84% and 125% in the Ang II content and the Ang II/Ang I ratio, respectively, were observed in SC rats (Table 4). The renal Ang 1–7 content was similar in C rats and SC rats (Table 4).

**Discussion**

The major findings of the present study were (1) rSNA, renal Ang II content, and PRA were increased by sucrose feeding; (2) acute captopril treatment caused a greater decline in MAP in SC rats compared with C rats, and no difference between groups was observed in response to acute sympathetic blockade; (3) CM and LVM were not altered by sucrose feeding, whereas cardiac Ang II content was decreased; and (4) despite enhancement of the epididymal adipose tissue mass, the Ang I and II contents were decreased and the Ang 1–7 content was increased.
Confirming previous reports from the medical literature, our results indicate that sucrose feeding was associated with hypertension and higher levels of plasma insulin, triglycerides, and Ang II. The increased volume of drinking water in SC was associated with the increase in urinary output providing the maintenance of fluid homeostasis. Urinary sodium excretion (mEq/day) and plasma sodium concentration were not changed by sucrose feeding. Therefore, in this experimental model, the RAS and rSNA activation were probably not mediated by changes in sodium balance. Increased plasma leptin levels and adipocyte diameter were also found in the present study.

Hyperinsulinemia and increased leptin levels are usually associated with an elevation in BP. Therefore, as shown by the present study and Hsieh, these hormonal changes, in addition to high plasma Ang II levels, seem to participate as mechanisms linked to hypertension induced by sucrose feeding.

The TPR increase found in this study could be another physiologic response associated with hypertension. However, it is not possible to differentiate whether the TPR increase was related to the peripheral SNS activation or to the high Ang II plasma levels, and it was not the aim of the present study. Considering that all of these determinations

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**Table 3.** Plasma renin and angiotensin-converting enzyme activities and angiotensin levels in control (C) and sucrose-fed (SC) rats

<table>
<thead>
<tr>
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<th>C</th>
<th>n</th>
<th>SC</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRA (ng/mL/h)</td>
<td>3.0 ± 0.3</td>
<td>5</td>
<td>12.3 ± 2.8*</td>
<td>5</td>
</tr>
<tr>
<td>Plasma ACE (M/min/mL) Abz</td>
<td>17.4 ± 0.5</td>
<td>5</td>
<td>17.6 ± 0.4</td>
<td>5</td>
</tr>
<tr>
<td>Plasma ACE (mU/mL) ZPhe-HL</td>
<td>30.8 ± 4.2</td>
<td>5</td>
<td>35.5 ± 3.0</td>
<td>5</td>
</tr>
<tr>
<td>Plasma Ang I (ng/mL)</td>
<td>193.5 ± 27.8</td>
<td>4</td>
<td>80.3 ± 9.8*</td>
<td>5</td>
</tr>
<tr>
<td>Plasma Ang II (ng/mL)</td>
<td>302.0 ± 10.2</td>
<td>4</td>
<td>421.6 ± 40.9*</td>
<td>5</td>
</tr>
<tr>
<td>Plasma Ang II/Ang I</td>
<td>1.6 ± 0.2</td>
<td>4</td>
<td>5.7 ± 1.1*</td>
<td>5</td>
</tr>
</tbody>
</table>

Abz = Abz-Phe-Arg-Hys(DnP)-Pro-OH; ACE = angiotensin-converting enzyme; Ang = angiotensin; PRA = plasma renin activity; ZPhe-HL = Z-Phe-His-Leu.

Data are presented as mean ± SEM.

* P < .05 v C.
were made after 30 days of sucrose feeding, it is possible that they are consequences of an autoregulatory mechanism elicited early on in this experimental procedure. New experiments in the early stages of this protocol are necessary to answer these questions.

The rSNA increase in SC rats was shown for the first time in the present study, and based on these results it is possible to postulate kidney participation as another mechanism in BP elevation. In fact, that rSNA increases renal sodium retention and renin release has already been shown in a canine obesity model in which the bilateral renal denervation completely prevented hypertension and renal sodium retention. Accordingly, the overall functional alterations described here, such as an increase in rSNA, PRA, plasma Ang II, and renal Ang II content, seem to be implicated in the BP elevation provoked by the sucrose feeding. These findings also confirm the hypothesis that increased intrarenal Ang II content is a major mechanism involved in BP elevations.

Although an increased sympathetic drive to the kidney was noted, the BP decrease in response to hexamethonium did not differ between groups. This probably indicates that in response to sucrose feeding, differential changes in sympathetic tonic activity occur according to the body territory represented, in this case, the kidney. Furthermore, we also observed that the baroreflex control of rSNA was blunted in SC compared with C rats. The rSNA decrease in response to phenylephrine (intravenously) was significantly reduced (SC = 55% ± 3.9% and C = 80% ± 3.5%) in SC. Similar results were obtained after sodium nitroprusside injection. In this case, the rSNA increase was significantly reduced in the SC group (SC = 17% ± 1.8% and C = 35% ± 5%). The data suggest that in association with a renal sympathetic activation in SC rats, there is some degree of impairment in the baroreflex control of rSNA.

The larger BP reduction caused by captopril in SC rats emphasizes the RAS activation in this model. However, considering that captopril can influence the bradykinin breakdown, we may not exclude the participation of this peptide in this response. Therefore, the role of other peptides involved in BP control, in this model, needs further investigation.

In the present study, despite the use of two distinct methods for ACE activity measurement, no differences between C and SC rats were found. This finding, in association with the high plasma Ang II levels, indicates the need for further investigation seeking to understand the mechanisms involved in the increased generation of Ang II in sucrose-fed rats. Furthermore, an increase in plasma ACE activity was observed in high-dose fructose-fed rats. Recently, it has been postulated that plasma Ang II exerts a positive feedback on the intrarenal RAS by an ACE-dependent mechanism. Renal ACE activity was not measured in this study, but data showing an increase in the renal Ang II content with no changes in plasma ACE activity suggest a dissociation between these two responses.

Based on the current results it is not possible to determine which system is primarily involved in the BP elevation induced by chronic sucrose feeding. However, an interaction between rSNA and renal RAS seems to be involved in the cardiovascular changes due to sucrose feeding. Therefore, the present findings emphasize that, in sucrose-fed rats, a renin-sympathetic cross-talk participates as a major hypertensive mechanism and is similar to what was proposed for BP and blood volume control in pathophysiologic conditions.

In this study, no change was found in LVM after sucrose feeding. This observation is in disagreement with studies that show left-ventricular hypertrophy (less dependent on systemic elevations of BP and more dependent on the cardiac tissue RAS) in fructose-fed rats. In our mild hypertensive model, the lower cardiac Ang II content should explain the absence of hypertrophy. This result suggests that most likely, for cardiac hypertrophy, RAS activation should be a more important stimulus than the increased BP. However, differences in animal strains and in composition and timing of the dietary carbohydrate

### Table 4. Tissue angiotensin I, II, and Ang 1–7 contents in controls (C) and sucrose-fed (SC) rats

<table>
<thead>
<tr>
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<th>C</th>
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<th>SC</th>
<th>n</th>
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<tbody>
<tr>
<td>Cardiac Ang I (ng/g)</td>
<td>290.2 ± 21.7</td>
<td>4</td>
<td>358.6 ± 30.6</td>
<td>5</td>
</tr>
<tr>
<td>Cardiac Ang II (ng/g)</td>
<td>769.5 ± 81.3</td>
<td>4</td>
<td>464.1 ± 48.7*</td>
<td>5</td>
</tr>
<tr>
<td>Cardiac Ang II/Ang I</td>
<td>2.5 ± 0.3</td>
<td>4</td>
<td>1.3 ± 0.2*</td>
<td>5</td>
</tr>
<tr>
<td>Cardiac Ang 1–7 (ng/g)</td>
<td>181.0 ± 17.1</td>
<td>4</td>
<td>201.3 ± 27.0</td>
<td>5</td>
</tr>
<tr>
<td>Epididymal Ang I (ng/g)</td>
<td>402.6 ± 45.0</td>
<td>4</td>
<td>220.4 ± 18.7*</td>
<td>5</td>
</tr>
<tr>
<td>Epididymal Ang II (ng/g)</td>
<td>594.8 ± 54.8</td>
<td>4</td>
<td>447.7 ± 19.1*</td>
<td>5</td>
</tr>
<tr>
<td>Epididymal Ang II/Ang I</td>
<td>1.6 ± 0.1</td>
<td>4</td>
<td>2.1 ± 0.2*</td>
<td>5</td>
</tr>
<tr>
<td>Epididymal Ang 1–7 (ng/g)</td>
<td>109.5 ± 12.2</td>
<td>4</td>
<td>188.9 ± 15.3*</td>
<td>5</td>
</tr>
<tr>
<td>Renal Ang I (ng/g)</td>
<td>211.2 ± 35.3</td>
<td>4</td>
<td>162.8 ± 6.6</td>
<td>5</td>
</tr>
<tr>
<td>Renal Ang II (ng/g)</td>
<td>396.9 ± 45.9</td>
<td>4</td>
<td>730.8 ± 46.3*</td>
<td>5</td>
</tr>
<tr>
<td>Renal Ang II/Ang I</td>
<td>2.0 ± 0.3</td>
<td>4</td>
<td>4.5 ± 0.3*</td>
<td>5</td>
</tr>
<tr>
<td>Renal Ang 1–7 (ng/g)</td>
<td>289.6 ± 16.6</td>
<td>4</td>
<td>340.9 ± 43.4</td>
<td>5</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SEM.

* *P < .05 vs C.
overload have to be taken into account when comparing these results.

In the present study, a decrease in the epididymal adipose tissue Ang II content was found, similar to that obtained in salt-restricted obese rats. Curiously, in both experimental models, high plasma Ang II levels associated with increased epididymal adipose tissue mass were also observed. On the other hand, marked activation of adipose and systemic RAS was described in high-fat obese and hypertensive rats.

In the epididymal adipocytes of SC rats an increase in Ang 1–7 content was observed. A possible explanation for these findings is that Ang I (or Ang II) is being rapidly converted into Ang 1–7, resulting in less Ang II formation. The increased Ang II/Ang I ratio seems to confirm this fact. To our knowledge, we are the first to report these changes, and, considering the vasodilator effect of this peptide, it is possible that modifications in tissue perfusion could favor lipogenesis.

Our findings demonstrate that sucrose feeding increases TPR, levels of plasma insulin, leptin, and Ang II, PRA, rSNA, and renal Ang II content. Differential changes in RAS with a specific increase in the Ang II content in the kidney, but not in the heart and in the epididymal adipose tissue, were observed. Furthermore, activation of the Ang 1–7 synthesis was only present in the epididymal adipose tissue. Although the precise mechanisms responsible for hypertension in response to chronic sucrose feeding are still unclear, the present study showed that a preferential increase in sympathetic drive to the kidney associated with an increase in plasma and renal Ang II content might play a major role.

Acknowledgments
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References