Table 2.

		Uric acid (mg%)	Cortisol (mg%)	Cholesterol (mg%)	STAI Anxiety	MAACL Anxiety	Depression	Hostility
Age group I (age 18-30)	High Stress	4.86±0.3	9.74±1.9	149.44± 9.9	29.6±1.5	7.0±0.6	14.3±0.9	9.1±0.9
	Low Stress	5.75±0.3	7.73±0.6	131.89±10.1	38.2±1.0	3.2±0.9	6.3±0.5	5.3±0.5
Age group II (Age 30-55)	High Stress	6.1 ±0.2	12.1 ±1.2	194.7 ± 9.1	46.8±2.0	10.3±0.6	17.3±1.2	9.6±0.7
	Low Stress	6.2 ±0.2	12.0 ±0.9	182.6 ± 7.2	27.3±0.7	2.2±0.6	6.2±0.7	3.9±0.5

Mean values (± SE) of psychological parameters and serum uric acid, cortisol and cholesterol parameters in high and low psychological stress groups.

ty, and depression raw scores at or above 7, 7, and 11 respectively.

Blood was obtained from the anticubital vein of subjects who had fasted 12-14 h at the time of the psychological testing. Total serum cholesterol was measured by continuous-flow analysis according to the lipid research protocol[11] with the use of the Libermann-Burchard Reagent. Cortisol was assayed by solid-phase radioimmunoassay according to the procedure of Rolleri et al.[12]. Serum uric acid was assayed according to the method of Henry et al.[13]. All changes were assayed for statistical significance by analysis of variance.

Results. The results recorded in table 1 indicate that the parameters of trait anxiety, depression, and hostility as measured by the MAACL were significantly ($p \leq 0.01$) correlated with the trait anxiety parameter as measured by the STAI.

Table 2 presents the mean STAI anxiety and MAACL scores of the total high and low psychological stress groups for the three highly interrelated mood and feeling parameters of trait anxiety, hostility, and depression. The data reveal that the goal of attaining 2 distinctly different psychological stress groups in each age group was attained. However, the serum indicators of stress among high and low psychological stress groups in both age groups were not significantly different.

Discussion. During the past 2 decades considerable progress has been made in the identification of the factors which predispose an individual to CHD. A list of generally accepted standard risk factors include psychological stress. Research attention has recently focused on the significance of psychological stress factors in the etiology of heart disease. The literature implies that psychological stress probably influences the level of certain serum components such as cholesterol, uric acid, and cortisol[4,5,14]. However, the data in table 2 indicate that trait characteristics of anxiety hostility and depression does not apparently chronicly elevate these serum parameters. It may not be the chronic trait of high psychological stress personality that influences the serum parameters but how these 2 personality types of individuals perceive or react to 'acute' stress[15]. The high stress individual may react differently to periods of acute stress that occur throughout a given work day; hence, the acquisition of a unitary data set may not detect such differences. This laboratory is in the process of attaining these data in a high and low stress group of subjects.

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Plasma catecholamines in conscious rats: Influence of sodium, stress and heredity[1]

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Summary. Plasma catecholamines are increased in sodium-loaded rats under both resting and stress conditions. Under stress, Na^+ resistant rats have lower plasma catecholamines than salt-sensitive ones.

Clinical and experimental data both strongly support the involvement of increased sympathetic activity in hypertension (for review, Axelrod[2]), and it has also been suggested that sodium (Na^+) may be one of the factors triggering this hyperactivity[3].

The available information concerning the effect of Na^+ on sympathetic activity is controversial. While some authors have reported that acute or chronic Na^+ loading enhances catecholamine excretion[4], increases plasma noradrenaline (NA)[5-7] and depletes heart catecholamine stores[8], others

found reduced NA excretion[9] decreased plasma NA[10], and unchanged catecholamine myocardial stores[11].

In the present investigation, plasma catecholamines were measured a) in severe hypertension, in both DOCA Na^+ rats and salt sensitive, genetically hypertensive SbH rats, b) in mild hypertension after prolonged sodium loading and c) in hypertension-resistant, salt resistant SbN rats.

Material and methods. This study was carried out on 2 groups of rats, a) unselected Wistar rats and b) the hypertension-prone (SbH) and -resistant (SbN) substrains derived from the Hebrew University Sabra strain (Sb) supplied by the Hadassah Medical School. Details regarding the selection, the breeding and the characteristics of these substrains have been reported elsewhere[12].

1 week after their arrival in the laboratory, rats (then aged 6 weeks) were submitted to 3 different diets. 1. Control rats were fed a control diet containing 0.02% Na^+ and had free access to tap water. 2. DOCA-Na^+ rats were uninephrectomized and fed the same diet but drank a 1% NaCl solution. They also received, once a week, an i.m. injection of deoxycorticosterone pivalate (25 mg/kg). 3. High Na^+ rats were fed a diet containing 2% Na^+ and with 1% saline to drink. The animals of groups 2 and 3 were maintained on the respective sodium regimens for a period of 7–9 weeks.

The mean systolic arterial pressures (mm Hg) of the different groups of rats were as follows: control 125 ± 8 ($n=4$); DOC.Na^+ 170 ± 15 ($n=14$); high Na^+ 148 ± 11 ($n=8$); SbH 182 ± 10 ($n=8$); SbN 112 ± 8 ($n=10$).

2 days after implanting a catheter in the carotic artery, blood sampling was performed a) under resting conditions on sleeping rats, accustomed to a quiet room, b) under stressful conditions; rats were transferred from the animal room to a laboratory room, and just afterwards blood was withdrawn. The experiment was randomized.

Samples of 0.4 ml of blood were collected. Blood was cooled to 4 °C and centrifuged at $3000 \times g$. Plasma was then centrifuged at $17{,}000 \times g$ for 5 min and deproteinized with 0.22 N perchloric acid containing 1% EGTA and 75 mM $MgCl_2$ in 8/1 vol/vol ratio. Measurements were performed by the Da Prada[13] technique with minor modifications. Sensitivity was 4 pg/ml for noradrenaline (NA) and 7 pg/ml for adrenaline (A). Interassay coefficient of variation was 8% for NA and 12% for A. Data were treated by analysis of variance.

Results. Resting levels of plasma NA and A of unselected Wistar and SbH and SbR Sabra rats are shown in figures 1 and 2. There is no difference between the NA levels of SbH, SbR and Wistar rats. In contrast, A-levels are lower in SbH rats ($p < 0.05$). After administration of DOC.Na^+ plasma NA was +44% and for A +54%. Higher increments were observed in high Na^+ rats (+55% for NA and 95% for A). It is noteworthy that the maximal changes in plasma catecholamines were associated with only a moderate rise in blood pressure which was significantly lower than the blood pressure response to DOC.Na^+. Under stress, a more pronounced increase in NA and A was observed in rats receiving DOC.Na^+ or a high Na^+ diet than in their controls (fig. 1). The mean values of plasma NA and A measured on SbR and SbH rats are represented in figure 2. They were significantly increased in both substrains. The Na increase induced by stress is much more considerable in SbH rats than in SbN rats. Plasma A increase was also more important in SbH than in SbN rats.

Discussion. The observed increase in plasma catecholamines in rats with chronic Na^+ loading is in agreement with previous reports[5,6]. But the present investigation shows that the phenomenon is apparent both at rest and under mild stress conditions and that it occurs independently of deoxycorticosterone administration. The elevation of blood pressure and that of plasma catecholamines do not appear to be directly related since the high Na^+ group, as compared to the DOCA-Na^+ groups, showed a considerably greater elevation in plasma catecholamines, in the presence of a milder degree of hypertension. If plasma norepinephrine and epinephrine express the activity of the sympathoadrenal system[14] one may conclude that the hypertensive effect of Na^+ is only partly explained by an activation of the sympathetic nervous system.

Plasma catecholamine levels were found to be identical in the hypertension-prone and -resistant substrains of adult Sabra rats when they were measured under resting conditions. Plasma adrenaline, however, was lower in SbH rats

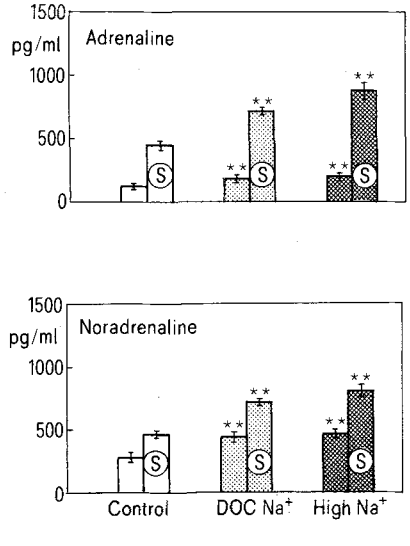

Figure 1. Noradrenaline and adrenaline in Wistar rats in resting and stress conditions. In control rats, in DOC.Na^+ rats (7 weeks of treatment), in rats fed a high Na diet for 7 weeks (high Na^+). Number of tested animals: $n=5$–10. Symbol S is used for stressed rats. Values are given as mean ± SEM. $p < 0.01$ experimental groups are compared to control.

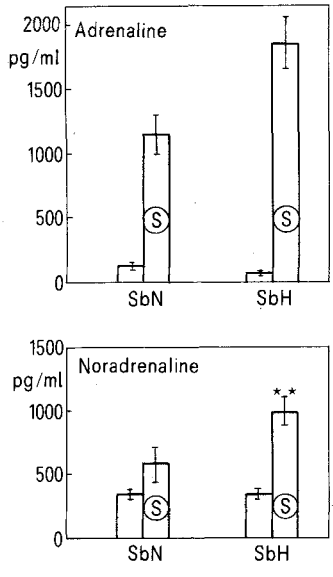

Figure 2. Noradrenaline and adrenaline in hypertension resistant SbR and hypertension sensitive SbH rats in resting and stress conditions. Number of tested animals: $n=5$–8. Symbol S is used for stressed rats. Values are given as mean ± SEM. $p < 0.01$ Sb stressed SbH are compared to stressed SbR.

than in SbR rats, possibly reflecting their lower adrenal catecholamine content (unpublished observation). However, under conditions of mild stress, plasma noradrenaline and adrenaline were found to be higher in SbH rats than in SbR rats suggesting that the sympathetic nervous system of SbH rats is hyperreactive to environmental stimuli. In this respect, Na^+ sensitive SbH rats do not differ from the Okamoto rats, where an increased activity of the nervous system has also been reported[15]. The present results concerning plasma catecholamines in Sabra rats are in agreement with other data obtained in SbH rats, such a reduction in cardiac noradrenaline content probably reflecting an increased turnover of the transmitter in nerve endings[16] and an increased tyrosine-hydroxylase activity in the medulla oblongata[17]. It was recently found that in all rats, except salt resistant rats, cell sodium content could be increased with excess sodium[18]. It appears therefore that hyperresponsiveness of the sympathetic nervous system accompanies the genetic sensitivity to Na^+.

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Tissue catecholamines following renal denervation in spontaneously hypertensive rats[1]

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Summary: The delay in blood pressure increase observed in spontaneously hypertensive rats following bilateral renal denervation appeared to be due to a temporary reduction of the renal catecholamines content.

We have previously reported that renal denervation delayed the increase in blood pressure by 2-3 weeks in spontaneously hypertensive rats (SHR) of the Okamoto strain[3], a finding which has been confirmed by others[4,5]. Although this result suggests that some action of the sympathetic system on renal functions was important in the development of hypertension, several questions remained unanswered: these concerned the completeness, the organ specificity, and the duration of the renal denervation brought about by our procedure. The present study was therefore undertaken to measure tissue catecholamines content in the kidney and other abdominal organs following the same maneuvre.

Methods: Male SHR's were used for these experiments. At the age of 5 weeks, the animals were divided into 2 groups. Group-1 (n = 24) was subject to bilateral renal denervation, and group-2 (n = 22) to a sham-denervation as previously described[3]. At 6, 8, 10, 14 and 17 weeks of age 4-5 rats in each group were anesthetized with pentobarbital, 40 mg/kg i.p. Arterial pressure was measured from a cannulated carotid artery. Then small portions of various abdominal organs were removed, rinsed in cold saline, blotted, weighed, placed into perchloric acid 0.4 N, and frozen at −30 °C until the catecholamines were measured. The organs assayed were the kidney, the small intestine, the adrenal and the spleen.

Tissue catecholamines (dopamine, and beta-hydroxylated catecholamines i.e. norepinephrine + epinephrine = NE + E) were measured according to the radio-enzymatic method described by Coyle and Henry[6]. NE accounts for the major portion of the beta-hydroxylated catecholamines in the kidney, the small intestine and the spleen; on the other hand, E is the major amine in the adrenal. The interassay coefficient of variation was 14% for dopamine, and 9.6% for NE (n = 20).

Results are given as mean ± SEM. Statistical comparison was made using either Student's t-test, or 1-way analysis of variance, followed by a Dunnett's test when a statistical significance for the mean effect was reached. Differences for p-value less than 0.05 were considered significant.

Results and discussion. As previously described[3], the mean blood pressure of SHR with surgical and chemical denervation of their 2 kidneys was significantly below that of sham-denervated animals at 6, 8, 10 and 14 weeks of age; however hypertension developed in both groups, and there was no significant difference between the 2 groups by 17 weeks of age (table). The table also summarizes the measurements of tissue catecholamines in the kidney, and in 2 abdominal organs. Only NE + E contents are shown since dopamine follows the same pattern as its major metabolites. The large variations in SEM shown on the table are probably related to a greater reactivity of tissue catecholamines of SHR to