Chronic Sucrose Ingestion Induces Mild Hypertension and Tachycardia in Rats

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SUMMARY As a means for increasing sympathetic activity, male weanling rats were given 8% sucrose solution to drink instead of water. After 5 weeks, systolic pressures measured with a tail-cuff method became appreciably elevated, and the elevation was verified when phasic pressures were later recorded directly from femoral catheters. Successful induction of sympathetic overactivity was considered a likely explanation because sucrose-ingesting rats, compared with untreated controls, had faster heart rates and larger hypotensive responses to α-adrenergic blockade with phentolamine. Upon graded electrical stimulation of the ventromedial hypothalamus under urethane anesthesia, resulting pressor and sympathetic nerve responses were also larger in sucrose-treated rats. By contrast, pressor responses to injections of norepinephrine or tyramine were unaffected, thereby indicating that cardiovascular sensitivity had not been enhanced by sucrose ingestion. During intravenous glucose tolerance tests, increases in plasma insulin were consistently lower in sucrose-treated than control rats even though corresponding increases in plasma glucose were just transiently higher. These results support the interpretation that chronic sucrose ingestion inhibits pancreatic insulin secretion and elevates blood pressure by stimulating the ventromedial hypothalamus to increase sympathetic activity. (Hypertension 5: 218-225, 1983)

KEY WORDS • blood pressure • insulin • heart rate • sucrose ingestion • sympathetic hyperactivity • ventromedial hypothalamus

WHY diabetics are more susceptible than nondiabetics to hypertension\(^1\) is unknown. As a working hypothesis we suggested that, since hypothalamic stimulation elevates blood pressure and blood sugar simultaneously, hypothalamic dysfunction may result in the simultaneous induction of both diseases.\(^1\) In studying interactions between hypertension and diabetes, a major difficulty is the lack of a suitable experimental model because, even though rats with streptozotocin-induced diabetes are predisposed to become hypertensive,\(^4\) they do not really resemble patients with diabetes mellitus.

Chronic sucrose ingestion increases systolic pressure by about 10–15 mm Hg in normotensive\(^5\)–\(^7\) or spontaneously hypertensive\(^6\)–\(^7\) rats, and, because cardiac norepinephrine turnover also increases,\(^10\) the blood pressure elevation has been attributed to sympathetic hyperactivity.\(^9\) The site from which sympathetic hyperactivity arises could be the ventromedial hypothalamus, since changes in norepinephrine turnover during fasting are suppressed by gold thioglucose which presumably destroys neurons in the ventromedial hypothalamus.\(^11\) This same hypothalamo-sympathetic activation may cause hyperglycemia by increasing hepatic glycogenolysis\(^12\) and inhibiting pancreatic insulin secretion.\(^13\) Thus, in especially selected rats sucrose feeding results in impaired glucose tolerance,\(^14\) and the level of serum glucose concentration rises.\(^15\) An analogous clinical counterpart apparently exists among Yemenite Jews in whom increased sucrose intake has been blamed for the greater incidence not only of hypertension\(^16\) but also of diabetes mellitus.\(^17\)

Inasmuch as the slight blood pressure elevation induced by sucrose ingestion has thus far been demonstrated only by indirect measurement with the tail-cuff method, we first confirmed its existence by direct measurement from indwelling femoral catheters. Upon finding that rats given sucrose indeed become mildly hypertensive, blood pressure responses to hypothalamic stimulation and α-adrenergic blockade with phentolamine were recorded to test the possibility that hypothalamic regulation of sympathetic activity had been altered. Additional experiments were then performed to determine whether our sucrose regimen had also affected pancreatic secretion of insulin.
Methods
Experiments were done on 36 3-week-old male Sprague-Dawley rats, weighing 56 ± 1 g, purchased from SASCO Inc. (Omaha, Nebraska). An initial group of 24 rats was divided evenly into two subgroups: 12 rats drank tap water while the other 12 drank 8% sucrose solution instead. Body weight, systolic pressure, and heart rate were measured weekly for 5 weeks after which terminal experiments were done to record sympathetic and cardiovascular responses to hypothalamic stimulation and α-adrenergic blockade with phentolamine. A second group of 12 rats (six drinking sucrose solution and six drinking water) was later treated similarly for 5 weeks, and then intravenous glucose tolerance tests were performed.

Chronic Measurements in Awake Rats
Weekly measurements of systolic pressure and heart rate were made using a photoelectric sensor (ITC Inc., Landing, New Jersey) which allows tail-cuff measurements in awake rats without preheating. After confinement in a holder for 30 minutes at a room temperature of 27°C, tail pulsations were large enough for accurate estimation of systolic pressure. By recording arterial pulsations and cuff pressure on separate channels of the recorder, systolic pressure was determined as the level at which pulsations reappeared during gradual deflation of the cuff. Each measurement was obtained by averaging five individual readings. Heart rate was calculated by multiplying by 12 the arterial pulsations recorded for 5 seconds.

During the 5-week period allotted for chronic measurements, rats were kept in an air-conditioned room and fed a standard chow (Rodent Laboratory Chow 5001, Ralston Purina Company, St. Louis, Missouri). On the last week, daily food and water intake were determined by measuring the food and water placed in each cage in the morning and then subtracting the amounts remaining 24 hours later. Total energy intake was calculated by multiplying daily food intake by 4.25 (gross energy of Purina Laboratory Chow 5001 in kcal/g). For sucrose-drinking rats, additional energy derived from the sucrose solution was calculated by multiplying daily fluid intake by 0.08 (concentration of sucrose solution) and then by 4.1 (1 g sucrose = 4.1 kcal).

Verification of Sucrose-Induced Cardiovascular Effects
Upon completing 5 weeks of chronic measurements, each rat was anesthetized with sodium pentobarbital (40 mg/kg i.p.), and an indwelling catheter was inserted into the right femoral artery with its outer end passed subcutaneously to emerge at the nape of the neck. One day later, each rat was kept in a round open-top cage, awake but partly restrained by a harness-and-swivel arrangement; a harness wrapped around the rat's chest was attached by a steel spring to a slip-ring swivel (Airflyte Electronics, Bayonne, New Jersey) placed above the cage. Tygon tubing inside the spring connected the indwelling femoral catheter to a pressure transducer (Statham P23Gb) located beside the swivel. Aside from pulsatile and mean pressures, heart rates were recorded simultaneously by triggering a biotachometer with the pressure signal from the transducer. In each experiment, phasic femoral pressures were first recorded for about 30 minutes while the rat was awake, and then recordings were repeated after the same rat had been anesthetized with urethane (see below).

Direct Recording of Responses to Hypothalamic Stimulation and Injected Drugs
While the rats were anesthetized for femoral cannulation, a concentric stainless steel electrode 0.5 mm in diameter (custom-made NE-100 with chronic connectors by Rhodes Medical Instruments, Woodland Hills, California) was implanted in the ventromedial hypothalamus at stereotaxic coordinates anteroposterior 6.0, lateral 1.0, and dorsoventral −3.7. Electrodes consisted of a center contact (exposed 0.5 mm length × 0.2 mm diameter) protruding from the shaft and separated by 0.5 mm from the lateral pole (exposed 0.5 mm length × 0.5 mm diameter). A day later, they were anesthetized with urethane (100 mg/100 g i.p.) so that another catheter could be inserted into the left femoral vein for drug injections. Pulsatile femoral pressure and sympathetic nerve activity were recorded continuously during graded hypothalamic stimulation and following intravenously-injected drugs. Hypothalamic stimulation was graded by using 10-second trains of 50–200 μA biphasic currents.

For recording sympathetic nerve activity, the inferior nerve bundle emerging from the coeliac ganglion was placed over a bipolar stainless steel electrode (uninsulated tips 1 mm apart). Nerves and electrode tips were immersed in mineral oil. Spontaneous respiratory movements were abolished by paralyzing skeletal muscles with decamethonium bromide (Syncurine, 0.2 mg/100 g i.v.) and connecting the rat to a respirator. Spike potentials were amplified (Grass P15AC amplifier, Grass Instrument Company, Quincy, Massachusetts) and recorded continuously on magnetic tapes that were later played back into an amplitude analyzer (F. Haer and Co., Brunswick, Maine) to convert individual spikes into uniform pulses. Number of individual pulses per second was counted with a rate analyzer whose output was recorded as a histogram on an ink-writing recorder, converted to digital form using a computer interface, and printed by a programmed calculator.

Test drugs used were norepinephrine bitartrate (Levophed), 100 and 200 ng; tyramine hydrochloride, 20 and 40 μg; and phentolamine mesylate (Regitine), 0.5 mg. To ensure induction of complete α-adrenergic blockade, phentolamine was given in divided doses until repeated injection no longer produced any further fall in blood pressure. All doses are expressed in terms of the respective salts per 100 g body weight.

Whenever hypothalamic stimulation had been done, a 0.5 mA direct current was passed through the hypothalamic electrode for 10 seconds to produce a small lesion at its tip. Through a thoracotomy, a 15-gauge
needle was inserted via the left ventricle into the ascending aorta and 10% formalin was perfused into the brain as described by Wolf. The whole brain was then removed, weighed, and stored in formalin (containing 1% potassium ferricyanide) until sectioning. Transverse sections (40 μ) stained with cresyl violet were compared with the atlas by Pellegrino et al. to locate lesion sites.

**Intravenous Glucose Tolerance Tests and Pancreatic Measurements**

A second group of 12 rats, after 5 weeks of sucrose ingestion, was anesthetized with sodium pentobarbital (4 mg/100 g i.p.). An indwelling cannula was then inserted into a femoral vein for slow injection of a 50% solution of D-glucose (0.2 ml/100 g) and collection of four 150 μl samples (at 0, 5, 20, and 60 minutes) of blood. Plasma concentrations of glucose were measured enzymatically using a Beckman autoanalyzer, and of insulin by radioimmunoassay using a double antibody system.

After each experiment, the pancreas was weighed and extracted with acid ethanol. Dilutions of the pancreatic extract with Krebs bicarbonate buffer containing pork crystalline insulin (Eli Lilly and Company, Indianapolis, Indiana) were then assayed using anti-insulin serum and [125I]-labeled insulin. Insulin content was expressed as μg/g wet weight of pancreas. Glucagon content was determined using a modified double antibody method.

**Statistics**

Data were routinely expressed as averages ± SEM and then analyzed using two-tailed t tests for comparing means of independent samples; differences at a 5% level (p < 0.05) were considered significant. Analysis of variance was used to detect possible changes at different weeks within each group. Duncan's multiple range test was used for F-ratios significant at 5% or less to determine the significance of differences between pairs of means.

**Results**

**Chronic Effects of Sucrose Ingestion**

Sucrose-drinking rats did not gain weight as rapidly as the controls. Even during the first week, their body weight was already significantly lower and decreased further through the fourth week, after which a 30 g difference was maintained until the experiments ended (table 1). When food and fluid intake were measured on the 5th week, sucrose-drinking rats were found to be eating less but drinking more than the controls. Food intake (g/rat/day) averaged 21 ± 2 in the control group and 12 ± 1 in the sucrose-drinking group; corresponding averages for fluid intake (ml/rat/day) were 39 ± 5 and 96 ± 9 respectively (p values for both comparisons < 0.001). However, total energy intake (kcal/day) did not differ significantly (p > 0.2), averaging 89 ± 8 in the control and 82 ± 7 in the sucrose-drinking group.

Attendant cardiovascular effects consisted of hypertension and tachycardia. Whereas systolic pressure remained unaltered in the control group it gradually became elevated in the sucrose-drinking group, and beginning on the 2nd week the difference between groups, though slight, was statistically significant. Similarly, from the 2nd week on, heart rates were consistently higher in the sucrose-drinking group (table 1).

**Verification by Direct Recording of Sucrose-induced Cardiovascular Effects**

Since only slight differences in blood pressure were recorded with the tail-cuff method, more accurate measurements were made by recording phasic pressures directly from indwelling femoral catheters, first while the rats were awake, and then again while they were anesthetized with urethane. Systolic pressures and heart rates still remained consistently higher in the sucrose-drinking group whether the rats were awake or anesthetized (table 2). Elevations in mean, diastolic, and pulse pressure were not as pronounced, but these results nonetheless confirmed the presence of systolic hypertension and tachycardia in sucrose-drinking rats.

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**Table 1. Chronic Effects of Sucrose Ingestion**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rat group</th>
<th>Age (weeks)</th>
<th>F ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td>control</td>
<td>95 ± 2</td>
<td>140 ± 3</td>
</tr>
<tr>
<td></td>
<td>sucrose</td>
<td>89 ± 2*</td>
<td>123 ± 3*</td>
</tr>
<tr>
<td>Systolic pressure</td>
<td>control</td>
<td>111 ± 3</td>
<td>108 ± 1</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td>sucrose</td>
<td>110 ± 4</td>
<td>116 ± 3*</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>control</td>
<td>425 ± 12</td>
<td>383 ± 7</td>
</tr>
<tr>
<td></td>
<td>sucrose</td>
<td>465 ± 8*</td>
<td>431 ± 9*</td>
</tr>
</tbody>
</table>

*Data expressed as averages ± SEM from 12 rats in each group. In analyzing data within each group, with f1 = 2 and f2 = 33-44, F ratios equal to or greater than 2.88 are significant at 5% while those equal to or greater than 4.42 are significant at 1%.

*p < 0.05 as compared with corresponding averages of the control group.
TABLE 2. Cardiovascular Changes Recorded from Indwelling Femoral Catheters in Control and Sucrose-Drinking Rats

<table>
<thead>
<tr>
<th>Variable</th>
<th>Awake</th>
<th>Anesthetized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Sucrose</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>404 ± 8</td>
<td>458 ± 8*</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>systolic</td>
<td>128 ± 4</td>
<td>150 ± 3*</td>
</tr>
<tr>
<td>mean</td>
<td>115 ± 4</td>
<td>126 ± 3*</td>
</tr>
<tr>
<td>diastolic</td>
<td>107 ± 3</td>
<td>112 ± 3</td>
</tr>
<tr>
<td>pulse</td>
<td>21 ± 3</td>
<td>38 ± 5*</td>
</tr>
</tbody>
</table>

Data expressed as in table 1. *p < 0.05 as compared with corresponding average for the controls.

Responses to Hypothalamic Stimulation or Drug Injections

Frequency of sympathetic nerve firing (spikes/sec) recorded after the rats were anesthetized with urethane was initially almost the same (p > 0.5) in both groups, averaging 19 ± 2 in control and 20 ± 2 in sucrose-drinking rats. As described previously, responses elicited by subsequent electrical stimulation of the ventromedial hypothalamus consisted of increases in mean blood pressure and sympathetic nerve firing, accompanied by bradycardia (fig. 1). Magnitude of these effects was generally larger in sucrose-drinking rats (table 3), but because of variability from rat to rat, enhancement of hypothalamic responses was statistically significant only for increases in blood pressure produced by 150 and 200 μA currents, and in sympathetic nerve firing produced by 150 μA.

Unlike the enhancement in hypothalamic responsiveness, responses to injected pressor drugs were unaffected by previous sucrose administration. Noradrenaline and tyramine produced dose-related increases in blood pressure accompanied by irregular changes in heart rate, but differences between groups were slight and insignificant (table 4). By contrast, hypotension occurring after α-adrenergic blockade with phentolamine was greater in the sucrose-drinking group so that subsequent levels of mean pressure became almost the same (i.e., 43 ± 4 in control and 39 ± 6 in sucrose-drinking rats; p > 0.5).

Upon postmortem examination, brains weighed (g) almost the same for the two groups, averaging 2.14 ± 0.01 for controls compared with 2.20 ± 0.02 for sucrose-drinking rats (p > 0.1). Similarly, sites of elec-

Figure 1. Cardiovascular and neural effects of hypothalamic stimulation in rats anesthetized with urethane. A. Control rat. B. Sucrose-ingesting rat. Tracings, from top to bottom, are of phasic femoral pressure (mm Hg), heart rate (bpm), original analog signal of sympathetic nerve activity, and histogram showing frequency of sympathetic nerve firing (spikes/sec). Large arrows indicate onset of 10-second periods of hypothalamic stimulation with numbers signifying current strengths (μA) used for stimulation. Small arrows indicate where the histogram went off scale because of very high increases in firing frequency.
TABLE 3. Sympathetic and Cardiovascular Responses to Ventromedial Hypothalamic Stimulation in Anesthetized Rats

<table>
<thead>
<tr>
<th>Current strength (μA)</th>
<th>Neural firing (spikes/sec)</th>
<th>Pressor response (mm Hg)</th>
<th>HR response (bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Sucrose</td>
<td>Control</td>
</tr>
<tr>
<td>50</td>
<td>3 ± 1</td>
<td>4 ± 2</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>45 ± 8</td>
<td>48 ± 8</td>
<td>16 ± 5</td>
</tr>
<tr>
<td>150</td>
<td>69 ± 7</td>
<td>95 ± 13</td>
<td>26 ± 3</td>
</tr>
<tr>
<td>200</td>
<td>81 ± 6</td>
<td>117 ± 12*</td>
<td>29 ± 1</td>
</tr>
</tbody>
</table>

Data are obtained from the same rats and presented as in table 2. All values are average changes from baselines given in table 2.

*p < 0.05 as compared with corresponding average for the control group.

TABLE 4. Cardiovascular Responses to Intravenously-Injected Drugs in Anesthetized Rats

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (100 g)</th>
<th>Pressor response (mm Hg)</th>
<th>Control</th>
<th>Sucrose</th>
<th>HR response (bpm)</th>
<th>Control</th>
<th>Sucrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>100</td>
<td>13 ± 3</td>
<td>10 ± 1</td>
<td>-6 ± 2</td>
<td>-18 ± 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tyramine (μg)</td>
<td>20</td>
<td>10 ± 1</td>
<td>11 ± 1</td>
<td>15 ± 4</td>
<td>19 ± 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentolamine (mg)</td>
<td>0.5</td>
<td>-56 ± 4</td>
<td>-70 ± 5*</td>
<td>-7 ± 6</td>
<td>-18 ± 6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05 as compared with corresponding average for control group.

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**POSTERIOR**

**FIGURE 2.** Diagram showing sites of electrode implantation determined in brains from control (○) and sucrose-ingesting (X) rats. Numbers at the top indicate the anteroposterior coordinate at which each cross section was made. Ventromedial hypothalamus is delineated by dotted lines, with cerebral ventricles (shaded), fornix (FX), and optic tract (OT) as landmarks. Vertical and horizontal scales in mm.

Reduced Plasma Insulin in Sucrose-Drinking Rats

Chronic effects similar to those described above occurred in a second group of rats subjected to the 5-week regimen of sucrose-ingestion. Average measurements on the 5th week obtained from six control and six sucrose-drinking rats respectively were: 259 ± 7 and 207 ± 11 g (p < 0.001) for body weight; 121 ± 1 and 138 ± 2 mm Hg (p < 0.001) for tail-cuff systolic pressure; and 372 ± 11 and 396 ± 10 (p > 0.2) for heart rate. Initial plasma glucose levels were also higher in sucrose-drinking rats but the elevation was not statistically significant. When 50% glucose was injected intravenously to determine tolerance, the ensuing hyperglycemia was more marked only at 5 minutes but not thereafter, while increases in plasma insulin at 5, 20, and 60 minutes were less in sucrose-drinking than in control rats (table 5). Considered together with lower food intake and reduced body...
weight, both these changes could mean that sucrose-drinking may have either inhibited pancreatic secretion of insulin, or enhanced sensitivity to its physiological effects. Postmortem measurements of pancreatic insulin and glucagon content did not show any appreciable differences between control and sucrose-drinking rats (table 6).

Discussion

Apart from confirming the induction of mild hypertension in rats given sucrose, our results also indicate other effects including: reduced food intake and body weight; tachycardia, which persisted despite the elevation in blood pressure (tables 1 and 2); enhanced pressor and sympathetic nerve responses to ventromedial hypothalamic stimulation (table 3); more pronounced hypotension in response to α-adrenergic blockade with phentolamine (table 4); and reduced plasma insulin levels in response to intravenously-injected glucose (table 5). By recording spike potentials from the splanchnic nerve, we showed that pressor responses elicited by electrical stimulation of the ventromedial hypothalamus were invariably preceded by increased sympathetic neural firing, and the magnitude of both responses was enhanced by sucrose ingestion. All our findings collectively support the interpretation that sucrose ingestion increases sympathetic activity by stimulating the ventromedial hypothalamus.

Instead of being caused directly by sucrose itself, some of the effects seen here could be secondary to changes in food or fluid intake. However, if reduced food intake made sucrose-drinking rats undernourished, then the ensuing hypertension and sympathetic overactivity would be difficult to explain because fasting lowers blood pressure and sympathetic nerve responses to ventromedial hypothalamic stimulation (table 3); more pronounced hypotension in response to α-adrenergic blockade with phentolamine (table 4); and reduced plasma insulin levels in response to intravenously-injected glucose (table 5). By recording spike potentials from the splanchnic nerve, we showed that pressor responses elicited by electrical stimulation of the ventromedial hypothalamus were invariably preceded by increased sympathetic neural firing, and the magnitude of both responses was enhanced by sucrose ingestion. All our findings collectively support the interpretation that sucrose ingestion increases sympathetic activity by stimulating the ventromedial hypothalamus.

To conclude that sympathetic overactivity exists even without an obvious elevation in basal rates of sympathetic neural firing may seem paradoxical. But because spike potentials recorded from multifiber preparations like the splanchnic nerve vary widely from rat to rat, baselines for sympathetic nerve firing seldom show significant differences unless activity has been markedly increased as in rats with established spontaneous or DOCA-salt hypertension. Thus, even though we failed to find differences in baselines for sympathetic neural firing, sucrose ingestion may still have increased sympathetic nerve activity, but the magnitude of enhancement was below levels detectable by multifiber recording.

According to the model advocated by Landsberg and Young, sucrose feeding increases sympathetic outflow by suppressing inhibitory pathways from the ventromedial hypothalamus. While our results agree with their model in regard to sympathetic overactivity, our opinions differ on what the underlying hypothalamic mechanism is. After finding norepinephrine turnover significantly increased in hearts, pancreas and liver from sucrose-fed rats they surmised that sympathetic activity is increased. Two of our findings also support a similar conclusion. First, despite the elevated blood pressure which would normally slow the heart through activation of pressor receptor reflexes, sucrose-ingesting rats consistently had tachycardia. And second, following α-adrenergic blockade with phentolamine the blood pressure fall in these rats was larger than in controls that had not taken sucrose thereby suggesting that sympathetic vasomotor tone had been increased.

On the other hand, their logic on the nature of hypothalamic involvement is not compatible with all that is now known. Based on the assumption that the ventromedial hypothalamus normally inhibits lower brainstem centers which regulate sympathetic outflow, Landsberg and Young proposed that sucrose feeding increases sympathetic activity by suppressing the ventromedial hypothalamus. Evidence for this proposal was derived in mice by injecting gold thioglucose intraperitoneally to destroy the ventromedial hypothalamus and then showing that the inhibition of cardiac norepinephrine turnover usually produced by fasting no longer occurs. Since gold thioglucose is taken up by glucose and insulin sensitive cells, their evidence for an inhibitory link between hypothalamic and medullary sympathetic centers depends on functional rather than anatomical localization. However, the changes in cardiac norepinephrine turnover produced by sucrose-feeding were not as clearly defined, and damage to other brain areas could not be ruled out since the extent of destruction was not verified histologically.
remains possible that the glucose- and insulin-sensitive cells they studied are not the same as those that were stimulated electrically in our experiments. Nonetheless, the idea that the ventromedial hypothalamus normally inhibits sympathetic outflow is difficult to reconcile with the cardiovascular changes resulting after hypothalamic ablation because electrolytic destruction of the ventromedial hypothalamic-median eminence region prevents, rather than augments, the development of renal hypertension.37 Furthermore, we found pressor and sympathetic nerve responsiveness to electrical stimulation of the ventromedial hypothalamus enhanced instead of being depressed, as would have been predicted from the Landsberg and Young hypothesis.

Perhaps a more plausible explanation is that sucrose ingestion increases sympathetic activity by enhancing hypothalamic responsiveness to stimulation. Once regarded as a "satiety center," the ventromedial hypothalamus when destroyed causes hyperinsulinemia, obesity, and hyperphagia, and when stimulated produces the opposite effects. Hypothalamic activation may explain why our weanling rats (unlike adult rats in whom sucrose feeding usually increases both energy intake and weight gain) neither ate as much nor gained weight as rapidly as the controls. As a further indication that removal of the ventromedial hypothalamus reduces sympathetic activity, ventromedial hypothalamic lesions have recently been shown to lower norepinephrine turnover rates in various organs. With the realization that hyperphagia is not essential for the development of hypothalamic obesity, hypothesis based on regulation of plasma insulin concentrations by reciprocal changes in parasympathetic and sympathetic nerve activity was proposed.

If the ventromedial hypothalamus really governs the level of sympathetic activity, then this hypothesis could explain not only the hypertension and tachycardia produced here by sucrose ingestion, but also why food intake, body weight, and plasma insulin levels (during intravenous glucose tolerance tests) were reduced. Such an interpretation may, however, be overly simplistic because with the complex interaction of facilitatory and inhibitory pathways which regulate blood pressure centrally, our findings could still be compatible with either increased facilitatory or decreased inhibitory inputs on the sympathetic pathway descending from the hypothalamus through synapses in the medulla, spinal cord, or thoracolumbar chains. Alternatively, chronic sucrose ingestion could act by enhancing sensitivity to the physiological effects of insulin but this would not account for either the hypertension or the tachycardia. We therefore conclude that, while sucrose ingestion may stimulate the ventromedial hypothalamus to increase sympathetic activity and elevate blood pressure, whether it will also induce experimental diabetes remains uncertain.

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References

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