Production of Sustained Hypertension by Lesions in the Nucleus Tractus Solitarii of the American Foxhound

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SUMMARY

The purpose of this study was to develop a model of sustained neurogenic hypertension in the dog. Thirteen female American foxhounds (mean arterial pressure 105 ± 12 mm Hg) with indwelling arterial and venous cannulas were maintained on a constant 82 mEq/day sodium intake. After a control period of at least 10 days, under pentothal anesthesia and direct visualization, the animals had placement of bilateral electrical lesions of the nucleus tractus solitarii (NTS) at the level of the obex. After recovery from anesthesia, the dogs could be divided into two groups on the basis of blood pressure response. Group I (n = 6) developed sustained hypertension with an increase of mean arterial pressure of 25-35% above control values (p < 0.01) for 10 days after placement of the lesions. Group II (n = 7) had a transient increase of blood pressure on postoperative Day 1 but became normotensive for the subsequent 9 days of observation. The hemodynamic features of the dogs in Group I were increased total peripheral resistance, decreased cardiac output and slightly decreased heart rate; these changes were reversed to control by phentolamine. Plasma renin activity, aldosterone concentration and blood pressure response to SQ20,881 were unchanged by NTS lesions. Group I dogs had sodium retention on postoperative Day 1, but no change in renal plasma flow or glomerular filtration rate was observed during the chronic hypertensive phase. One Group I dog remained hypertensive for 8 weeks. All dogs in Group I were hypertensive and all in Group II were normotensive at sacrifice. Histologic sections from Group I dogs showed complete cellular destruction of the nucleus and the tractus solitarius bilaterally at the obex. In Group II, unilateral or incomplete cellular destruction of the NTS at the obex, or bilateral NTS lesions caudal to the obex were present.

Bilateral NTS lesions at the obex in the American foxhound result in sustained arterial hypertension characterized by increased peripheral sympathetic nervous system activity and lack of dependence on the renin-angiotensin-aldosterone system. (Hypertension 1: 246-254, 1979)

KEY WORDS • hypertension • central nervous system • nucleus tractus solitarius • dog • renin-angiotensin system • catecholamines

THE sympathetic nervous system may play a critical role in the initiation and/or maintenance of several models of hypertension in experimental animals and possibly also of essential hypertension in man. The lines of evidence include correlation of sympathetic nerve activity with blood pressure as spontaneously hypertensive rats develop hypertension; the production of sustained hypertension by continuous stimulation of renal and splanchnic nerves or stellate ganglia; or by chronic intrarenal norepinephrine infusion in conscious dogs; correlation of diastolic blood pressure with plasma concentration of norepinephrine and dopamine beta-hydroxylase activity in patients with essential hypertension; and the common hemodynamic characteristics of patients with labile hypertension, including tachycardia, high cardiac output, venoconstriction and normal peripheral vascular resistance. These changes are likely to be mediated by increased activity of the sympathetic nervous system.

Central catecholaminergic neurons are important components of the central connections of the sympathetic nervous system and in the regulation of blood pressure. Selective ablation of central catecholaminergic neurons profoundly alters blood pressure in a number of experimental animal models. Central deafferentation of baroreceptor reflexes by

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means of bilateral lesions of the nucleus tractus solitarii (NTS) abolishes inhibitory influences and presumably leads to increased activity of the peripheral sympathetic nerves. However, studies to date have not documented chronic sustained hypertension in animals with NTS lesions. Specifically, rats develop fulminant hypertension and die of cardiac failure within 36 hours after placement of the lesions. On the other hand, cats with NTS lesions develop chronic labile hypertension characterized by wide swings in blood pressure between normal and abnormal.

This study was designed to determine whether bilateral lesions of the NTS in the dog would produce neurogenic hypertension that would last for a longer period of time than in the rat without the lability observed in the cat. Since we were able to demonstrate that NTS lesions in the dog produce hypertension, we performed studies of the peripheral mechanisms that might be responsible for the hypertensive process.

Methods

Animal Preparation

Thirteen female American foxhounds selected for their calm and gentle nature were used for these experiments (body weight 19 ± 2 (SEM) kg). At surgery, the dogs were given pentobarbital anesthesia, the trachea was intubated, and under sterile conditions a fasciectomy was performed in the area of the right femoral artery and vein. Teflon catheters (0.074 cm outer diameter) were inserted through the femoral artery and vein into the aorta and inferior vena cava, respectively. The aortic and inferior vena caval catheters were placed about 10 cm infrarenally. The two catheters were exteriorized through a stab wound near the right costovertebral angle. A canvas jacket was placed around the dog to protect the catheters. The dog was allowed to recover for at least 7 days prior to beginning studies.

After recovery from surgery, the dogs were placed on a constant 82 mEq sodium intake per day by food containing 5 mEq of sodium supplemented by 77 mEq of sodium intravenously in the form of 0.9% sodium chloride per day.

Collection of Data

When measurements were made during the course of an experiment, the dogs were placed in a canvas sling with their feet touching the floor enabling the dog to stand or rest. They were calm in this position and allowed to acclimate for 30 minutes before the measurements. The room in which these procedures were performed was quiet during the measurements.

Measurements

Arterial blood pressure and blood samples were obtained through the aortic catheter. Blood pressure was monitored using a strain gauge transducer (Statham P23Db) at the heart level and blood pressures were displayed on a dual channel carrier amplifier-recorder (Sanborn 321). Glomerular filtration rate and renal plasma flow were measured after the blood pressure measurements by means of standard clearance techniques with the isotopes $^1$H-inulin and $^3$H-p-aminohippuric acid ($^3$H-PAH). Urine collections for these clearances were obtained with a bladder catheter. Cardiac output was measured by injection of 2.5 mg of indocyamine green into the inferior vena cava and withdrawal of blood from the aortic catheter through a Gilford densitometer. Plasma renin activity was measured from the angiotensin I generated by incubation at 37°C and pH 5.7 according to the method of Sealey et al. Radioimmunoassay of plasma aldosterone was performed by the method of Bühler et al. Serum and urine sodium and potassium were determined by flame photometry.

Experimental Protocol

After recovery from surgery and at least 5 days of balanced sodium intake, the following control measurements were made: cardiac output, arterial blood pressure response to a continuous 30-minute I.V. infusion of the angiotensin converting enzyme inhibitor, SQ20,881 (6 μg/kg/min), and arterial blood pressure response to phentolamine (5 mg) given by I.V. bolus injection. Resting arterial blood pressure and heart rate were measured from 30 minutes to 2 hours daily for at least 10 days during the control period. During the measurements, the dogs were calm and awake, or asleep.

Immediately before NTS surgery, body weight, arterial blood pressure and heart rate were measured. Control plasma samples for renin activity, aldosterone and norepinephrine and serum samples for sodium and potassium were obtained. The dogs were placed in metabolic cages the day before NTS surgery for measurement of consecutive 24-hour urinary sodium excretion.

At 1–2 days before NTS surgery, a prophylactic antibiotic, sterile procaine penicillin G (200,000 units) and dihydrostreptomycin (250 mg), were administered intramuscularly. On the morning of NTS surgery, the dogs were anesthetized with sodium pentobarbital (30 mg/kg I.V.) and were placed on an operating table in a stereotaxic frame with the head flexed at 45°. During surgery, the dogs were maintained on a Harvard 613 respirator (Harvard Apparatus, Dover, MA) and body temperature was monitored with a rectal probe. Under sterile conditions, a suboccipital craniotomy was performed to expose the area of the obex under direct visualization. Hemostasis was secured by electrical cauterization. The inferior vermis of the cerebellum was retracted rostrally and did not interfere with manipulations in the area of the obex. A Teflon-coated stainless steel wire (diameter 0.006 inch) insulated to within 0.2 mm of its tip was attached to a stereotaxic electrode micromanipulator. The midline was identified by direct visualization, and the steel wire was passed stereotaxically into the region of the NTS on the left side of the brain stem in the area of the obex. The tip of the wire was placed 2.75–3 mm...
I dogs.

to bilateral electrical lesions of the NTS in two of the Group

health. In all other respects, the animals were in good

and recovered normal eating and drinking habits and

maintained on daily infusions of 500 ml of 0.9% saline I.V.,

which time spontaneous movements were reduced and

all had mild to moderate ataxia. The dogs were main-

tained on saline (0.9%, 500 ml I.V.) throughout

surgery. No other I.V. fluids were administered on the

day of surgery. All dogs after placement of these

lesions failed to eat or drink for 48 hours, during

which time spontaneous movements were reduced and

and all had mild to moderate ataxia. The dogs were main-

tained on daily infusions of 500 ml of 0.9% saline I.V.,

and recovered normal eating and drinking habits and

normal ambulation approximately 48 hours after sur-

gery. In all other respects, the animals were in good

health.

On the morning of the day following NTS surgery

and daily thereafter, arterial blood pressure and heart

rate were measured under the same conditions as

preoperatively. After surgery, 24-hour urine collec-
tions were obtained daily for 3 days, and then the

animals were returned to their regular cages because

they tended to stop eating if kept longer in these

moderately cramped quarters. At 7 days after NTS

surgery, plasma was obtained for renin activity,

aldosterone and norepinephrine, and studies of car-
diac output and blood pressure responses to pheno-
tolamine were performed. Eight days after NTS

surgery, renal function studies were repeated. Body

weight was measured daily. Repeated hemodynamic

and hormonal studies were obtained at weekly inter-

vals as long as the dogs maintained good health.

Histological Examination

The dogs were sacrificed by an injection of sodium

pentobarbital (40 mg/kg I.V.). The brain was per-
fused immediately with 0.9% saline and then with 10%

formalin. The brain was removed and was placed in

10% formalin for at least 2 weeks. The localization of

the lesions was confirmed on sections cut every 33 μ

and stained for neuronal cell bodies by the cresyl violet

method.

Statistical Evaluation

Data are expressed as mean ± se. Statistical

analysis of the data was performed with the paired

Student's t test. Changes were considered to be signifi-
cant if the p values were less than 0.05 using a double-
tailed test. Group statistics were compared by averag-
ing the means for all dogs belonging to the same

group. Data for dogs in the awake and asleep stage

were pooled for analysis.

Results

Subsequent to attempted placement of NTS lesions,

the animals were divided into two groups on the basis

of their blood pressure responses to brain-stem sur-
gery. Group I, composed of six dogs, had sustained

hypertension for at least 10 days after lesioning.

Group II, composed of seven dogs, had no significant

increase in blood pressure 48 hours or more after

lesioning.

Acute Phase Studies

Acute phase is defined as the time period in the

operating room preceding, during and immediately

after brain-stem surgery. The duration of this phase

was 3–5 hours. Pentobarbital anesthesia increased

mean arterial blood pressure in all dogs. Average

mean arterial blood pressure in conscious animals

during the control period prior to anesthesia was

105 ± 4 mm Hg. Average mean arterial blood

pressure in anesthetized animals just before brain-

stem lesioning was 135 ± 7 mm Hg. In Group I dogs

(fig. 1) there was no change or only a transient in-

crease in blood pressure with placement of the initial

lesion on the left side of the brain stem. However, with

placement of the contralateral lesions, blood pressure

increased within 60 seconds of initiation of the anodal

DC current and remained elevated above baseline for

the duration of the acute phase. Blood pressure in-

FIGURE 1. Representative acute blood pressure responses to bilateral electrical lesions of the NTS in two of the Group I dogs.
creased to a maximum of 160 ± 10 mm Hg (p < 0.01) at 1 hour after placement of the lesions. Heart rate in Group I animals also increased during the acute phase from 160 ± 12 to 210 ± 22 beats/min (p < 0.01) after NTS lesions.

In Group II dogs only a transient increase in blood pressure and heart rate was observed during the period of application of the electrical current on each side of the brain stem. Blood pressure promptly returned to baseline after a few minutes and remained unchanged during the remainder of the acute phase.

**Chronic Phase Studies**

**Hemodynamic Changes**

The chronic changes in mean arterial blood pressure following brain-stem surgery for the two groups of dogs are illustrated in figure 2. In Group I dogs, the mean arterial blood pressure during the preoperative control period was 100 ± 6 mm Hg. At 24 hours after surgery, when the dogs were fully conscious, mean arterial pressure had risen to 139 ± 4 mm Hg (p < 0.001). On postoperative Day 2, the blood pressure remained elevated at 136 ± 6 mm Hg. Thereafter, blood pressure decreased slightly, but remained significantly elevated above baseline levels for 10 days after surgery (p < 0.01). No difference in the lability of blood pressure between the control and postoperative period was observed for the Group I dogs. The blood pressure curves were steady within a range of ± 5 mm Hg for each dog when measured at different times on the same day and were not altered appreciably by environmental stimuli. Two dogs, monitored for 18 and 56 days, respectively, had sustained elevation of blood pressure each day. Heart rate decreased slightly from 108 ± 6 to 95 ± 4 beats/min (p < 0.05) after NTS surgery.

The mean arterial blood pressure of Group II dogs increased from 111 ± 4 to 120 ± 4 mm Hg (p < 0.01) at 24 hours after brain-stem surgery similar to Group I dogs. However, blood pressure had decreased to 103 ± 3 mm Hg at 48 hours and was unchanged from control values during the remainder of the chronic period of observation. Heart rate was unchanged from control measurements of 110 ± 5 beats/min during the chronic phase.

Some hemodynamic changes in Group I dogs with chronic sustained hypertension are shown in figure 3. In the control period blood pressure decreased by 9 ± 3 mm Hg (p < 0.05) within 1 minute of phentolamine (5 mg I.V.) without significant change in cardiac output or total peripheral vascular resistance. The increase in mean arterial blood pressure after NTS lesioning was associated with a significant decrease in cardiac output and an increase in total peripheral resistance. In dogs with NTS hypertension, phentolamine administration resulted in a 45 ± 3 mm Hg (p < 0.001) decrease in mean arterial blood pressure accompanied by an increase in cardiac output and a decrease in peripheral resistance. Heart rate also was reversed to control by phentolamine.

**Figure 2.** Chronic responses of blood pressure to bilateral electrical lesions of the NTS in Group I (solid line; n = 6) and Group II (dashed line; n = 7) dogs. Control blood pressures were not significantly different, but Group I dogs had significantly greater blood pressures than Group II dogs on and after postoperative Day 1 (p < 0.05).

**Figure 3.** Hemodynamic changes in dogs with NTS lesions (Group I; n = 6) with acute administration of phentolamine (5 mg I.V.). Asterisks = p < 0.05.
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Plasma renin activity and aldosterone concentration to NTS lesions and responses of blood pressure to SQ20,881 (6 μg/kg/min I.V.) for 30 minutes in Group I dogs (n = 6). None of the changes were significant statistically.

**Hormonal Changes**

In Group I hypertensive dogs, the increase in blood pressure was not dependent upon the renin-angiotensin-aldosterone system (fig. 4). Plasma renin activity was 1.59 ± 0.30 ng/ml/hr before NTS surgery and was unchanged after NTS lesions. Plasma aldosterone concentrations were 4.7 ± 0.2 ng/100 ml during the control period and also were unchanged by NTS surgery. Infusion of SQ20,881 produced no significant change in mean arterial blood pressure either during the control period or after the NTS lesions.

**Renal Function and Sodium Balance Studies**

In Group I hypertensive dogs, renal blood flow during the control period was 336 ± 41 ml/min and after NTS lesions was 295 ± 30 ml/min (p = NS). Glomerular filtration rate was 87 ± 15 ml/min in the control period and was 82 ± 10 ml/min (p = NS) following NTS surgery. Urinary sodium excretion was 85 ± 2 mEq in the 24 hours just before NTS surgery and was 42 ± 8 mEq (p < 0.05) in the 24 hours immediately following NTS lesioning. Thereafter, 24-hour urinary sodium excretion returned to control levels of 84 ± 2 and 83 ± 2 mEq on the succeeding 2 days. In contrast, Group II dogs showed no sodium retention on the day after brain-stem surgery; control 24-hour renal sodium excretion was 82 ± 3 mEq, and after brain-stem surgery sodium excretion was 90 ± 8 mEq (p = NS).

**Histological Studies**

All Group I hypertensive dogs had bilateral destruction of the NTS cell bodies and neuronal tracts at the level of the obex. In the dog brain stem at the obex the NTS lies 2.0–2.5 mm lateral to the midline and 3 mm below the ependymal surface. Representative lesions are shown in figure 6. On microscopic section, the NTS cell bodies surrounding the area of the NTS are destroyed. In all dogs in Group I, structures surrounding the NTS, including the dorsal motor nucleus of the vagus, the intermediary nucleus, the medial cuneate nucleus, and the area postrema were intact. In contrast, histological sections from the brain stem of Group II dogs did not show bilateral destruction of the NTS at the obex (fig. 7). Instead, a combination of lesions in different locations were present. Five of the Group II dogs had no NTS lesions at the obex but had bilateral lesions 200–400 μ caudal to the obex. One animal had only a unilateral lesion of the NTS at the obex and no lesion on the contralateral side at any level. The remaining dog had bilateral incomplete destruction of the NTS cell bodies at the obex.

**Discussion**

The primary objective of the present study was to develop an experimental animal model of sustained neurogenic hypertension by means of bilateral lesions of the NTS. The American foxhound was selected because of its usual stability of blood pressure, its quiet, gentle nature even in the presence of experimental manipulations and the extensive experience of this laboratory in working with this species. Furthermore,
if the canine model of neurogenic hypertension could be developed, it would afford the opportunity for identification of central and peripheral mechanisms associated with the hypertensive process.

The present experiments have shown that the American foxhound responds to placement of bilateral NTS lesions with an immediate increase in blood pressure, which is maximal during the first 24–48 hours after surgery. Subsequently, the blood pressure remains significantly elevated for 10 days without apparent increase in lability over control values. The hypertension has been demonstrated to be present for over 2 weeks in some of the animals, which are otherwise healthy during the chronic period of observation.

Up to the present time, attempts to establish an animal model of neurogenic hypertension with sustained elevation of blood pressure have been difficult and generally unsuccessful. Sinoaortic denervation (peripheral baroreceptor deafferentation) in several animal species has led to mild labile hypertension with wide swings in blood pressure between normal and abnormal. Similarly, bilateral lesions of the NTS in cats have produced chronic hypertension with marked lability of blood pressure. Classical Pavlovian conditioning of cats with NTS hypertension accentuates the acute blood pressure increase associated with the conditioned stimulus. In the rat, NTS lesions usually have resulted in acute fulminant hypertension with death within 4–6 hours secondary to acute left ventricular failure. In a provisional report, when reserpine was given prior to placement of the NTS lesions to prevent the acute lethal rise in blood pressure, rats developed chronic elevation of blood pressure for several weeks. However, the characteristics of this form of hypertension in rats, particularly the degree of blood pressure lability, have not been evaluated systematically. Thus, although others have shown a comparable increase in the average level of arterial pressure, the present study, in which persistent elevation of blood pressure is demonstrated following bilateral NTS lesions, is the first demonstration of production of sustained neurogenic hypertension without apparent lability in an experimental animal model.

During the acute phase of neurogenic hypertension in the present study, the stable elevation of arterial blood pressure was similar in magnitude to that described for the rat and the cat. However, after placement of the NTS lesion and discontinuation of anesthesia in the rat and cat, the blood pressure increased gradually to maximum levels over a period of approximately 30 minutes. In the present experiments, the blood pressure elevation was immediate and achieved a maximum pressure within several minutes of bilateral lesion placement. Also, unlike the present observations in dogs, in cats the blood pressure returned to normal by 24–48 hours postoperatively, although the pressure was elevated by 34 mm Hg at the end of the first postoperative week. In other respects, however, the acute phase of dog hypertension was similar to that reported for cats: both species developed sustained tachycardia and tolerated the immediate postoperative period without evidence of acute heart failure.

Subsequent to the acute phase of stable hypertension, dogs with bilateral NTS lesions entered the chronic phase, characterized by apparent sustained elevation of mean arterial blood pressure. In contrast to the chronic hypertension reported for cats, in dogs the blood pressure did not show minute-to-minute lability, exaggerated swings in blood pressure in response to environmental stimuli or sustained tachycardia. On the contrary, the chronic-phase
Arterial hypertension in the present studies was characterized by a persistent increase in blood pressure with little variability from minute-to-minute or from day-to-day. However, longer blood pressure recordings and analysis of variation of blood pressure by means of frequency histograms will have to be done in future studies to confirm this impression. The reason for differences in the characteristics of the hypertension between the cat and the dog model are not clear. It simply might be related to species differences. Another explanation might be differences in the degree of baroreceptor deafferentation. Lability of blood pressure is a principle manifestation of sinoaortic denervation, which blocks baroreceptor activity from the carotid sinus and the aortic arch. In the cat with NTS hypertension, the baroreceptor reflexes are abolished as quantified by the lack of bradycardia in response to pressor doses of norepinephrine. Baroreceptor reflexes in dog NTS hypertension have not been tested by this method. In fact, the neuroanatomical termination of the baroreceptor neurons in the dog brain has not been studied up to the present time, and there is some known variation in the location of the baroreceptor terminals within the NTS depending on species differences. Therefore, it remains possible that the NTS lesions in the present experiments did not attenuate baroreceptor reflexes sufficiently to produce labile blood pressure. In this case, the elevation of blood pressure in dogs with NTS lesions would depend on another mechanism besides alteration in baroreceptor control. The NTS receives a high density of catecholaminergic nerve terminals, some originating from higher centers in the central nervous system. Since norepinephrine has a predominantly inhibitory role in the central control of blood
pressure, it is possible that the NTS lesions in the present studies destroyed catecholaminergic pathways exerting inhibitory influence on sympathetic vaso-

motor activity, thereby producing hypertension. Alternatively, it is possible that the NTS lesions produced in this study destroyed a portion of the noradrenergic input to the NTS, causing a disturbance in the noradrenergic modulation of the baroreceptor reflex arc and resulting in sustained hypertension. A further unlikely possibility is that an unknown mechanism independent of baroreceptor or cate-

cholaminergic input to the NTS is involved in the production of the hypertension. Further studies of the baroreceptor control of blood pressure will be necessary to clarify the mechanism of the sustained hypertension in dogs with NTS lesions.

The hemodynamic features of this experimental model of neurogenic hypertension include a sustained mean arterial pressure 25–30 mm Hg above control values, decreased cardiac output, normal to decreased heart rate, increased pulse pressure and markedly elevated total peripheral vascular resistance. The hemodynamic changes were present 7–14 days after initiation of the hypertensive process and are similar to those changes reported from this laboratory after chronic intrarenal norepinephrine infusion in conscious dogs. The chronic decrease in cardiac output is most likely related to afterload mechanisms. The mechanism most likely responsible for the increased total vascular resistance is vasoconstriction resulting from an increase in α-adrenergic activity. Although plasma norepinephrine concentration increased in four of the five dogs in which it was measured, the increase was not significant statistically because of the decrease of plasma norepinephrine in one of the dogs. However, the importance of α-adrenergic vasocons-

triction in the production of the hypertension is evident in the marked decrease in blood pressure associated with a decrease in peripheral resistance and an increase in cardiac output associated with phenyl-

talamine administration. After establishing that bilateral NTS lesions produce elevation of blood pressure, we performed studies to elucidate other mechanisms that might play a role in the increase in peripheral resistance. Plasma renin activity and aldosterone concentration were similar before and after NTS lesions. The blood pressure response to the angiotensin converting en-

zyme inhibitor, SQ20,881, also was unchanged after NTS lesions. Therefore, it is highly unlikely that the peripheral vasoconstriction in this form of hypertension is dependent on the renin-angiotensin-aldosterone system. These data are consistent with the observation that acute rat NTS hypertension is not blocked by bilateral adrenonephrectomy immediately before placement of the lesions.

In the first 24 hours postoperatively, we were able to demonstrate renal sodium retention in the NTS hypertensive dogs. This positive sodium balance could have contributed to the maintenance of elevated blood pressure either by increasing intravascular volume or by increasing vascular sensitivity to endogenous pressor substances such as norepinephrine. The mechanism for renal sodium retention with NTS lesions is not clear. Renal plasma flow and glomerular filtration rate were unchanged 1 week after placement of the NTS lesions. However, renal function studies were not performed in the first 24 hours after surgery, and it is possible that an acute change in renal hemodynamics accounts for the sodium retention observed during this period. It is also possible that the H2-p-aminohippuric acid (PAH) clearance technique was not sensitive enough to measure a small decrease in renal blood flow which might have been detected with the flow probe technique. Nevertheless, studies of regional blood flow by the isotope dilution technique in rats with NTS hypertension suggest that the max-

imum vasoconstriction occurs in skin, skeletal muscle and lower bowel, and that blood flow to the kidneys is normal in these animals. The present data in dogs with NTS hypertension are similar to previous results in dogs with chronic norepinephrine infusion in that acute sodium retention was demonstrated in both studies. However, in dogs with intrarenal norepinephrine infusion, a consistent 25% reduction in renal plasma flow was demonstrated at 1, 5 and 11 days of infusion of this sympathetic neurotransmitter. An explana-

tion of the differences in renal plasma flow between these two models of experimental hyperten-

sion, both of which are dependent on increased α-adrenergic activity, probably is related to the greater quantity of norepinephrine available at intrarenal α-adrenergic receptor sites in the model of chronic intrarenal norepinephrine infusion. In the present study, we have demonstrated that bilateral lesions of the NTS in dogs produce hypertension, which is characterized by increased peripheral sympathetic nervous system activity. This dog model of neurogenic hypertension may prove valuable in future studies of the mechanisms of neurogenic hypertension in animals, and may ultimately contribute to an increased understanding of the mech-

anisms underlying the initiation and maintenance of essential hypertension in man.

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