Dissociation between Compensatory Renal Growth and Induction of $(Na^+ + K^+)$-ATPase in Rat Kidney after Uninefrectomy

Following uninefrectomy in rats, the activity of $(Na^+ + K^+)$-ATPase in the microsomal fraction prepared from the enlarging kidney is increased[1,2]. This enzyme system is involved in the active transport of sodium[3], and the finding was interpreted as a selective induction of enzyme secondary to the increased demand for reabsorption of sodium by the remaining kidney[1]. This inference was not supported by FANESTIL[2], who found that induction of $(Na^+ + K^+)$-ATPase in the remaining kidney after uninefrectomy was not a result of the shift of the excretory load to a single kidney. It has, however, not been possible to dissociate compensatory renal enlargement from induction of $(Na^+ + K^+)$-ATPase.

In this report, the relationship between compensatory enlargement and the level of $(Na^+ + K^+)$-ATPase was studied after uninefrectomy combined with bilateral adrenalectomy. This experiment may solve the above-mentioned discrepancy, because adrenalectomy causes a considerable decrease in activity of $(Na^+ + K^+)$-ATPase in rat kidney[4–6], while compensatory renal enlargement is unaffected in adrenalectomized rats supported with saline[7–9].

Methods. Male Wistar rats, weighing 180–200 g, were divided into 3 groups. Shamoperation, right nefrectomy and bilateral adrenalectomy were performed by lumbar approach. The adrenalectomized rats had free access to both tap water and 0.9% NaCl solution. 10 days after the operation the rats were anaesthetized with ether. Blood samples for measurement of plasma (Na^+) and (K^+) were taken from vena cava and the left kidney was removed after exsanguination from the aorta. After cooling, the kidney was decapsulated and weighed on a torsion balance. Preparation of homogenate and of the heavy microsomal fraction was previously described[6]. For measurement of ATPase activity[6], aliquots of the preparations were incubated with 3 m*M* EDTA, 2.4 m*M* deoxycholate, 50 m*M* imidazole (pH 7.5, 20 °C) in a total volume of 1 ml. After 30 min at 0 °C, 50 µl was transferred to test tubes containing 3 m*M* Mg^{++} 100 m*M* Na^+, 20 m*M* K^+, 3 m*M* ATP (*tris* salt), 30 m*M* histidine (pH 7.5, 37 °C). After incubation for 15 min at 37 °C, the reaction was stopped by addition of TCA and Pi was determined[10]. $(Na^+ + K^+)$-ATPase was calculated as the difference in activity with and without 1 m*M* ouabain added to this medium[6]. Mg^{++}-ATPase denotes the activity measured with 1 m*M* ouabain in the medium, equal to the activity with Mg^{++} alone. Glucose-6-phosphatase was measured by the method of HARPER[11], and protein by the micro-Kjeldahl method. Mean values ± standard error of the mean are given and the significance of differences between means was calculated by Students' *t*-test.

Results and discussion. Table I shows that the increase in absolute as well as in relative weight of the left kidney 10 days after uninefrectomy and bilateral adrenalectomy was about the same as after uninefrectomy alone. The well-known changes in plasma electrolytes were seen in the adrenalectomized group.

The results of measurements of enzyme activity in kidneys of the same rats are shown in Table II. In agreement with previous observations[1,2], an increase in activity of $(Na^+ + K^+)$-ATPase was found in the microsomal fraction after uninefrectomy. This was accompanied by an increase in the specific activity of glucose-6-phosphatase, while the level of Mg^{++}-ATPase remained

Table I. The weight of the left kidney and the concentration of Na^+ and K^+ in plasma 10 days after uninefrectomy and uninefrectomy combined with bilateral adrenalectomy

	Body weight (g)	Kidney weight (mg)	Relative kidney weight (mg/100 g body weight)	Plasma Na^+ (m*M*)	Plasma K^+ (m*M*)
Shamoperation	250 ± 6	772 ± 16	310 ± 12	139 ± 0.5	3.7 ± 0.1
Uninefrectomy	251 ± 7	1059 ± 37 (+37%)[c]	422 ± 13 (+36%)[c]	139 ± 0.7	3.3 ± 0.1
Uninefrectomy and adrenalectony	214 ± 9	940 ± 72 (+22%)[a]	439 ± 15 (+41%)[c]	135 ± 0.7	5.5 ± 0.3

Results are given as means ± S.E.M. Significance of differences from the group of shamoperated rats: [a] $p < 0.05$; [c] $p < 0.001$. $N = 5$ for each group.

Table II. The effect of uninefrectomy and uninefrectomy combined with adrenalectomy on the activity of $(Na^+ + K^+)$-ATPase, Mg^{++}-ATPase, and glucose-6-phosphatase in homogenate and in the microsomal fraction prepared from the left kidney

	Homogenate		Microsomal fraction		
	$(Na^+ + K^+)$ ATPase µmoles Pi/mg kidney/h	Mg^{++}-ATPase	$(Na^+ + K^+)$-ATPase µmoles Pi/mg protein/h	Mg^{++}-ATPase	Glucose-6-phosphatase
Shamoperation	3.23 ± 0.02	4.32 ± 0.14	43.0 ± 2.1	42.3 ± 2.0	21.6 ± 0.5
Uninefrectomy	3.22 ± 0.17	4.73 ± 0.34	53.0 ± 1.3 (+23%)[b]	42.8 ± 3.1	30.9 ± 1.7 (+43%)[b]
Uninefrectomy and adrenalectony	2.34 ± 0.10 (−28%)[c]	4.72 ± 0.21	32.2 ± 0.6 (−25%)[c]	40.1 ± 1.2	26.9 ± 0.5 (+25%)[a]

All values given are means ± S.E.M. $N = 5$ for each group. The significance of differences from the group of shamoperated rats: [a] $p < 0.05$; [b] $p < 0.005$; [c] $p < 0.001$.

unchanged. Data on the activity of $(Na^+ + K^+)$-ATPase in whole homogenate after uninefrectomy have not been published before. In Table II it is seen that the activity per mg kidney remained unchanged. These findings suggest a preferential increase in the specific activity of enzyme in cellular constituents collected in the microsomal fraction. $(Na^+ + K^+)$-ATPase seems not to be selectively induced in the enlarging kidney[1]; but it increases in amount, along with the increase in kidney weight, after uninefrectomy.

After uninefrectomy and bilateral adrenalectomy, the activity of $(Na^+ + K^+)$-ATPase both in whole homogenate and in the microsomal fraction was significantly lower than the corresponding activity in kidneys of sham-operated and uninefrectomized rats (Table II). This decrease in activity dissociated not only from the increase in kidney weight (Table I), but also from a moderate increase in activity of glucose-6-phosphatase in the microsomal fraction (Table II). As the level of Mg^{++}-ATPase in homogenate and in the microsomal fraction was unchanged, it is unlikely that the changes in activity of $(Na^+ + K^+)$-ATPase are due to unspecific alterations in the composition of the preparations[6].

Thus, the stimulus causing compensatory hypertrophy of the remaining kidney after uninefrectomy could not prevent the decrease in activity of $(Na^+ + K^+)$-ATPase after adrenalectomy. On the contrary, a dissociation between compensatory renal enlargement and the level of $(Na^+ + K^+)$-ATPase was found. It is therefore unlikely that a causal relationship exists between compensatory renal enlargement after uninefrectomy and induction of $(Na^+ + K^+)$-ATPase. The enzyme activity seems to be under control of the adrenal cortical steroids. It is, however, not possible at present to decide whether this control is exerted directly, or whether the changes in activity reflect adaptation to sustained changes in the functional demands on the enzyme[12].

Zusammenfassung. Nach Uninephrektomie und bilateraler Adrenalektomie entsteht eine Dissoziation zwischen der Nierenvergrösserung und der $(Na^+ + K^+)$-ATPase Aktivität. Es besteht wahrscheinlich kein Zusammenhang zwischen der Nierenvergrösserung und der Induktion von $(Na^+ + K^+)$-ATPase. Auch in der vergrösserten Niere sind die Nebennierenhormone notwendig, um die $(Na^+ + K^+)$-ATPase zu erhalten.

PETER L. JØRGENSEN

Institute of Physiology, University of Aarhus, DK-8000 Aarhus (Denmark), 13 November 1970.

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Reciprocal Autoregulation of Blood Flow and Blood Pressure

The following results led us to the conclusion that the peripheral regulation of blood flow through different arterial beds depends on an equilibrium of 2 reciprocally acting autoregulatory control mechanisms. The arterial input impedance

$$R_i(p, \dot{Q}) = p/\dot{Q}\,, \qquad 1$$

as defined in the frequency domain[1,2], is the quotient of the complex arterial pressure p and the complex arterial flow $\dot{Q}$. The existence of local control mechanisms is expressed by assuming R_i in equation 1 to be an implicite function of pressure and flow[2]. Considering only small perturbations of pressure and flow, the following relation can be derived from equation 1:

$$dp/d\dot{Q} = R_{iin} = R_{io}\frac{1 + G_q}{1 + G_p}. \qquad 2$$

R_{iin} is the 'linearized' input impedance. R_{io} is the impedance set value around which small perturbations of pressure and flow are examined. Q_o and p_o are the corresponding set values of flow and pressure.

$$G_q = (\dot{Q}_o/R_{io})\,\delta R_i/\delta\dot{Q} \qquad 3$$

is defined as the gain of the autoregulation of flow and reflects the controlling influence of arterial flow on the impedance R_i.

$$G_p = -(p_o/R_{io})\,\delta R_i/\delta\dot{Q} \qquad 4$$

is defined as the gain of the autoregulation of pressure and reflects the controlling influence of the arterial pressure on the impedance. The choice of a negative sign in the definition of G_p is suggested by the direction of the expected response, as explained in Figure 1.

Equation 2 was used to examine the autoregulatory frequency response of different arteries. We perfused the A. mesenterica sup., the A. femoralis and the A. renalis of different anesthetized dogs (Morphin-Chloralose) with arterial blood. The blood flow was provided by a peristaltic

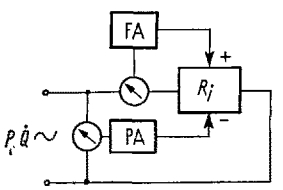

Fig. 1. Schematic diagram demonstrating possible controlling influences of autoregulation of flow (FA) and hypothetic autoregulation of pressure (PA) on the input impedance R_i of an arterial bed.

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