ABSTRACT
Bilateral electrolytic lesions of the anterior hypothalamus in unrestrained rats resulted in the development, within 2 hours, of arterial hypertension, tachycardia, hyperthermia, and increased locomotor activity, often leading to pulmonary edema and death. Similar lesions in paralyzed, artificially ventilated rats produced comparable changes in arterial blood pressure and body temperature with a similar time course. The arterial hypertension was a consequence of an increase in total peripheral resistance to 15% of control with a reduction in cardiac output to 49% of control. Arterial hypertension, elevated peripheral resistance, and diminished cardiac output were reversed toward normal by alpha-receptor blockade with phentolamine (1 mg/kg, iv). Bilateral adrenalectomy, adrenal demedullation, or adrenal denervation performed prior to lesion placement prevented the development of arterial hypertension and pulmonary edema as well as the changes in peripheral resistance, cardiac output, and body temperature. We conclude that arterial hypertension following lesions of the anterior hypothalamus is due to a neurally mediated increase in peripheral resistance initiated by the release of adrenal medullary catecholamines and that pulmonary edema is due to myocardial failure secondary to the ensuing ventricular overload. Structures originating in or passing through the anterior hypothalamus may exert selective control over the adrenal medulla independent of vasomotor neurons.

In 1954, Maire and Patton (1) demonstrated that bilateral electrolytic lesions of the anterior hypothalamus (AH) result in the development of a syndrome of hyperactivity, hyperthermia, and fatal pulmonary edema in the rat. Although cardiovascular measurements were not made, Maire and Patton attributed the pulmonary edema to a neurogenically mediated shift of blood from the capacitance vessels into the pulmonary circulation (2). More recently, Doba and Reis (3, 4) have observed that fulminating pulmonary edema can also be produced in the rat by bilateral lesions of the nucleus tractus solitarii (NTS), a brainstem nucleus in the medulla oblongata serving as a site of termination of arterial baroreceptors. In this instance, the pulmonary edema is due to the rapid development of neurogenic arterial hypertension with a marked increase in total peripheral resistance leading to a reduction in cardiac output and myocardial failure. Thus, the possibility exists that the pulmonary edema observed by Maire and Patton (1, 2) after lesion of the AH was secondary to the development of arterial hypertension.

In the present study, we investigated the hemodynamic changes following placement of lesions in the AH in the rat. Such lesions produced pulmonary edema as a consequence of arterial hypertension, and the hypertension was due to a neurally mediated release of adrenomedullary catecholamines.

Methods

Animals
Experiments were performed on Sprague-Dawley rats (Carsworth Farms) of both sexes weighing 240–350 g. The rats were housed in groups of six in a light-cycled (on at 0700, off at 1900 hours), thermally regulated (20°C) room with free access to food and water.

Studies in Freely Moving Rats
Measurement of Arterial Blood Pressure, Heart Rate, and Motility.—In the initial operation, rats were anesthetized with halothane (2–3% in a mixture of 50% O2–50% N2 blown over the nose through a face mask). For recording arterial blood pressure, one end of a polyethylene cannula (PE 50, 0.023 inches, i.d.) was inserted through the right common carotid artery into the ascending aorta. The other end of the cannula was brought out through the skin at a point midway between the scapulas and fed through a flexible metal spring attached to a saddle device strapped on the rat’s back. The anesthesia was then discontinued, and the rat was placed in a plastic cage (47 x 20 x 25 cm). The free end of the spring cannula was attached to one end of a
STUDIES IN ARTIFICIALLY VENTILATED RATS

RATION was confirmed at autopsy. Verification of the completeness of denervation. After completion of the adrenal surgery, bilateral lesions were placed in the thalamus lying dorsal to the AH or in the cerebral cortex. Adrenomedullary release was impaired by bilateral electrolytic lesions made in the AH as described earlier. In selected rats, a bilateral adrenalectomy was performed prior to the placement of AH lesions.

The rats were then paralyzed with curare (tubocurarine chloride, 0.4-0.8 mg/kg, iv). The tracheal tube was connected to a small-animal respirator (Harvard Apparatus Company no. 680), and the halothane was discontinued. To avert the hypoxia produced by the pulmonary atelectasis invariably associated with artificial ventilation of a rat with room air (5), these rats were artificially ventilated with a gas mixture of 50% O₂-50% N₂ at an average tidal volume of 1.75 ml and a respiratory frequency of 80/min (average minute volume of 140 ml). Tidal volumes were selected according to body weight by use of the nomogram of Kleinman and Radford (Harvard Apparatus Company).

Cardiac output was measured 2 hours after placement of the lesions by a thermal dilution technique (6-8) adapted for the rat and described in detail elsewhere (3). In brief, normal saline (0.1 ml) at room temperature was injected as a bolus into the right atrium through the venous cannula, and the temperature change of the bolus when it reached the aortic arch was measured with the thermistor. The resultant thermal dilution curve was displayed on the polygraph.

BLOOD GAS ANALYSIS.—To ascertain that blood gases were within the physiological range in the paralyzed, ventilated rats, an 0.2-ml blood sample was withdrawn from the arterial cannula into a 1-ml heparinized glass syringe 2.5-3 hours after placement of the lesion. The oxygen tension (PO₂), the carbon dioxide tension (PCO₂), and the pH were measured in a Radiometer blood microsystem (type BMS3) (9).

OTHER PROCEDURES

Core body temperature before and after lesion placement was measured in some rats with a rectal thermistor probe connected to a temperature display unit (Yellow Springs model 8420). In other unlesioned rats, the core temperature was measured while they were exposed to an infrared heat source. In some experiments, phenolamine (1 mg/kg, iv) was administered in a volume that never exceeded 0.2 ml.

Great care was taken to ensure the comfort of the paralyzed unanesthetized rats. All wounds were packed with cotton saturated with aqueous procaine (2%), and...
the eyes were covered with procaine ointment (5%). The inspired air was humidified. Body temperature was maintained at 38 ± 0.5°C through the use of a rectal probe connected to a thermostatically regulated electric heating pad. To ensure paralysis, needle electrodes were inserted into muscles of the posterior thigh, and the electromyogram was displayed on the polygraph; additional curare (0.4 mg/kg, iv) was administered as required. Control rats were prepared and maintained in a similar manner except that no lesions were made.

POSTMORTEM EXAMINATION

An autopsy was performed on all of the rats that died spontaneously or were killed by an intravenous or intra-arterial injection of sodium pentobarbital. After ligating the inferior and superior caval veins, the ascending aorta, and the trachea, the lungs were rapidly removed from the body and weighed. The lung weight-body weight ratio (×100) was used to assess the presence of pulmonary edema (3, 10).

The brain was removed and, along with the lungs, placed in 10% Formalin for at least 2 weeks. The localization of brain lesions was confirmed on frozen sections cut every 50μ and stained for cells by the Nissl method (11). The lungs were embedded in paraffin, stained with hematoxylin and eosin, and examined for pulmonary edema.

STATISTICAL EVALUATION OF DATA

The significance of changes in the cardiovascular responses and other variables resulting from brain lesions was determined by an unpaired t-test (12) or the Mann Whitney U-test for independent samples (13). Changes were considered to be significant at \( P < 0.05 \).

Results

EFFECTS OF LESIONS OF THE ANTERIOR HYPOTHALAMUS IN FREELY MOVING RATS

The Syndrome.—Bilateral lesions of the AH in the rat invariably resulted in the gradual development of arterial hypertension, tachycardia, and increased motor activity (Fig. 1). The onset of hypertension (Fig. 1B) was evident 30 minutes after cessation of anesthesia, whereas heart rate (Fig. 1C) and motility (Fig. 1A) began to increase above control levels after 60 minutes. Arterial blood pressure and motility continued to increase over the next several hours; maximum elevations of blood pressure were achieved between 1 and 2.5 hours and of motility between 2 and 3 hours after placement of the lesion. In contrast, the tachycardia developed more gradually (Fig. 1C), reaching a maximum after 4 hours at a time when the arterial blood pressure was already declining (Fig. 1B).

At the time when arterial blood pressure and hypermotility were maximum, all of the rats displayed signs of intense autonomic arousal including piloerection, increased sweating, exophthalmia, and hyperthermia (Table 1). The rats were aggressive and irritable, and they would attack inanimate objects without hesitancy or provocation. When they were undisturbed, they ran compulsively without ceasing to rest or to consume food or water.

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BRAIN LESIONS AND HYPERTENSION

TABLE 1

<table>
<thead>
<tr>
<th>Experimental preparation</th>
<th>Temperature (°C)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unparalyzed rats</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>37.9 ± 0.16</td>
<td>7</td>
</tr>
<tr>
<td>AH lesions</td>
<td>39.4 ± 0.34*</td>
<td>14</td>
</tr>
<tr>
<td>AH lesions + adrenalectomy</td>
<td>37.9 ± 1.01</td>
<td>9</td>
</tr>
<tr>
<td>Paralyzed rats</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>37.8 ± 0.22</td>
<td>9</td>
</tr>
<tr>
<td>AH lesions</td>
<td>39.0 ± 0.24*</td>
<td>7</td>
</tr>
<tr>
<td>AH lesions + adrenal denervation</td>
<td>38.5 ± 0.50</td>
<td>5</td>
</tr>
</tbody>
</table>

All values are means ± SE; N = number of rats tested. Rectal temperature was measured 2 hours after the lesions had been produced.

* P < 0.01 compared with the unparalyzed or the paralyzed control value.

The time required for the development of the arterial hypertension after placement of the lesions in the AH was delayed in comparison with the much more rapid evolution of hypertension in rats with NTS lesions (3, 4). We sought therefore to evaluate whether the delay was a consequence of unusually prolonged recovery from halothane. Bilateral lesions were placed in the AH in six rats, the anesthesia was discontinued, and arterial hypertension was permitted to develop. At 2 hours after placement of the lesions, when the circulatory effects were maximum (Figs. 1B and 2A), the rats were reanesthetized for 20–30 minutes. As seen in Figure 2B, the arterial blood pressure of the AH-lesioned rats returned to control levels during anesthesia. However, 1–2 minutes after the anesthesia was terminated, arterial blood pressure began to rise. Within 7–10 minutes, the hypertension was reestablished. This experiment indicates that (1) arterial hypertension produced by lesions of the AH is reversible and sensitive to halothane anesthesia and (2) any lingering depressant effect of halothane on the cardiovascular responses to AH lesions is brief, lasting only 7–10 minutes. Therefore, the delayed development of hypertension after AH lesions cannot be attributed to halothane.

Arterial blood pressure and motility gradually began to fall (Fig. 1A and B) 3–4 hours after the placement of the lesions. Within 4–5 hours, 59% of the rats were dead and many others lay exhausted on the floor of the cage. Even though a number of the rats made futile attempts to run, they were unable to move themselves through the light beam, and the recorded motility decreased markedly (Fig. 1A).

The sequence of preterminal events in one of the rats that died is illustrated in Figure 3. Nearly 5 hours after the lesions had been placed and following a period of arterial hypertension, the arterial blood pressure fell precipitously to levels of 30–55 mm Hg, cardiac rate decreased, and cardiac ar-

![Figure 2](http://circres.ahajournals.org/)

**FIGURE 2**

Effect of halothane anesthesia on arterial blood pressure and heart rate after AH lesions in the rat. Two hours after placement of AH lesions and discontinuation of halothane anesthesia, the hypertension was well established (A). The rat was reanesthetized, paralyzed, and artificially ventilated for 10 minutes, and the anesthetic was then discontinued (B). Note the rapid reestablishment of hypertension.

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rhythms developed; the rat lay motionless on the floor of the cage. At this time, clinical signs of pulmonary edema including labored breathing, audible gurgling, and the appearance of pink frothy fluid exuding from the nostrils were evident. At postmortem examination, this rat, as well as many of the other rats that died, had boggy lungs with frothy fluid often filling the trachea and the bronchi. The average lung weight–body weight ratio in the rats that died acutely 4–5 hours after placement of the AH lesions was significantly elevated (0.92 ± 0.06, N = 8) compared with the control value (0.73 ± 0.4, N = 6, P < 0.05). Microscopically, the lungs were characterized by an intense, diffuse interstitial and perivascular edema. Generalized vascular congestion and intra-alveolar edema were also often seen. These changes are characteristic of pulmonary edema (14) and identical to those occurring in rats following NTS lesions (3).

Localization of Effective Lesions.—In all instances, the electrolytic lesions effective in producing the hypertensive syndrome destroyed the bulk of the nucleus of the AH and the adjacent periven-

tricular nucleus of the hypothalamus. A typical lesion is illustrated in Figure 4. Rarely and variably, the lesions also damaged the adjacent optic tract, the fornix, the superchiasmatic nuclei, the caudal pole of the preoptic nucleus, or the rostral pole of the ventromedial hypothalamic nucleus. In two rats, the lesions were inadvertently placed asymmetrically in the AH. In these cases, one electrode penetrated the third ventricle and the other lodged in the lateral hypothalamus. The result was bilateral destruction of the periventricular nuclei and the medial part of the nucleus of the AH by the medial electrode and unilateral destruction of the lateral hypothalamic area by the lateral electrode. The degree of hypertension and motility developed by these rats was indistinguishable from that produced by the bilateral AH lesions. These observations suggest that destruction of either the medial portion of the AH or the periventricular nuclei may be responsible for the syndrome.

In the control rats, large lesions in the overlying thalamus, including the anterior medial nucleus, the reticular nucleus, and the ventral nucleus, did not result in changes in arterial blood pressure or motility. Lesions of the cerebral cortex were similarly without effect.

Effects of Adrenalectomy, Adrenal Demedullation, or Adrenal Denervation.—We next sought to examine the contribution of adrenal medullary catecholamine release to the syndrome produced by AH lesions. In the first of these particular experiments, we discovered that bilateral adrenalectomy performed just prior to placement of the AH lesions completely blocked the development of arterial hypertension but not the associated tachycardia and hypermotility produced by the AH lesions. Comparable effects were observed with selective adrenal demedullation or with bilateral denervation of the adrenal glands (Fig. 5). Preventing the release of adrenal catecholamines by any of these treatments attenuated the associated piloerection, proptosis, and mydriasis. Adrenalectomy also abolished the hyperthermia elicited by the lesions (Table 1). The findings therefore suggest that the arterial hypertension and some of the peripheral signs of sympathetic activation resulting from AH lesions are a consequence of the release of catecholamines from the adrenal medulla.

No evidence of pulmonary edema was seen in any of the rats in which adrenomedullary function was impaired, and lung weight–body weight ratios were normal (0.62 ± 0.02). However, 53% of these rats were dead 4–5 hours after lesion placement.
The high rate of mortality may have been due to the stress of running, since all of the paralyzed, adrenalectomized rats with AH lesions survived.

**Effects of Hyperthermia.**—To assess the effects of elevation of body temperature on arterial blood pressure, four unlesioned rats were exposed to an infrared heat source until their body temperatures were elevated to 40.4 ± 0.21°C. The mean arterial blood pressure recorded from these rats at this time was only 114 ± 3 mm Hg. Thus, it is unlikely that the changes in arterial blood pressure observed after AH lesions were a consequence of the accompanying hyperthermia.

**EFFECTS OF LESIONS OF THE ANTERIOR HYPOTHALAMUS IN PARALYzed RATS**

Changes in Arterial Blood Pressure, Heart Rate, and Body Temperature.—Next, we studied the effects of AH lesions in paralyzed, artificially ventilated rats to assess the contribution of muscular movement to the changes in arterial blood pressure, heart rate, and body temperature. As illustrated in Figure 6, bilateral lesions of the AH in paralyzed rats resulted, after discontinuation of the anesthetic, in the development of arterial hypertension comparable to that seen in the unrestrained rats (Fig. 1B) and significantly different from that seen in the paralyzed controls, who tended to develop a mild elevation of arterial blood pressure. Although the heart rate also increased in lesioned, paralyzed rats, the differences from controls were not significant, because the control rats gradually developed a moderate tachycardia. The...
Changes in arterial blood pressure in paralyzed, artificially ventilated, lesioned rats (solid circles, \( N = 13 \)) compared with those in sham-operated, paralyzed controls (open circles, \( N = 12 \)). Note that the time course for the development of arterial hypertension after anterior hypothalamus (AH) lesions in paralyzed rats is identical to that in unrestrained rats (Fig. 1). * \( P < 0.01 \) compared with control, and ** \( P < 0.001 \) compared with control.

Lesioned, paralyzed rats were also hyperthermic (Table 1); they exhibited a mean body temperature almost identical to that observed in the unrestrained, lesioned rats and significantly different from that seen in the paralyzed, unlesioned controls. These findings indicate, therefore, that the lesion-elicited hypermotility was not the cause per se of the cardiovascular changes or the hyperthermia.

**Cardiodynamic Changes during the Acute Hypertensive State.**—We next sought to determine if the arterial hypertension produced by AH lesions was due to an increase in total peripheral resistance or to an increase in cardiac output. The cardiodynamic changes were measured in control rats and in rats with AH lesions 2 hours following cessation of the anesthetic at a time when the arterial hypertension was fully developed.

As indicated in Table 2, AH lesions in paralyzed rats resulted in significant elevations in systolic, diastolic, and mean arterial blood pressures with an increase in total peripheral resistance to 157% of control and a reduction in cardiac output to 49% of control. Central venous pressure was unchanged. The cardiovascular changes could not be attributed to alterations in blood gases, which were within normal limits.

**Effect of Phentolamine on Arterial Blood Pressure, Cardiac Output, and Total Peripheral Resistance.**—Administration of the alpha-adrenergic blocking agent, phentolamine (1 mg/kg, iv), immediately reversed toward normal the arterial hypertension, the elevation in total peripheral resistance, and the decrease in cardiac output resulting from bilateral lesions of the AH (Fig. 7). Heart rate remained unchanged. These findings indicate that the low cardiac output characterizing the acute hypertensive state associated with AH lesions is

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**TABLE 2**

*Effects of Bilateral Lesions of the Nucleus of the Anterior Hypothalamus (AH) with and without Bilateral Adrenalectomy on Cardiovascular Dynamics and Blood Gases*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>AH lesions</th>
<th>AH lesions + adrenalectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic arterial blood pressure (mm Hg)</td>
<td>161 ± 5 (9)</td>
<td>183 ± 7* (9)</td>
<td>144 ± 13 (4)</td>
</tr>
<tr>
<td>Diastolic arterial blood pressure (mm Hg)</td>
<td>122 ± 6 (9)</td>
<td>142 ± 5t (9)</td>
<td>118 ± 8 (4)</td>
</tr>
<tr>
<td>Mean arterial blood pressure (mm Hg)</td>
<td>133 ± 4 (12)</td>
<td>159 ± 44 (13)</td>
<td>130 ± 6 (5)</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>399 ± 21 (12)</td>
<td>440 ± 21 (13)</td>
<td>529 ± 22S (5)</td>
</tr>
<tr>
<td>Cardiac output (ml/min)</td>
<td>90 ± 21 (6)</td>
<td>44 ± 4* (6)</td>
<td>65 ± 8 (5)</td>
</tr>
<tr>
<td>Total peripheral resistance (mm Hg · min/ml)</td>
<td>2.000 ± 0.386 (6)</td>
<td>3.138 ± 0.671* (6)</td>
<td>2.092 ± 0.156 (5)</td>
</tr>
<tr>
<td>Central venous pressure (cm H2O)</td>
<td>2.4 ± 0.80 (6)</td>
<td>2.5 ± 0.36 (6)</td>
<td>1.4 ± 0.52 (5)</td>
</tr>
<tr>
<td>Arterial PCO2 (mm Hg)</td>
<td>96 ± 9 (7)</td>
<td>104 ± 6 (9)</td>
<td>158 ± 15 (4)</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>39 ± 3 (7)</td>
<td>40 ± 3 (9)</td>
<td></td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.37 ± 0.01 (7)</td>
<td>7.36 ± 0.02 (9)</td>
<td>7.42 ± 0.09 (3)</td>
</tr>
</tbody>
</table>

All cardiovascular measurements were made in paralyzed, artificially ventilated rats 2 hours after placement of lesions in the AH. Adrenalectomy was performed just prior to placement of the lesions. Blood gas measurements were made 2–3 hours after lesion production. Due to technical difficulties, PCO2 measurements from rats with AH lesions + adrenalectomy could not be made. All values are means ± SE; the number of rats in each group is given in parentheses.

* \( P < 0.05 \) compared with control.
† \( P < 0.02 \) compared with control.
‡ \( P < 0.001 \) compared with control.
§ \( P < 0.01 \) compared with control.
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Effects of phentolamine (1 mg/kg, i.v.) on mean blood pressure (BPm), cardiac output (CO), and total peripheral resistance (TPR) in rats with hypertension produced by bilateral lesions of the AH. Rats were anesthetized with halothane and cannulated, and lesions were placed in the AH. The rats were then paralyzed and artificially ventilated. The control rats were similarly treated except that no lesions were made. Two hours after discontinuation of the anesthetic, measurements were obtained in all rats. Phentolamine was then administered to the rats with lesions, and cardiovascular activity was determined within the next 10 minutes. Note the reversal of hypertension, the decrease in total peripheral resistance, and the increase in cardiac output produced by the drug.

Discussion

The present study demonstrates that bilateral electrolytic lesions of the AH in the rat result in the development of acute arterial hypertension, often leading, within hours, to pulmonary edema and death. Although the acute changes in arterial blood pressure and heart rate that follow lesions of the AH have not been previously described, the other manifestations of the lesions, particularly pulmonary edema as well as increased locomotor activity, hyperthermia, widespread sympathetic activation, and emotional hyperreactivity, have been described by Maire and Patton (1, 2, 15) following the placement of lesions in regions variously identified as the preoptic area (2) or the rostral hypothalamus (15). Since these regions, according to current opinion, are part of the AH (16), the pulmonary edema produced by Maire and Patton and the edema observed in the present study were probably caused by placement of lesions in the same general area. It is also highly probable that the pulmonary edema reported by Maire and Patton was preceded by a period of arterial hypertension.

The arterial hypertension produced by AH lesions is, like that produced by NTS lesions, entirely due to increased peripheral resistance and not to an elevation of cardiac output. Indeed, cardiac output is reduced by half, probably as a consequence of a reduced stroke volume resulting from the ventricular overload imposed by the elevated peripheral resistance, since reduction of peripheral resistance and arterial blood pressure by alpha-receptor blockade returns the cardiac output toward normal levels. Pulmonary edema appeared as a terminal event in over half of our rats 4-5 hours after placement of the lesions. It was probably the consequence of left heart failure with subsequent congestion of the pulmonary circulation, perivascular edema, and, terminally, exudation of fluid into the alveolar spaces.

The arterial hypertension as well as some of the peripheral effects of sympathetic activity depend on a neurally mediated release of catecholamines from the adrenal glands and can be blocked by adrenal surgery. Moreover, the release of catecholamines appears to be a direct result of the AH lesion and not secondary to associated components of the syndrome. It is not a consequence of muscular activity, since hypertension was produced by AH lesions in paralyzed rats. It is not due to changes in blood gases, possibly consequent to catecholamine release (17), since these were normal at a time when the rats were hypertensive, and it is probably not due to the elevated body temperature, since heating rats to over 40°C was not associated with hypertension.

The absence of any elevation in arterial blood pressure after lesions are placed in rats with adrenal denervation suggests that the AH lesions initiate a differentiated activation of the sympathetic nervous system with a preponderant dis-
charge of preganglionic sympathetic neurons to the adrenal gland. This pattern is entirely different from that associated with the hypertension produced by NTS lesions. In the latter instance, the hypertension appears primarily to result from augmented sympathetic vasomotor activity with little adrenal involvement (3).

The central mechanisms through which AH lesions lead to the development of the AH syndrome are uncertain. One interpretation (15) is that structures either originating in or passing through the region of the AH exert a tonic inhibitory effect on other brain areas which themselves provide excitation for the neural networks mediating component parts of the syndrome. One such area which might be disinhibited by the AH lesion is the adjacent lateral hypothalamus. There are known anatomical connections between the lateral and the medial hypothalamus (18), and electrical stimulation of the antero- and the posterolateral hypothalamus has been demonstrated to produce a release of adrenomedullary catecholamines (18–21). However, if the AH syndrome is simply due to disinhibition, then it is difficult to explain the long latency required for the full development of the responses; we have clearly established that it is not attributable to anesthesia.

Another possibility is that the AH syndrome is due to lesion-induced excitation rather than disinhibition of pathways responsible for the expression of the observed behaviors. Excitation might result from the slowly accelerating release of neurotransmitters from the terminals of damaged axons, degeneration activation (22), or from the deposition of iron at the electrode site, which has been implicated in producing prolonged excitatory effects in the central nervous system (23–26).

Whatever the mechanism responsible for the production of the AH syndrome, the fact remains that elimination of the adrenal medullary secretion can entirely abolish the arterial hypertension associated with the AH lesion. That fact is of considerable importance in the framework of the central neural organization of the cardiovascular system. The finding suggests, first, that the central neural representations of the adrenal medulla and the vasomotor systems are in part distinct. This feature of the central organization of the autonomic nervous system is not widely appreciated, but it is implicit in findings that adrenal catecholamines may be released reflexively through activation of receptors within the central nervous system by hypoglycemia induced by insulin or 2-deoxy-D-glucose (26–32) in the absence of significant hypertension (27). Second, it indicates that pathways originating in or passing through the AH exert control over the adrenal medulla, thereby pointing to a specific area of the brain involved in adrenomedullary control.

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References

4. DOBA N, REIS DJ: Role of central and peripheral adrenergic mechanisms in neurogenic hypertension produced by brainstem lesions in rats. Circ Res 34:293–301, 1974
5. NATHAN MA, REIS DJ: Hypoxemia, atelectasis and the elevation of arterial pressure and heart rate in paralyzed, artificially ventilated rats. Life Sci 16:1103–1120, 1975
7. IMMS FJ, JONES MT, NEAME RLB: Determination of cardiac output in the anesthetized rat (abstr). J Physiol (Lond) 215:8P, 1971
8. KÖRNER PI: Effect of section of the carotid sinus and aortic nerves on the cardiac output of the rabbit. J Physiol (Lond) 180:266–278, 1965

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