Obesity & Sympathetic Nerve Activity

Cafeteria Diet Increases Fat Mass and Chronically Elevates Lumbar Sympathetic Nerve Activity in Rats

Martin S. Muntzel, Omar Ali S. Al-Naimi, Alicia Barclay, David Ajasin

Abstract—Obesity causes sympathetic activation that promotes atherosclerosis, end-organ damage, and hypertension. Because high-fat induced weight gain in rats elevates plasma leptin at 1 to 3 days after the onset of calorie-dense diets, we hypothesized that diet-induced overfeeding will increase sympathetic activity within 1 week after the onset of the regimen. To test this, we continuously measured sympathetic activity and blood pressure before and during the onset of diet-induced obesity using a high-calorie, cafeteria-style diet. Female Wistar rats, in which radiotelemeters had been implanted for continuous monitoring of lumbar sympathetic activity, mean arterial pressure, and heart rate, were randomly assigned to groups that received regular chow (control) or a cafeteria diet for a period of 15 days. This short-term, cafeteria-feeding regimen caused modest but nonsignificant increases in body weight (P<0.07) and a doubling of brown and white adipose tissue (P<0.01). The increases in fat mass were accompanied by elevations in plasma leptin (P<0.001) but no change in glucose. Overall heart rates and blood pressure were higher in cafeteria rats compared with controls (P<0.05). Cafeteria diet-induced weight gain caused increases in lumbar sympathetic nerve activity that became significant by the 12th day of the diet (P<0.001). These data show, for the first time, that the high-fat, cafeteria-style diet stimulates sustained increases in lumbar sympathetic neural drive in rats. (Hypertension. 2012;60:1498-1502.)

Key Words: obesity ■ cafeteria diet ■ sympathetic nerve activity ■ leptin ■ blood pressure

Accumulating evidence indicates that weight gain and obesity result in activation of the sympathetic nervous system. For example, obese hypertensive patients have increased muscle sympathetic nerve activity (SNA) compared with lean controls, and weight loss causes marked reductions in SNA. In addition, experimental animals and humans fed high-fat diets show increases in renal and muscle SNA. This sympathetic overactivity, caused by obesity, may contribute to several complications that characterize this disease, including atherosclerosis, end-organ damage, left ventricular hypertrophy, and hypertension. In support of this, sympathetic activation causes growth promotion in vascular smooth muscle and myocardium, stimulation of platelet number and aggregability, and mechanical injury of the vascular wall. Finally, increases in renal SNA may contribute to impaired pressure natriuresis that predisposes toward the development of hypertension.

Despite the importance of the link between obesity and sympathetic activation, the mechanisms responsible for the increases in SNA are not completely understood. For example, obesity-induced elevations in leptin, insulin, angiotensin II, adiponectin, and inflammation have been proposed as potential activators of sympathoexcitation. One way to better understand how weight gain increases SNA is to establish the time course of sympathetic increases during the initial stages of diet-induced obesity. Prior et al demonstrated that 3 weeks of high-fat feeding to rabbits caused increases in both leptin and renal SNA. However, it is unknown whether the SNA increased before its measurement at 3 weeks. Because high-fat feeding in rats significantly elevates abdominal fat mass by 3 to 7 days with corresponding increases in plasma leptin at 1 to 3 days after the onset of the diets, we hypothesized that diet-induced overfeeding will increase SNA within 1 week after the onset of the regimen. To test this possibility, we continuously measured lumbar SNA, using telemetry, before and during the first 2 weeks of diet-induced obesity in freely moving rats. We selected female Wistar rats and the cafeteria diet because this combination produces rapid increases in both body weight and fat mass.

Methods

Animals
Female Wistar rats, weighing 200 to 225 g, were purchased from Harlan Laboratories (Indianapolis, IN). On arrival, the rats were placed on regular rat chow (5001 LabDiet, PMI Nutrition International, Brentwood, MO) and given water ad libitum for ≥1 week before entry into the...
protocol. They were housed individually in standard polycarbonate cages on pine-shaving bedding in a temperature-controlled colony room illuminated on a 12:12 light:dark cycle. All procedures were performed in accordance with the Lehman College Institutional Animal Care and Use Committee and the National Institutes of Health guidelines for the care and use of experimental animals.

**Experimental Procedure**

After 1 week of habituation, a telemetry-based recording electrode and blood pressure monitor (model TR46SP; Telemetry Research, Auckland, New Zealand) was placed on the lumbar sympathetic nerve and in the abdominal aorta, respectively, under isoflurane anesthesia (please see the online-only Data Supplement for surgery and SNA recording details). After surgery, rats were housed individually and lumbar SNA and blood pressure were recorded continuously with a radiotelemetry system, consisting of the implanted device, a battery-charging device placed underneath the cage (model TR802, Telemetry Research), and a telemetry receiver for both blood pressure and SNA (model TR162, Telemetry Research) connected to a PowerLab data acquisition system (AD Instruments, Castle Hill, New South Wales, Australia) interfaced to a Macintosh computer. Heart rate was calculated from the blood pressure pulse using the PowerLab system. During surgery for implantation of the radiotelemetry device (described above), a 0.5-mL fasting blood sample was taken, centrifuged, and the plasma stored at −80°C.

The animals were allowed 4 days of postsurgery recovery, followed by a 2-day baseline period, during which blood pressure, heart rate, and lumbar SNA were recorded continuously. The rats were then randomly assigned to 2 experimental groups, a control group (n=7) that received water and regular rat chow (5001 Lab Diet) and a cafeteria group (n=7) that received, along with regular rat chow and water, vanilla wafers, crackers, buttered popcorn, cheetos, chocolate, salami, smoked fish, peanuts, shredded wheat, condensed milk (mixed 1:1 in water), and soda pop. To encourage overconsumption, 5 of the 9 solid items were randomly offered each day and the choices were alternated on a daily basis. In addition, these items were given in excess and were replaced every day. The control diet contained (% weight) 23.0% protein, 48.7% carbohydrate, 4.5% lipid, and 23.8% other components without caloric value; the average composition of the cafeteria diet was (% weight) 9.5% protein, 48.1% carbohydrate, 23.4% lipid, and 19% water and other materials. The control diet contained 4.0 mg sodium/g diet, and the cafeteria diet averaged 5.2 mg of sodium/g of diet. Blood pressure, heart rate, and lumbar SNA were recorded continuously for 15 days on these dietary regimens.

At study completion, overnight fasted rats were anesthetized (isoflurane), a 0.5-mL blood sample was taken, and SNA and blood pressure signal quality were assessed (please see the online-only Data Supplement). The gonadal and perirenal white adipose tissues, as well as the interscapular brown adipose tissues, were excised, rinsed in saline, patted dry, and weighed. Plasma leptin was analyzed using a radioimmunoassay kit with antibodies to authentic rat leptin (Millipore, Billerica, MA). Plasma glucose was determined using a GM9 autoanalyzer (Analox Instruments, London, United Kingdom). The intra-assay and interassay coefficient of variation values for leptin were 4.3% and 6.0%, respectively, and for glucose, they were 0.6% and 3.0%, respectively.

**Statistical Analysis**

All data were analyzed using appropriate single or repeated-measures ANOVA, and post hoc comparisons were made using the Holm-Bonferroni method when the global F ratio was significant (GraphPad PRISM 5; GraphPad Software Inc, San Diego, CA). Data are presented as means±SEM. Differences between groups were considered significant at the P<0.05 level.

**Results**

**Effect of the Cafeteria Diet on Body Weight, Adipose Tissue, and Hormones**

Body weights did not differ between the groups before the onset of the diets. During the 15-day feeding period, cafeteria diet–fed rats gained slightly more weight than controls (Table). ANOVA of these data revealed a significant effect for time (P<0.0001) and a borderline significant group by repeated measures interaction (P=0.07), indicating a tendency for more weight gain in cafeteria rats. Cafeteria rats also showed 2- to 3-fold greater white adipose tissue and interscapular brown adipose tissue weights than controls after 15 days on the diets (Table; P<0.01).

Cafeteria diet feeding did not affect plasma glucose. In contrast, plasma leptin levels nearly doubled in cafeteria rats (P<0.001) but did not change in control animals (Table).

**Effect of the Cafeteria Diet on Lumbar SNA, Mean Arterial Pressure, and Heart Rate**

Representative lumbar SNA and mean arterial pressure responses to the cafeteria diet in a single rat are shown in Figure 1. Analysis of the group data revealed that lumbar SNA, expressed as percentage change from baseline, decreased slightly in control rats during baseline, followed by unchanged SNA until the end of the study (Figure 2). In contrast, cafeteria rats displayed mild decreases during baseline, followed by increases in lumbar SNA that became significant by the 12th day on the diet. Because we used a postsurgery recovery period of 4 days, it is possible that the decreases in SNA in both groups during the first 2 and 3 days were attributed to postsurgery recovery. Nevertheless, the control and cafeteria rats received exactly the same postsurgery recovery period, and analysis of the raw SNA values during the 2-day baseline period failed to reveal significant differences between the 2 groups (please see the online-only Data Supplement). ANOVA of the group data revealed a significant effect for group (P=0.03) and a group by repeated-measures interaction (P<0.001), reflecting increasing SNA in the cafeteria group that became significant (P<0.05) during the last 4 days of observation (Figure 2). Analysis of the area under the integrated SNA curves, expressed as μV·seconds, revealed a similar group by time interaction (P=0.001), indicating increasing SNA in the cafeteria group (please see the online-only Data Supplement). Further analyses comparing

**Table. Effect of Cafeteria Feeding on Body Weight, Fat Mass, and Blood Levels of Glucose and Leptin**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Control Females Day 1</th>
<th>Day 17</th>
<th>Cafeteria Females Day 1</th>
<th>Day 17</th>
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<tbody>
<tr>
<td>Body weight, g</td>
<td>257.0±8.1</td>
<td>284.3±6.1</td>
<td>259.3±9.7</td>
<td>305.7±11.5</td>
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<td>Gonadal WAT, g</td>
<td>1.0±0.1</td>
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<td>2.2±0.2</td>
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<td>Perirenal WAT, g</td>
<td>3.6±0.9</td>
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<td>6.8±0.6</td>
<td></td>
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<tr>
<td>IBAT, g</td>
<td>0.4±0.02</td>
<td></td>
<td>1.3±0.2</td>
<td></td>
</tr>
<tr>
<td>Plasma glucose, mmol/L</td>
<td>8.4±0.6</td>
<td>9.4±0.5</td>
<td>9.1±0.5</td>
<td>7.3±0.6</td>
</tr>
<tr>
<td>Plasma leptin, ng/mL</td>
<td>0.87±0.17</td>
<td>0.64±0.15</td>
<td>1.03±0.23</td>
<td>1.93±0.19†</td>
</tr>
</tbody>
</table>

WAT indicates white adipose tissue; IBAT, interscapular brown adipose tissue. All values are means±SEM.

*P<0.01 vs control day 17.
†P<0.001 vs control day 17.
SNA at baseline (day 2) with the last day of observation (day 17) revealed that cafeteria feeding increased lumbar SNA primarily through increases in burst amplitude and not through changes in burst frequency (Figure 3). For both total lumbar SNA and amplitude of SNA bursts in Figure 3, there were significant group by time interactions (P=0.02 and P=0.006, respectively). Our data also indicated that cafeteria feeding increased lumbar SNA during the entire 24-hour period. In support of this, separate ANOVAs of the 12-hour day periods and 12-hour night periods revealed precisely the same findings (please see the online-only Data Supplement). In addition, ANOVA of the rise in SNA from the day periods to the night periods showed no difference between the 2 groups (data not shown). A testing of nerve signal quality on the final day of the study showed blood pressure decreases to intravenous sodium nitroprusside (from 94.0±5.4 to 76.8±7.2 mm Hg) and to intravenous hexamethonium bromide (to 55.0±3.8 mm Hg).

Lumbar SNA responses to baroreceptor unloading with sodium nitroprusside (100% to 127.9±6.7%) and to ganglionic blockade using hexamethonium (100% to 15.3±3.1%) were appropriate and similar to previously published values (please see the online-only Data Supplement).19,20

Twenty-four-hour mean arterial pressure tended to decrease in controls contrasting with no change in cafeteria diet–fed rats (Figure 2). ANOVA of these data revealed a significant effect for group (P=0.002), reflecting overall higher levels in cafeteria rats, for time (P=0.02), and a borderline significant group by time interaction (P=0.09). Overall heart rates were higher in cafeteria rats, as reflected by a significant effect for group (P=0.03), but there was no interaction (Figure 2).

Discussion

The major finding from this study is that short-term, cafeteria-style feeding stimulated increases in directly recorded lumbar SNA from conscious rats. Furthermore, these radiotelemetry data revealed that lumbar SNA elevations in cafeteria rats were sustained throughout the 24-hour period, during both the day and night cycles. These SNA increases occurred with only modest elevations in body weight but with large increases in white adipose tissues, brown adipose tissues, and plasma leptin.

Previous studies with rats have shown that high-fat diets for 10 to 20 weeks stimulate increases in renal SNA.3,5,7 In humans, 10 to 12 weeks of overfeeding with Boost Plus resulted in modest weight gain and elevated muscle SNA.4 In a shorter term study, 3 weeks of high-fat feeding to rabbits also produced significant
increases in renal SNA.\(^6\) The present study extended these findings by showing that sympathetic increases to overfeeding are significant by the 12th day on the diet and are sustained over each of the 24-hour periods. The elevation in lumbar SNA can be attributed to increased sympathetic burst amplitude (Figure 3), indicating an increasing number of recruited nerve fibers.\(^{21}\) This pattern of increased sympathetic burst amplitude without a change in burst frequency is similar to that in rabbits fed high fat and in obese humans\(^6,22\) but differs from humans given Boost Plus who exhibited increases in muscle SNA burst frequency.\(^4\)

Although it is unclear how increased adiposity elevates lumbar SNA, several lines of evidence point to the hormone leptin. We observed a near doubling of plasma leptin after only 15 days of cafeteria feeding, which agrees with others reporting increasing leptin after only 7 days on a high-fat diet.\(^{21}\) Supporting a sympathoexcitatory role for leptin, both intravenous and intracerebroventricular leptin administration have been shown to increase directly recorded brown adipose tissue, renal, and lumbar SNA.\(^{24,25}\) Passage of leptin through the blood-brain barrier allows concentrations of cerebrospinal fluid leptin to closely follow changes in blood levels of the hormone.\(^{26}\) Once in the central nervous system, leptin may act in the ventromedial hypothalamus and arcuate nucleus to increase SNA. In support of this, microinjection of leptin into these 2 areas increases SNA, whereas lesions of the ventromedial hypothalamus and arcuate nucleus abolishes increases in SNA to intravenous leptin.\(^{27-29}\)

Although cafeteria diet feeding stimulated chronic increases in lumbar SNA, the regimen did not clearly elevate mean arterial pressure compared with controls. It is likely that a longer period of overfeeding is necessary to stimulate increases in blood pressure, because most\(^{10,31}\) but not all\(^12\) cafeteria diet studies demonstrated elevations in blood pressure after 8 to 20 weeks on the diets. As with SNA increases, blood pressure elevations may be secondary to increases in circulating leptin, because both intravenous and intracerebroventricular administration of leptin to rats have been shown to produce slowly developing increases in arterial pressure.\(^{33,34}\) In support of a prohypertensive role for leptin, deletion of leptin receptors in the arcuate nucleus of mice abolished both sympathoexcitatory responses to intracerebroventricular leptin and increases in blood pressure to 20 weeks of diet-induced obesity.\(^{27}\)

There were several limitations to the present study. First, our sample size was relatively small because of the difficulty in obtaining long-term SNA recordings. A second limitation was that we included only female Wistar rats. Previous studies have shown that cafeteria feeding stimulates smaller decreases in adiponectin and resistin in female Wistar rats compared with males\(^7\) and smaller increases in blood pressure in females.\(^{35}\) Therefore, sympathoexcitatory increases to the cafeteria diet may also be different in males, and our finding should not be extrapolated beyond the population studied. Third, we did not measure food or calorie intake in the present study. Nevertheless, several previous experiments using similar cafeteria diets over the same time period as in our experiment documented 30% to 40% increases in daily energy intake compared with rats on regular chow.\(^{36,37}\) In addition, the elevations in body weight, white adipose tissues, and interscapular brown adipose tissues observed in the current study were very similar to those, over identical time periods, in the same published studies.\(^{36,37}\) A final limitation was that we recorded SNA only from the lumbar nerve, which sends sympathetic signals to muscle and skin vasculature in the hind limb of the rat. We therefore cannot extrapolate the present SNA findings to other vascular beds, although others have reported increases in renal and muscle SNA after high-fat diet-induced obesity.\(^3,5-7\)

**Perspectives**

By using telemetry-based 24-hour recordings of SNA in freely moving rats, the current work established that feeding a high-calorie cafeteria diet produces increases in both fat mass and lumbar SNA. The present data therefore provide further key evidence that diet-induced increases in adiposity activate chronic increases in SNA, indicating that the current obesity epidemic may also result in an epidemic of sympathetic overactivation. The mechanism of this early rise in sympathetic activity is likely to involve rapid increases in plasma leptin levels, although other hormones may play a role in later stages of the sympathoexcitation. A determination of whether diet-induced elevations in sympathetic activity can be abolished, such as by eliminating the actions of leptin in the hypothalamus, will require further research.

**Acknowledgments**

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**Sources of Funding**

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**Disclosures**

None.
References


Novelty and Significance

What Is New?

- To our knowledge, these are the first telemetry-based 24-hour recordings of sympathetic nerve activity in freely moving rats.
- The high-calorie, cafeteria-style diet stimulated immediate increases in lumbar sympathetic nerve activity that became significant by the 12th day on the diet.
- The increases in sympathetic activity, caused by the cafeteria diet, were sustained over the entirety of the 24-hour periods.

What Is Relevant?

- The increases in sympathetic activity that accompany weight gain are thought to be a primary mechanism through which obesity results in hypertension.

Summary

- The cafeteria diet stimulated rapid increases in fat mass and plasma leptin levels in rats.
- The increases in fat mass and leptin were accompanied by rapid elevations in lumbar sympathetic nerve activity, measured by telemetry.
- Despite the increase in sympathetic activity, 15 days of cafeteria feeding did not clearly affect arterial blood pressure or heart rate.
Cafeteria Diet Increases Fat Mass and Chronically Elevates Lumbar Sympathetic Nerve Activity in Rats

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THE CAFETERIA DIET INCREASES FAT MASS AND CHRONICALLY ELEVATES LUMBAR SYMPATHETIC NERVE ACTIVITY IN RATS

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Short Title: Cafeteria Diet and Sympathoexcitation
METHODS

Implantation and Use of Telemetry Devices

After one week of habituation, over-night fasted rats were anesthetized (isoflurane, 1.4% in oxygen), were given analgesic (ketoprofen, 5 mg/kg) and antibiotic (Baytril, 10 mg/kg), and prepared for placement of a recording electrode on the lumbar nerve and an arterial catheter using sterile techniques. In brief, a midline abdominal incision was made, the intestines were retracted, and the abdominal aorta and vena cava were pulled aside to expose the left lumbar nerve (Figure S1). A 2 mm section of the nerve was carefully dissected from underlying connective tissue using glass probes. Electrode wires from a telemetry device that measures blood pressure and SNA (model TR46SP, Telemetry Research, Auckland, New Zealand) were anchored to the aorta using approximately seven 6-O sutures placed through the aortic adventitia. Then, the 2 ends from the wires were placed underneath the sympathetic trunk (between L3 and L4) and the ends and nerve were covered with a silicone elastomer (Kwik-Sil, WPI, Sarasota, FL). The ground electrode from the device was sutured to the abdominal muscles just exterior to the wound. The quality of the signal was monitored during surgery by visualizing raw nerve activity and from assessing sound quality using an audiomonitor (Grass model AM8, Warwick, RI). After this, a section of the abdominal aorta caudal to the nerve electrode was carefully separated from the vena cava. The tip of the catheter from the radiotelemetry device was inserted through a hole made by a 23-gauge needle, and the catheter was then fixed to the artery with cyanoacrylate cement (Vetbond, 3M, St. Paul, MN) so as to not occlude the flow of blood.

Lumbar SNA signals were sampled at 500 Hz and continuously displayed on the PowerLab system. The original lumbar SNA signal was amplified, filtered between 50-2,000 Hz, full-wave rectified, and integrated using a low-pass filter with a 20-ms time constant. Chronic lumbar SNA was analyzed using a method adapted from Yoshimoto and colleagues. In brief, the area under the integrated SNA curves was calculated every 1 sec using the PowerLab system, and the background noise level was set to be the lowest value from each 1 sec segment of the integrated SNA curves. The validity of this assumption was tested by comparing these lowest values during normal recording with values obtained after euthanasia in the same rat. The lack of difference obtained during the two conditions indicated that the lowest level during each 1 sec SNA segment was a good estimate of the background noise. Using this method, the background noise was therefore subtracted from the total activity every second. A post-study analysis of background noise demonstrated that these levels were not different between the 2 groups and did not change during the study (Figure S2). Means of the area under the integrated SNA curves were calculated for every hour of the 17-day recording period. To quantify lumbar SNA responses to the control and cafeteria diets, percentage changes in SNA were calculated by taking the mean of these values during the 2-day baseline period as 100%.

For the control group, there were 7 successful recordings and 11 recordings that failed and were removed from the study. For the cafeteria group, there were 7 successful recordings
and 8 recordings that failed and were removed from the study. To determine nerve viability, we performed daily written records for each subject that included raw noise voltages and spike voltages, integrated noise voltages and spike voltages, as well as assessment of nerve quality through sound. Criteria for inclusion in the study were 21 days of nerve recordings in each rat showing the following on a daily basis: 1) signal to noise ratio > 2:1 from the raw nerve signal where the signal is the microvolt value (peak to peak) of the lumbar SNA bursts and the noise is the microvolt value (peak to peak) of the background noise, 2) clearly visible SNA spikes on the raw nerve signal having a typical lumbar SNA appearance, which includes conspicuous SNA bursts occurring in a semi-cyclic fashion with the signal falling to the level of the background noise in-between SNA bursts, 3) clearly visible SNA bursts on the integrated signal showing the same characteristics, 4) audible nerve bursts that correspond exactly to the visible bursts on both the raw and integrated channels. Recordings that contained electrocardiogram signals or electrical noise or movement artifact (continuous voltage increases of 1 sec. or longer) were excluded from the protocol.

At study completion, SNA signal quality was assessed in isoflurane anesthetized rats by examining lumbar nerve responses to intravenous sodium nitroprusside, hexamethonium bromide, and to euthanasia. To do this, a catheter was placed in the left femoral vein and baseline blood pressure and SNA were recorded for 15 min. Then, sodium nitroprusside (200 µg/ml, iv) was given as 2.5 to 80 µg/kg/min over 1-2 min, followed by recovery of blood pressure, and then administration of hexamethonium (30 mg/kg, iv). Euthanasia was achieved by an overdose of sodium pentobarbitone (100 mg/kg, iv). Accuracy of blood pressure calibration in the TR46SP devices was tested in each unit before and after implantation against a mercury manometer.

REFERENCES

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<tr>
<th>Values are per 1g of food item</th>
<th>Total Kcal</th>
<th>Fat Kcal</th>
<th>Total Fat g</th>
<th>Total Carb g</th>
<th>Protein g</th>
<th>Dietary Fiber g</th>
<th>Sugars g</th>
<th>Saturated Fat g</th>
<th>Cholesterol mg</th>
<th>Sodium mg</th>
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<td>Lab Diet 500 l (Purina)</td>
<td>4.07</td>
<td>0.45</td>
<td>0.05</td>
<td>0.49</td>
<td>0.24</td>
<td>0.05</td>
<td>0.00</td>
<td>0.02</td>
<td>0.00</td>
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<td>5.00</td>
<td>2.10</td>
<td>0.26</td>
<td>0.64</td>
<td>0.07</td>
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<td>0.14</td>
<td>0.00</td>
<td>0.00</td>
<td>0.06</td>
</tr>
</tbody>
</table>

NA, not available
FIGURE S1.

Schematic representation of the lumbar sympathetic electrode and arterial catheter. The 6 – O silk was anchored through the adventitia of the abdominal aorta.
FIGURE S2.

Group data showing background noise level in the 2 groups. Background noise was set to be the lowest value from each 1 sec segment of the integrated SNA curves. Means of these values were calculated for every hour of the 17-day recording period.
FIGURE S3.

Group data showing lumbar sympathetic nerve activity (LSNA) responses as area under the integrated SNA curves, both before (days 1-2) and during (days 3-17) control diet or cafeteria diets in rats. Values are means ± SEM.
FIGURE S4.

Lumbar sympathetic nerve activity (LSNA) responses before (days 1-2) and during (days 3-17) control diet or cafeteria diets during the 12-hour day periods (top) and the 12-hour dark periods (bottom). Values are means ± SEM. * P < 0.05, cafeteria rats vs. control rats.
FIGURE S5

Representative raw (top) and integrated (bottom) lumbar SNA signals from a control and cafeteria subject on the final day of the study (day 17).
FIGURE S6

Representative arterial pressure (AP) and integrated lumbar SNA responses to sodium nitroprusside (SNP)(top) and to hexamethonium bromide (bottom) from a control subject on the final day of the study (day 17). The increase in SNA to SNP can be seen as an increase in spike density (frequency) rather than an increase in amplitude.