*BIOBEHAVIORAL EFFECTS OF EXTENDED SALT LOADING AND
CONFLICT STRESS IN INTACT BABOONS*

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Behavioral stressors may inhibit sodium excretion, potentially increasing plasma volume and elevating blood pressure during chronic exposure. Blood pressure regulation may be especially deranged during manipulations that further challenge the kidney, such as a diet high in salt content. The effects on blood pressure and other variables of combined behavioral stress (food/shock conflict) and dietary salt (12 g NaCl per day; 218 mEq Na⁺ per day) were examined in adult male baboons over the course of 1 year. Mean arterial pressure was not significantly elevated over baseline after 5 months of high dietary salt alone (6 ± 5 mmHg) but was maximally elevated by an average of $17 (\pm 3 \text{ SEM})$ mmHg after 5 months of combined salt and conflict stress. Control baboons showed no significant trends in mean arterial pressure across the same time period. Individual subjects whose blood pressure was "salt+stress resistant" or "salt+stress sensitive" were differentiated by their degree of pressure diuresis and natriuresis, urinary free cortisol, and a behavioral index of stress sensitivity. The data indicate additive effects of chronic high dietary salt intake and behavioral stressors on blood pressure in nonhuman primates that are dependent on renal function and pituitary-adrenocortical activity.

Key words: hypertension, blood pressure, sodium chloride, behavioral stress, food/shock conflict, lever pull, baboons

Recent analyses of international epidemiological studies have shown positive and highly significant correlations between dietary salt and both systolic and diastolic blood pressure (Elliott, 1991; Intersalt Cooperative Research Group, 1988b). Of some public health concern are consistent findings that Americans ingest markedly more salt per day than is physiologically needed or recommended (Fregly & Fregly, 1982). Such ingrained potentially unhealthy dietary habits exist in combination with chronic stress in many individuals. Evidence from some suggestive laboratory studies in rodents, canines, and humans, and from nonhuman primate studies in our own laboratory, point to the potential for stress exposure concurrent with high levels of dietary salt to produce deleterious cardiovascular outcomes (DiBona & Jones, 1991; Ely, Friberg, Nilsson, & Folkow, 1985; Ely & Weigand, 1983; Hudak & Buckley, 1961; Koepke, Jones, & DiBona, 1988; Rothlin, Cerletti, & Emmenegger, 1956; Sanders, Cox, & Lawler, 1988).

A recent study in borderline hypertensive rats established that a high-salt diet (8%) combined with air-jet stress increased renal sympathetic nerve activity, sodium retention, and mean arterial pressure (DiBona & Jones, 1991). Moreover, a lower salt dose (1%) failed to produce sodium retention during stress and limited expected increases in renal sympathetic nerve activity and blood pressure. Studies with intact dogs provided additional impetus to the hypothesis that a high salt intake and stress may exacerbate each other's deleterious effects on tonic blood pressure control mechanisms: Intraarterial isotonic saline infusions combined with chronic shock-avoidance stress elevated blood pressure of dogs over a period of weeks. The animals displayed no tonic blood pressure increases with saline infusions alone or with avoidance conditioning alone (Anderson, 1986; Anderson, Gomez-Sanchez, & Dietz, 1986; Anderson, Kearns, & Better, 1983).

A series of studies in our laboratories established an additive effect on blood pressure of chronic behavioral stress and dietary salt in nonhuman primates (Turkkan, 1991; Turkkan & Goldstein, 1991a, 1991b). Baboons consumed high levels of salt (12 to 15 g NaCl per day) or experienced food/shock conflict stress during extended periods; each manipulation produced small changes in mean arterial pressure (MAP). When baboons then underwent a combination of the conflict stress and dietary salt, progressive, persistent increases in blood pressure occurred. Specifically, these earlier

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studies also established that (a) the blood pressure elevations when salt and stress were administered concurrently were not dependent on the preceding order of exposure to stress versus salt; (b) blood pressure increases during combined salt and stress were generally accompanied by decreases in heart rate and large-scale increases in ad libitum water ingestion; (c) the blood pressure elevations were reversible when salt and stress were discontinued; but (d) these elevations were not reversible by beta-1 blockade with atenolol or by the diuretic hydrochlorothiazide. These results supported the hypothesis that long-term dietary salt loading and repeated episodes of mild psychological stress can interact and evoke chronically elevated blood pressure in otherwise healthy primates undergoing noninvasive procedures.

Also noted in our previous work have been individual differences in behavioral and physiological sensitivity to conflict stress alone. Animals that displayed enhanced "stress responses" during food/shock conflict (such as elevated blood pressure, urinary free cortisol, plasma renin activity [PRA], urinary catecholamines, sodium retention, and behavioral indices) displayed the largest blood pressure elevations when salt and stress were subsequently combined (Turkkan, 1991).

The current study aimed to confirm and to extend these previous observations (a) by lengthening the duration of exposure to salt alone prior to combination with stress and also by extending the duration of combined stress and high-salt diet as more realistic of chronic human exposure; (b) by lowering the salt dose by 3 g per day in order to avoid complete suppression of PRA levels, as we observed at higher doses in our previous studies; and (c) by characterizing the time course of developing underlying physiological differences between salt+stress-sensitive versus -resistant animals during chronic exposure.

In addition to blood pressure, urinary excretion of cortisol was measured, because the pituitary-adrenocortical systems are activated during aversive situations. Long-term exposure to behavioral stress, particularly situations involving low stress controllability (Henry & Grim, 1990), has been demonstrated to activate the pituitary-adrenocortical system (Mason, 1968) and is thought to interact with sodium consumption to potentiate blood pres-

sure elevations (Henry & Grim, 1990). Experimental evidence indicates that adrenocorticotrophic hormone (ACTH) administered to nonhuman animals (Whitworth et al., 1990) or to humans (Whitworth, Saines, Thatcher, Butkus, & Scoggins, 1983), and cortisol administered to humans (Whitworth, Saines, & Scoggins, 1984), can be hypertensinogenic. Because of the role of the renin-angiotensin-aldosterone system in regulation of blood pressure and alterations in activity of this system during stress and high salt intake, PRA was also measured. The role of natriuretic and diuretic responses in the blood pressure elevations observed during salt loading and stress was assessed with 24-hr urine excretion volumes, 24-hr fluid intake, sodium balance, and serum sodium/potassium ratio. A behavioral index of stress was the degree of "conflict" during experimental sessions, defined as lever-pull pause duration following a stimulus (S^D) that set the occasion for shock punishment through the lever.

METHOD

Subjects

Seven adult male baboons (*Papio* of *cynocephalus* and *anubis* subtypes) weighing 20 to 24 kg served as subjects. Four baboons served as experimental subjects and underwent food/shock conflict concurrent with high dietary salt intake, and 3 baboons housed in the same area served as controls. All baboons were surgically intact. Standard monkey chow (Purina® 5037) contained 5% fat, 0.22% sodium, 0.34% chlorine, 0.5% potassium, and 83 ppm cholesterol. Animals received chow and one piece of fruit daily at 3:00 p.m. on weekdays and at 9:00 a.m. on weekends. Tap water was available for drinking ad libitum. The laboratory was on a 12:12-hr light/dark cycle (lights on at 6:00 a.m.). Three of the 4 experimental baboons had been exposed to a high-salt diet and conflict stress approximately 4 months prior to the current study; baseline blood pressure was within 5 mmHg of original resting levels at the start of this study. Eight weeks has been suggested to be a required stress-recovery interval for baboons (Steyn, 1975). The control baboons and 1 experimental baboon (DU) were naive to stress or a high-salt diet.

Apparatus

Baboons were housed singly in stainless-steel cages (122 cm long by 89 cm wide by 142 cm high) with a seating bench. On an aluminum panel (25 cm by 38 cm) attached to the outside of each cage were mounted, facing into the cage, a Lindsley response lever modified for presentation of mild electric shock, a hinged lucite panel (7.6 cm by 12.7 cm) at eye level that could be transilluminated with red or green stimulus hues, and a small hinged opening for the animal to extend its arm outside of the cage for blood pressure measurement. Mounted on the panel on the outside of the cage were an automated (BRS) food-pellet dispenser and a food well to receive banana-flavored pellets (Bio-Serv, 1 g) or chow. A shelf for arm support was periodically attached to the cage for blood pressure measurement. Systolic and diastolic (Phase V) blood pressure measurement was accomplished with standard auscultatory equipment consisting of a stethoscope (Tycos, Model 5079-28), a child cuff (40.5 cm by 10.5 cm), bladder (17.5 cm by 9 cm), and a mercury (W. A. Baum, "Standby") manometer. Blood pressure also was measured with a random-zero Hawksley sphygmomanometer to check for bias in blood pressure measurements. Apple IIE® computers controlled experimental events and stored data on floppy disks that were later ported to an Apple Macintosh® computer for descriptive statistics, hypothesis testing, and graphics.

Urine was collected for measurement of concentrations of cortisol and electrolytes and for estimates of fluid and sodium balance. Collection pans of galvanized sheet metal (0.8 m wide by 1.2 m long) were covered with a double layer of wire mesh to screen all material other than urine, and were constructed with a sloped back and sides to ensure pooling and to limit evaporation.

Procedure

Experimental baboons experienced twice-daily experimental sessions consisting of a fixed-ratio (FR) schedule of food reinforcement for a period of 6 weeks (baseline). Next, subjects underwent a daily dietary salt regimen, described below, for 5 months while food-reinforcement sessions continued (salt alone). Subjects then underwent the dietary salt reg-

imen concurrent with food/shock conflict sessions for 5 months (salt+stress). Baseline recovery, consisting of food-reinforcement sessions without salt or stress, next occurred for 3 weeks. Baboons in the control condition underwent daily sessions of food reinforcement and received the same daily diet as did the experimental animals, but did not undergo conflict stress or added salt.

Experimental sessions occurred in each experimental animal's cage twice daily and were signaled by the onset of a green light on the panel. In all experimental conditions, animals earned one food pellet for each 100 lever pulls (FR 100). Session length was 90 reinforcements or 180 min, whichever occurred first. During salt+stress sessions, 30% of trials introduced an electric shock punishment contingency for pulling the lever that was correlated with a change in the S^D from green to red. Thus, each of the last three lever pulls to complete a trial had a 35% probability of producing mild electric shock (i.e., Lever Pulls 98, 99, or 100, or any combination of these three responses, could produce shock). When the animal pulled the lever in the presence of the red S^D , constant-current electric shock was administered through the lever for 500 ms (intensity range, 2 to 3 mA). Food-reinforcement contingencies remained in effect on trials containing the punishment contingency. If the animal did not pull the lever, the session timed out with no further experimental consequences. The low shock intensity was chosen to ensure that animals would continue to respond on the lever. Because fewer pellets were earned during the conflict conditions, evening food rations were adjusted daily in order to maintain a constant diet.

Dietary salt loading was accomplished by administering hypertonic saline (Abbott Laboratories) for oral ingestion in orange-flavored and colored water placed in a bottle with a nozzle and attached to the animals' cages daily at 7 a.m. Saline (270 mL) was combined with powdered orange drink (Tang®) and tap water (150 mL) to yield a daily dose of 12 g NaCl per day (218 mEq Na^+ per day). The American adult daily diet has been estimated at 8 to 9 g NaCl per day based on 24-hr urine samples (Intersalt Cooperative Research Group, 1988a). The control (vehicle) fluid consisted of 400 mL of Tang® in tap water

administered daily at 7:00 a.m. The control drink was administered to control animals and to experimental animals during experimental conditions that did not include salt loading. The control diet contained approximately 1 g NaCl per day.

Brachial blood pressures were measured from the seated animal prior to the onset of each session (8:30 a.m.; presession) and 15 min after the start of the second daily experimental session at 12:15 p.m. (midsession). (See Turkkan, 1990, and Turkkan, Ator, Brady, & Craven, 1989, for full details of the measurement procedures.) Random-zero sphygmomanometry was done on a quasi-random schedule. Heart rate (beats per minute; BPM) was obtained by palpation of the brachial artery for 60 s prior to blood pressure measurement.

Assay procedures. Urine collection pans were inserted under the cages at 6:30 a.m.; urine was pumped into collection bottles at 11:00 a.m., 2:00 p.m., and 6:30 a.m. the following day. Urinary sodium (Na^+) and potassium (K^+) were assayed by flame photometry. Assays of urinary free cortisol were accomplished once per week by radioimmunoassay at the Pediatric Endocrine Laboratory of the Johns Hopkins Hospital. Serum chemistries from femoral arterial blood included PRA and electrolytes. To collect blood, the animal was sedated with ketamine HCl (5 mg/kg i.m.) and kept in a supine position for 30 min during halothane anesthesia while effects of ketamine dissipated. Arterial blood was then collected into coded, chilled glass tubes containing EDTA. Plasma was stored at -70°C until assayed. PRA was measured by the rate of angiotensin I generation using radioimmunoassay (Smith/Kline Laboratories). Blood was collected twice during baseline, after the 3rd and 5th months of salt and salt+stress, and once during baseline recovery.

Data Analysis

Mean arterial pressure (MAP) was calculated as diastolic blood pressure (DBP) plus one third pulse pressure (systolic blood pressure $-$ DBP). Urinary sodium excretion was calculated by measuring the concentration of electrolyte in urine and multiplying by the volume ($U_{\text{Na}}V$). For data that were taken daily or weekly (blood pressure, heart rate, water intake, and urinary measures), medians for each animal were calculated across successive

nonoverlapping 5-day (weekday) periods. Data were analyzed using mixed-model (between-groups factor = experimental group vs. control group; within-group factor = successive experimental conditions) repeated measures analyses of variance (ANOVA). Data were entered for the last 4 weeks (median) of baseline, the 3rd and 5th months of salt alone, the 3rd and 5th months of salt+stress, and baseline recovery. Random-zero blood pressures did not differ from other readings and were pooled in the analyses. Reported probabilities use the Huynh-Feldt conservative probability correction for repeated measures and 95% confidence intervals for planned comparisons of means after overall ANOVAs were found to be significant. Planned comparisons were conducted on all statistically significant measures in order to determine whether the salt-alone and salt+stress conditions significantly changed the measure from baseline levels. Planned comparisons also aimed to determine whether measures taken during the salt+stress period were significantly different from the preceding salt-alone period. Neither baseline recovery data nor data from control baboons were entered into the planned comparisons.

RESULTS

Results will be presented as follows: The effects on cardiovascular measures of salt alone and salt+stress in experimental versus control animals will be described, with accompanying changes in neuroendocrine and sodium excretion measures. Following this, 2 baboons that showed a markedly different cardiovascular pattern during salt+stress will be directly compared in detail to determine whether changes in accompanying variables are potential indicators of the source of differences in their blood pressure patterns.

Cardiovascular Effects

Across all experimental conditions, average midsession MAPs of experimental baboons were significantly changed, whereas average MAPs of control baboons remained unchanged across the same period (conditions $\times$ group interaction $F(5, 25) = 7.57$; $p < .0005$; Figure 1, upper panel). Means comparisons revealed that average MAPs were not statistically different in comparison to baseline after 3 months (change from baseline = -3 ± 4

mmHg) and also after 5 months (change from baseline = 6 ± 5 mmHg) of salt loading alone. During subsequent salt+stress, however, MAPs were significantly elevated over baseline by 14 ± 2 mmHg after 3 months and by 17 ± 3 mmHg after 5 months; it was also significantly elevated in comparison to salt alone (Figure 1). Presession MAP levels also rose progressively across salt+stress months (not shown) and were generally lower than midsession MAPs by approximately 10 mmHg.

Heart rates of experimental animals were inversely related to MAP across experimental conditions, whereas heart rates of control animals were stable across the same time period (Figure 1, lower panel) (condition $\times$ group interaction $F(5, 25) = 6.29$; $p < .005$). Heart rates of experimental animals were maximally and significantly lowered from their baseline levels after 5 months of salt alone (change of -17 BPM) and remained lowered from baseline during salt+stress. Heart rates of experimental animals returned to baseline during baseline recovery.

Electrolytes and Renal Function

Serum Na^+ was elevated in the majority of experimental animals to 148 ± 2 mEq/L after 5 months of salt alone (change from baseline = $+2$ mEq/L), whereas serum Na^+ of control animals decreased to 145 ± 0.5 mEq/L during the salt-alone period (change of -2 mEq/L). Serum Na^+ and serum K^+ progressively fell across subsequent conditions in all animals. The proportion of serum Na^+ to serum K^+ was different for experimental animals compared to control baboons: For experimental animals, serum Na^+ was elevated in proportion to serum K^+ during the 5th month of salt+stress, whereas serum Na^+ declined in proportion to serum K^+ during this same period in control baboons. During all conditions in which salt was administered, PRA of experimental animals fell to an average of 6 ± 1 ng/mL/hr (change from baseline = -6 ng/mL/hr) and recovered baseline levels after salt was terminated; no statistically significant differences in PRA between salt-alone and salt+stress conditions were evident.

Twenty-four hour urine volume (UVOL) and water intake were highly correlated across conditions. Each measure was maximal during the 3rd month of salt+stress, and was elevated over baseline by 538 mL per day and 563 mL

Fig. 1. Average ($\pm$ SEM) mean arterial pressure (top) and heart rate (bottom) across successive experimental conditions for experimental (left) and control (right) baboons. Statistically significant individual means planned comparisons are shown with brackets. Five-day medians were averaged over 4 weeks, with the exception of baseline recovery (3 weeks). Data were then averaged over 4 subjects in the experimental group, and over 3 subjects in the control group.

per day for urine volume and water intake, respectively (Figure 2). Daily urine volume and water intake of control animals (not shown) remained constant across parallel observation periods (conditions $\times$ group interaction $F_{\text{UVOL}}(5, 25) = 3.26$; $p < .05$; $F_{\text{H}_2\text{O}}(5, 25) = 5.66$; $p < .01$). Urinary sodium excretion of experimental animals was elevated in all conditions that included salt loading; sodium excretion of control animals remained roughly constant across observations (conditions $\times$ group interaction $F(5, 25) = 42.4$; $p < .0001$). Sodium excretion of experimental animals was maximally elevated during the 5th month of salt+stress (change of $+191$ mEq Na^+ /day). Trends in sodium balance (intake $-$ output) for experimental animals across conditions

Fig. 2. Mean sodium excretion ($U_{NA}V$), sodium balance, 24-hr urine volume, and 24-hr water intake of experimental baboons across successive experimental conditions. Each point is an average of 4 weeks for an individual animal. Solid lines are an average over the 4 experimental subjects.

(Figure 2) were not significantly different from controls ($p > .10$).

Salt+Stress Effects: Individual Differences

Two baboons (SY and IM) whose MAPs were changed to a small degree (± 5 mmHg) after 5 months of salt loading displayed markedly different physiological and behavioral trends during the subsequent salt+stress condition (Figure 3). The MAP of Baboon SY increased progressively across salt+stress months, reaching its highest level (131 mmHg) in the 5th month (change from baseline = 21

mmHg; a change of 26 mmHg over the last month of salt alone). The MAP of Baboon IM, by contrast, was elevated maximally by 11 mmHg over baseline levels after 5 months of salt+stress (+6 mmHg over the last month of salt alone).

Neuroendocrine levels during salt+stress also differentiated these 2 baboons. Urinary free cortisol of Baboon IM was lower than that of Baboon SY during the final month of salt+stress by approximately 200 μg per 24 hr (Figure 3). Further, Baboon IM's PRA level fell following the addition of food/shock

Fig. 4. Scatterplots of pressure natriuresis (MAP $\times$ urine sodium excretion) and pressure diuresis (MAP $\times$ urine volume) curves for Baboons SY (filled points) and IM (unfilled points). Each point is a median over 4 weeks. Second-order polynomial regression curves are fit to the data.

conflict stress and was lower by 3 ng/mL/hr in the last month of salt+stress compared to increases in PRA levels obtained for Baboon SY. Finally, lever-pull pause duration during the conflict S^D was lower for Baboon IM than for Baboon SY by an average of 1.3 s in the final month of salt+stress.

Pressure natriuresis and diuresis curves for these animals (Figure 4) reflected Baboon IM's

Fig. 3. Midsession mean arterial pressure, urinary free cortisol, and time in conflict S^D (duration of lever pausing during the shock S^D) as a function of successive months of salt+stress. Baboons SY (filled data points) and IM (unfilled points) are contrasted in separate functions. Each point is a median over 4 weeks.

greater sodium and water excretion compared to Baboon SY correlated with rising blood pressure. Based on the regression slopes, for a 5-mmHg rise in MAP (e.g., between 95 and 100 mmHg), daily sodium excretion increased by 60 mEq in Baboon IM and decreased by 30 mEq in Baboon SY. This indicated sodium retention in Baboon SY instead of sodium excretion. Note also Baboon SY's pressure natriuresis curve shifted to the right, such that a higher MAP was required to maintain sodium excretion at the same levels as Baboon IM. With regard to urine volume (pressure diuresis), the same 5-mmHg rise in MAP brought an increase in urine volume excretion in Baboon IM of approximately $\frac{1}{4}$ L in comparison to the $\frac{1}{8}$ L increase in urine volume excretion in Baboon SY.

Food reinforcers earned per day and shocks received per day were not systematically different between these 2 animals, and both had similar conditioning histories prior to the current study. Average shock intensities across the entire stress period were 2.3 and 2.4 mA for Baboons SY and IM, respectively.

DISCUSSION

The MAP measured during food-reinforcement sessions in genetically unselected, freely mobile baboons was modestly but not statistically significantly elevated during a 5-month salt-loading period without a programmed stressor. MAP increased markedly above baseline levels after food/shock conflict stress was added to the daily salt-loading protocol. Parallel measures taken from control baboons that experienced no food/shock conflict stress or added dietary salt were generally stable. These findings again confirm salt+stress blood pressure additivity, which has now been obtained both in human (Haythornthwaite, Pratley, & Anderson, 1992) and in nonhuman animal studies (Anderson et al., 1983; DiBona & Jones, 1991; Ely & Weigand, 1983; Turkkan & Goldstein, 1991a, 1991b). Although the salt levels administered both here and earlier were approximately 3.5 times the American daily dietary intake, such high dietary levels are needed to produce a blood pressure response to salt within a relatively brief period of time.

Blood pressures rose not only during experimental sessions but also, to a lesser degree, during daily pre-session periods (cf. Forsyth, 1969), suggesting that blood pressure may have

been elevated throughout the day. This would cause a steadily higher load on the systemic arterial tree rather than intermittently higher blood pressure levels elicited only during the experimental sessions. In agreement with our previous findings (Turkkan, 1991), a behavioral stress index (i.e., lever-pull pausing during a cued period which set the occasion for shock) was differentially elevated in a blood-pressure-sensitive animal compared to a resistant animal. The effect size previously observed during a conflict S^D for this pausing measure was not, however, replicated. Gross indices such as food reinforcers and shocks received per session did not differentiate blood-pressure-sensitive and -resistant animals. Future studies might incorporate more sensitive objective behavioral measures in order to index differences in stress sensitivity as correlates of physiological changes.

Although short-duration manipulations of stress and brief alterations in salt diet are commonplace and their effects have been examined in acute studies, our studies aimed to simulate, in freely mobile animals without invasive measurements, extended changes in salt diet in combination with chronic stress. This study revealed that blood pressure elevations in the salt+stress condition were progressive, but did not rise above salt-alone levels for the majority of animals until after 3 months of added stress. Further, MAPs of 2 of the 4 experimental baboons had not plateaued in the final 3 weeks of the 5-month stress+salt period. Note also Forsyth's (1969) early study, which found blood pressure of rhesus monkeys elevated over baseline levels only after 4 continuous months of daily shock-avoidance stress. The current findings argue for extended studies in which long-term trends in cardiovascular and hormonal changes can be revealed.

The kidney has been implicated in the long-term regulation of blood pressure through its actions on salt and fluid regulation (Guyton, 1991). In the presence of both a high salt intake and stress exposure, alterations in kidney function may produce nonreversible changes in blood pressure during stress due to impairments of renal blood flow, thus causing sodium retention and volume expansion (Anderson, 1984). The extracellular fluid volume is controlled almost exclusively by alterations in body sodium balance (daily sodium intake minus daily sodium excretion). When the arterial blood pressure rises, there is an immediate and

predictable increase in renal sodium (and water) excretion, known as the renal pressure natriuresis phenomenon; this reduces extracellular fluid volume and lowers blood pressure to normal. In normal individuals, sodium intake can increase dramatically without consequent elevations in blood pressure through pressure natriuresis, which matches renal sodium output to intake at a set arterial blood pressure. When the capacity of the kidney to excrete sodium is reduced, however, the arterial blood pressure set point for renal sodium excretion is raised, so that neutral sodium balance (intake = output) is achieved at a higher level of blood pressure (Guyton et al., 1986). Several mechanisms can reduce the renal capacity to excrete sodium. Prior experiments both in nonhuman animals and in humans have shown that behavioral stress reduces the renal capacity to excrete sodium, at least in some individuals, thus resetting the renal pressure-volume mechanism. For example, shock-avoidance conditioning decreases renal blood flow in monkeys (Forsyth, 1971; Vatner, 1978) and decreases renal excretion of sodium and water in dogs (Koepke, 1985). In studies with humans, borderline hypertensives (Light, Koepke, Obrist, & Willis, 1983) and normotensive young adults both with (Light et al., 1983) and without (Harshfield, Pulliam, & Alpert, 1991) a family history of hypertension have exhibited reduced sodium excretion rates during laboratory stressors.

In the current study, MAP of 1 animal (Baboon IM) rose less than all other animals. An examination of this "salt+stress-resistant" animal revealed that he ingested large volumes of water and showed greater diuresis throughout the study. Most notable was his extremely responsive pressure natriuresis, suggesting a maximally functioning kidney, in comparison to the salt+stress-sensitive animal who displayed sodium retention across part of the range of MAP. This salt+stress-sensitive animal (Baboon SY) was notable in that he showed the highest levels of urinary free cortisol in the final months of salt+stress. Moreover, he was the only experimental animal whose PRA was elevated over salt-alone levels (and markedly above baseline levels) during salt+stress. Thus, PRA was inappropriately high for the high salt intake that he was ingesting, which also implicates the renin-angiotensin-aldosterone system in the observed blood pressure elevations.

We have shown previously, with a variety of behavioral and physiological indexes, that some animals are sensitive to stress manipulations. Further, these stress-sensitive animals show differentially greater blood pressure elevations when stress is administered concurrent with a high-salt diet (Turkkan, 1991). With regard to dietary salt sensitivity, although the panoply of measures that have been brought to bear on this question (Sullivan, 1991) were not obtained here, it was apparent that salt sensitivity per se was a weak predictor of the magnitude of blood pressure elevation under salt+stress. First, the baboons who were the most salt sensitive (change in MAP > 10 mmHg after 5 months of salt alone) did not show the largest increases in blood pressure during subsequent salt+stress. Second, the most salt+stress-sensitive and -resistant animals showed comparable blood pressure elevations during salt alone. Studies must be conducted in a large number of subjects with counterbalanced order of salt and stress alone and combined for firm conclusions to be drawn. Nevertheless the present data and our earlier findings suggest that heightened sensitivity to stress—accompanied by heightened activity of the pituitary-adrenocortical and renin-angiotensin-aldosterone systems and inadequate regulation of extracellular fluid volume—may be the more important hypertensinogenic factor in the stress+salt equation.

Recently, the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure has recommended reduction of sodium chloride intake <6 g per day (Joint National Committee, 1993). Future studies may profitably examine the interaction of a range of salt intake doses with behavioral stress in the genesis of high blood pressure. The broader implications of these studies relate to a general understanding of neurogenic, behavioral, and renal interactions during stress.

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