exhibit responses to acoustic stimuli that are not readily distinguished from responses observed in classical auditory pathways[11–15]. The physiological sensory input we used, acoustic stimulation, served as a tool to initiate synaptic activities in neural structures which may control appetite as well as in other structures not apparently related to appetite. The doses of gastrointestinal hormones we administered are doses which drive their respective normal target organs maximally in the rat. They are doses which are likely to be encountered in the body under normal conditions. In conclusion, our findings suggest that there may be a basis for the concept that the gastrointestinal tract can modulate central neuronal activity during feeding by release of a hormone, CCK. Injection of CCK-OP in conscious rats modified the AAER in several structures, notably areas of the hypothalamus linked to control of appetite.

Zusammenfassung. Bei Ratten wurde die Tätigkeit des ZNS mit Hilfe von in diverse Hirnzonen implantierten Elektroden registriert, wobei die sensorische Reizung im Wachzustand zur Aktivierung der elektrischen Aktivität benutzt wurde. Injektionen von Cholecystokinin Oktapeptid in Zonen mit Appetitregulation führte zu systematischer Veränderung der durchschnittlichen Reizbeantwortung.

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Increased Erythrocytes Sodium Efflux in Genetic Hypertensive Rats of the Hebrew University Strain

Several investigators have attempted to establish a correlation between hypertension and an abnormal intracellular sodium distribution. Increased sodium content in the arterial wall has been reported in hypertensive subjects[1] and in various types of experimental hypertension[2–4]. Increased sodium content has been also found in the erythrocytes of hypertensive subjects and their normotensive relatives[5,6] and more recently in the leucocytes of hypertensive subjects[7]. In one study, the high erythrocyte sodium concentration was attributed to an increased sodium influx[6]. Recent studies from this laboratory have shown an increased efflux of Na^{22} from erythrocytes of subjects with uncomplicated essential hypertension[8]. These studies have now been extended to experimental hypertension in rats.

We have recently developed in this laboratory 2 strains of rats with markedly dissimilar susceptibility to Doca-salt hypertension[9]. The hypertension-prone (H) rat invariably develops hypertension on Doca-salt treatment whereas the normotensive (N) rat maintains normal blood pressure on the same regimen. The H rat also tends to develop mild spontaneous hypertension under regular laboratory conditions. The results presented here show an increased erythrocyte sodium efflux in the hypertension-prone rats.

Materials and methods. Male rats from the hypertension-prone (H) and hypertension resistant (N) strains developed in this laboratory were used[9]. The animals were kept in an artificially illuminated environment and maintained on regular laboratory chow and tap water. All experiments were run in pairs of H and N rats of approximately comparable age and weight. In the H group we have chosen rats with the highest levels of spontaneous hypertension. None of the animals had been subjected to any manipulation prior to this study. Systolic blood pressure was determined by the tail microphonic method of FRIEDMAN and FRIED.

Sodium efflux was studied by a modification of the methods of SACHS and WELT[10] and GARDNER et al.[11]. Heparinized blood was obtained by cardiac puncture under light ether anesthesia. The plasma and buffy coat were removed after centrifugation at 3000 rpm for 5 min at room temperature. Erythrocytes were washed three times with chilled isosmotic $MgCl_2$ and suspended in a ratio of 1:3 in a solution containing 10% sodium phosphate buffer (pH 7.4), 90% isosmotic sodium chloride and 500 mg/100 ml glucose. Approximately 10 μCi of Na^{22} were added and the suspension incubated in a rotor for 3 h at 37 °C. The cells were separated by centrifugation and washed 3 times with iced isosmotic $MgCl_2$ solution containing 10 m*M tris* buffer (pH 7.4). The erythrocytes were resuspended in an incubation medium at a hematocrit of 3–5%. The medium had the following composition (m*M*): *Tris* buffer (pH 7.4), 23; NaCl, 146; KCl 6; KH_2PO_4, 0.3. After thorough mixing, 2 samples of 2 ml each were taken from the suspension at time zero. In one sample, the cells were lysed with saponin, and, after thorough mixing, 1 ml of the hemolysate was counted. The second sample was chilled in crushed ice for 2–3 min centrifuged and 1 ml of the supernatant transferred into a counting vial. The suspension of cells was placed in an oscillating water bath at 37 °C and additional 2 ml samples were obtained at 15, 30, 45, 60 and 75 min. Each sample was chilled, centrifuged and 1 ml of the supernatant removed for counting as above. Radioactivity was measured with a Packard model 3004 liquid scintillation spectrometer.

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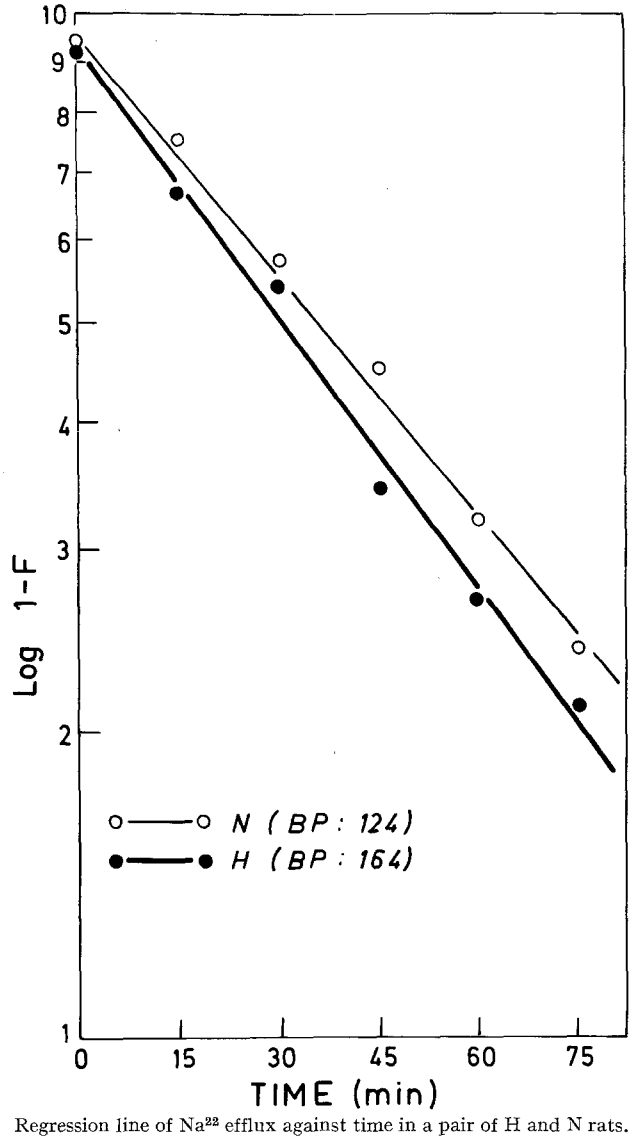
Efflux of Na^{22} from erythrocytes in 9 pairs of hypertensive (H) and normotensive (N) rats

Pair No.	Blood pressure (mm Hg)		Weight (g)		HKT [a] (%)		Na^{22} — 1/2T min		Rate constant of Na efflux (h)	
	H	N	H	N	H	N	H	N	H	N
1	172	126	213	245	45	48	31	39	1.32	1.02
2	164	124	248	226	47	47	34	38	1.20	1.08
3	168	128	280	204	42	42	22	34	1.92	1.20
4	158	135	194	228	45	44	33	41	1.26	1.02
5	154	126	189	195	42	46	36	39	1.14	1.06
6	168	126	235	260	45	44	36	44	1.14	0.94
7	158	116	288	245	42	43	32	41	1.26	1.02
8	146	112	240	257	—	—	25	40	1.62	1.04
9	138	118	242	222	40	39	26	45	1.56	0.92
M ±	158	123	236	231	43.5	44.1	30.5	40.1	1.38	1.03
S.D.	11	7	34	22	2.3	2.9	2.9	5	0.26	0.08
Significance of difference	$p < 0.01$		$p = 0.5$		$p = 0.6$		$p < 0.01$		$p < 0.01$	

[a] Hematocrit



Regression line of Na^{22} efflux against time in a pair of H and N rats. Efflux = 1-F, where $F = \frac{Na^{22} \text{ in supernatant}}{Na^{22} \text{ in hemolysate}}$.

Sodium efflux was calculated from the equation: Efflux = 1-F, where $F = \frac{\text{radioactivity of supernatant.}}{\text{radioactivity of hemolysate}}$ The rate constant ($hour^{-1}$) and Na^{22}-halftime were calculated from the regression line of sodium efflux against time. For statistical analysis, the sign test method with binomial $p = 1/2$ was used.

Results and discussion. The Table summarizes the data obtained in 9 pairs of H and N rats. The results of a representative experiment are illustrated in the Figure. The rate constant for sodium efflux was consistently higher in the hypertensive member of each pair ($p < 0.01$). Conversely, the half-time of Na^{22} extrusion from erythrocytes was significantly lower in the normotensive partner in each experiment ($p < 0.01$).

The data indicate that the erythrocytes of the hypertensive animals extrude more sodium per unit of time when compared to the normotensive ones. Since the erythrocytes sodium content was comparable in the 2 groups (H: 3.2 ± 0.4 mEq/kg rbc; N: 3.1 ± 0.4 mEq/kg rbc), the results suggest an enhanced erythrocyte sodium influx in the hypertensive group.

The possibility was considered that differences in sodium efflux may reflect differences in erythrocyte counts or volume. It has been shown that spontaneously hypertensive rats (SH) have a significant increase in red cell count as opposed to normal rats, although hematocrit values were comparable [12]. Since H and N rats have similar red cell counts, hematocrit and mean cell volumes, the increased sodium efflux in the H cannot be ascribed to a larger cell surface per unit volume.

Our results in rats with hereditary hypertension corroborate the findings of AVIRAM [8] in hypertensive subjects and are consistent with the concept of an altered sodium transport in hypertension. At the present time it is impossible to conclude whether the increased sodium efflux is a primary anomaly in active transport, or whether it is secondary to increased passive diffusion. Obviously, additional work is required to clarify the underlying mechanism responsible for the difference in the sodium efflux between hypertensive (H) and normotensive (N) rats. It is, however, tempting to speculate that

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the inherited susceptibility of the H rats to hypertension may be associated with an inherited anomaly in sodium transport.

Résumé. Nous avons étudié le flux du sodium (Na^{22}) dans des hématies provenant de 2 souches de rats obtenues par croisement consanguin et possédant une susceptibilité différente à l'hypertension artérielle. La tension artérielle chez les rats hypertendus était 158 ± 11 mm Hg vs 123 ± 7 mm Hg chez les rats normotensifs ($p < 0.01$). L'efflux du sodium, par heure, était plus rapide chez les animaux hypertendus (1.38 ± 0.26) que chez les normotensifs (1.03 ± 0.08, $p < 0.01$).

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Inhibitors of the Adhesiveness of Enteropathogenic *E. coli*

Many species of enterobacteriacae have nonflagellar appendages called fimbriae. The roles of fimbriae are at the present not well-defined. Strong evidence has been provided by DUGUID[1] that they confer adhesive properties on bacilli and that only the fimbriate bacteria are able to adhere to different types of cells, including the epithelial cells of intestinal mucosa. Mutations can affect the synthesis of fimbriae[1]. DAREKAR et al.[2,3] have shown in mice challenged with the fimbriate strain of *S. typhimurium* or the non-fimbriate mutant derived from it, that the fimbriate strain produced greater number of infections and had greater opportunities for dissemination and spread to susceptible hosts. FUBARA and FRETER[4] have given indirect evidence that the adhesive properties play a

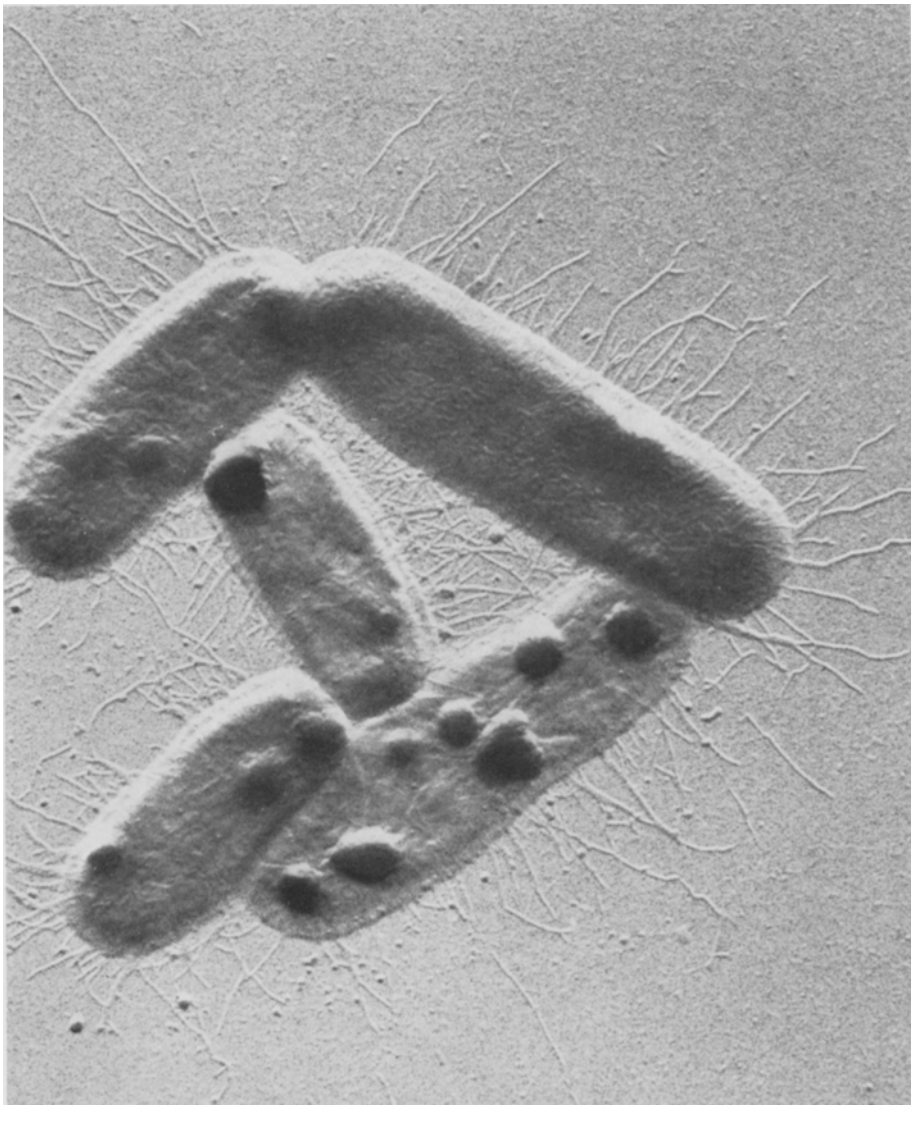

Fig. 1. Electron-microphotograph of fimbriate-*Escherichia coli* 0125: K70. Shadow-cast, ×27,000.