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The Functional Morphology of the Kidneys and the Hypothalamic Neurosecretory System in Rabbits with Ischemic Cerebral Hypertension

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Summary. Rabbits with cerebral ischemic hypertension exhibited increased volume of the nucleus supraopticus of the hypothalamus with hypertrophy of its neurones and morphological signs of enhanced secretory activity of the hypothalamo-hypophyseal neurosecretory system.

The kidney of rabbits with cerebral ischemic hypertension undergoes a substantial morphological adaptation suggesting the existence of a special regime of kidney functioning. The main feature of such adaptation is pronounced hypertrophy of the medullary layer, particularly of the renal papilla, which is indicative of functional overloading of the inner medulla in such animals including an enhancement of its resorptive function.

The above changes in the "hypothalamic secretory system—renal medulla complex" appear to be associated with the mechanism of escape from the corticosteroid overloading due to enhancement of the secretory function of the adrenal cortex in rabbits with this form of arterial hypertension.

The possible appearance of chronic arterial hypertension as a direct result of reduced blood supply and ischemia of the brain has been demonstrated in a number of experimental studies (Nowak and Walker, 1939; Fishback, Dutra and MacCamy, 1943; Crandall *et al.*, 1957; Rosenfeld, 1952; Tupikova, 1963; Suchkov, 1970). The suggestion which has been advanced in this connection that cerebral ischemia in atherosclerotic stenosis of supplying arteries may be critical for the development of the hypertensive disease (Myasnikov, 1965; Dickinson, 1965) has found strong support in clinical-experimental and morphological investigations (Dickinson and Thomson, 1960; Meyer, Sheehan, Bauer, 1960; McDowell, Potes and Groch, 1961; Dickinson, 1965). Hence the interest in the study of cerebral ischemic hypertension in experiment.

Being a neurogenic in the method of its reproduction, ischemic cerebral hypertension in rabbits with reduced brain blood supply according to Rosenfeld involves a considerable hypertrophy of the adrenal cortex and a changed electrolyte balance in the arterial wall (Postnov and Suchkov, 1967), i.e. it develops with a direct or indirect involvement of the system regulating the water-salt metabolism. This points to the existence of some features in the pathogenesis of this hypertension to a certain degree common with those in the pathogenesis of other forms of arterial hypertension.

The object of this study was to ascertain the state of the hypothalamic system secreting the antidiuretic hormone in ischemic cerebral hypertension and attempt to elucidate the functional regime of the kidney on the basis of morphological criteria, in particular of its medullary layer which is the site of application of ADH action.

The main method used in this study for making a general assessment of the functional state of the above objects, was morphometry which in addition to histological and histochemical procedures, was supplemented by an enzymohistochemical study.

Material and Methods

Thirty two Chinchilla male rabbits kept on an ordinary laboratory diet were used. In 16 rabbits with an initial weight of 2.9 ± 0.11 kg, cerebral ischemic hypertension was induced by the method of Rosenfeld (1952) wherein under local anesthesia the branches of the internal and external carotid artery were ligated unilaterally distal to the carotid sinus. Ten days later, an analogous operation was performed on the other side. During the operation, visual control was made to insure intactness of the carotid sinus and of its nervous communications.

The remaining 16 rabbits with an initial weight of 2.9 ± 0.09 kg were used as controls. A sham-operation was performed on these animals (the carotid arteries were ligated but not tightened).

Systolic blood pressure in both groups of rabbits was measured according to McGregor (1928) twice weekly by compressing the abdominal aorta and listening to the sounds on the femoral artery. All measurements were made by the same persons in the morning before feeding. To eliminate the emotional hypertension associated with fixation of the animal and compression of abdominal organs, rabbits of both groups had been habituated to the procedure of measurement for 8 weeks prior to the experiment. The systolic blood pressure each time was the mean value of three measurements. The diagram of Fig. 1 was constructed on the basis of mean values during one week.

The rabbits were killed by decapitation on the 9th to 10th week following the second operation. At autopsy the heart, kidneys, adrenals and pituitary were weighed.

For the purpose of histological and morphometric study of kidneys, 10 rabbits with hypertension and 10 control animals were employed. Morphometric and histologic study of the nucleus supraopticus was performed in all 32 animals. Directly after sacrifice, the middle renal segment with the renal papilla, the adrenals and the pituitary of these rabbits were fixed in 10% formalin, the brain was fixed in Bouin's fluid, and all the pieces of these tissues were embedded in paraffin. Kidney sections 4 μ thick were staind with hematoxylin-eosin, trichrome Masson, by the method of Hale and PAS-reaction; pituitary sections, in addition, were stained by azan according to Heidenhein and by aldehyd-fuchsin according to Gömori. One of the adrenals was cut on a freezing microtome and stained with oil red.

The *morphometry of renal structures* was done on histological slides obtained from cross sections of kidney passing exactly through the papillary summit. The width of the renal cortex was measured with an ocularmicrometer in 20 sectors of the cross section, and the mean width was calculated for each case. The total area of the kidney cross section and the areas of the cortex and of the external and internal medulla were measured with a planimeter on photographs of histological slides magnified 8 times.

The height of the collecting tubules epithelium was measured in the middle segment of the renal papilla in tubules of the same order of magnitude. At least 100 cells were measured in each case. The mean diameters of cortical and juxtamedullary glomeruli were measured separately by means of a screw ocular-micrometer MOB-1–15 and objective × 20. The biggest and the smallest diameters were measured in each glomerule and than average size was taken. 100 cortical and 100 juxtamedullary glomeruli were measured during each observation. Glomeruli cut through the middle were taken into account. The width of the glomerular zone of adrenals was measured by means of the screw ocular-micrometer in the slides stained with oil red. The mean value of 15 measurements was calculated in each case.

The *morphometric study of the nucleus supraopticus* of the hypothalamus was made on serial brain sections 7 μ thick stained with Gomori's chrome-hematoxylin phloxine. The paraventricular nucleus was not studied morphometrically because of the small number and scattering of its neurones in rabbits. The neurosecretory material was detected by aldehyde fuchsin according to Gomori.

The volume of n. supraopticus was measured by the method of secondary planimetry according to Kesarev (1964), using every 10th section of a series. The mean diameter of the neurone and of its nucleus was determined by measuring the greater and lesser diameters with a screw ocular-micrometer. In each case, measurements were made of the mean diameter for 300 nuclei and the mean diameter of the neurone for 100 cells of the nucleus supraopticus. Results of these measurements were used to prepare spectra of nuclear and neuronal sizes for n. supraopticus in rabbits with hypertension and in control animals. All data were processed by the variation statistics method and are presented in tables and diagrams.

The enzymohistochemical study of the kidneys was made in 6 rabbits with hypertension (with systolic blood pressure of 175 ± 5 mm before sacrifice) and in 6 control rabbits. The middle portion of the kidney with the papilla was isolated just after decapitation in both control and test animals, mounted in blocks in pairs and frozen with carbonic acid, and sections were prepared in a cryostat at —18° C.

In the non-fixed sections of the kidney the following enzymes were assayed: NAD′H- and NADP′H-diaphorase (Scarpelli *et al.*, 1958), succinate dehydrogenase (SDH) (Nachlas *et al.*, 1957), and isocitrate dehydrogenase (IDH), lactate dehydrogenase (LDH) and glucose-6-phosphate dehydrogenase (G-6-PDH) (Hess *et al.*, 1959). In sections fixed for 15 min, in 10% cold formalin, ATP-ase was demonstrated (Wachstein and Meisel, 1957).

Results

Systolic blood pressure prior to operation was in the range of 95–120 mm, with a mean of 105 ± 1.3 mm.

After the second stage of ligation of the carotid arteries, arterial pressure rose progressively to a maximum in the 6th week, and fell thereafter to reach 186 ± 5 mm by the time of sacrifice. The sham-operated control rabbits showed a moderate transitory elevation of systolic blood pressure to 140 mm. Blood pressure returned to the initial level in these rabbits on the average on the 10th day after the second operation, constituting 106 ± 3.0 mm by the time of sacrifice (Fig. 1). At autopsy, the rabbits with hypertension showed increased weights of the heart, kidneys, adrenals and pituitary (Table 1).

Kidneys

a) Histological and Morphometric Studies. A general histological study of rabbits with hypertension revealed no changes in cortical tubules; measurements,

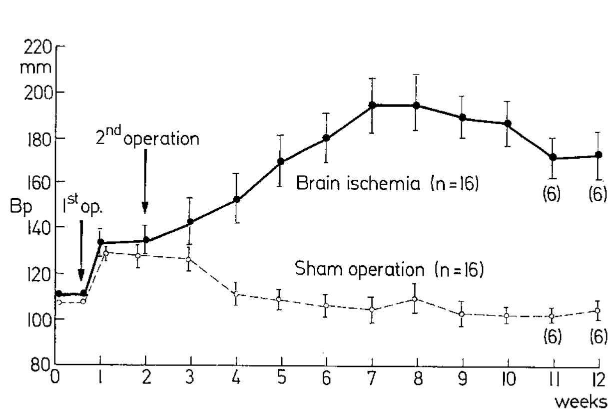


Fig. 1. Systolic blood pressure in rabbits with cerebral ischemia and in control rabbits. In parentheses — the number of animals remaining by end of experiment (IIth and 12th weeks)

Table 1. Bodyweight and weight of kidneys, heart, adrenals and pituitary in rabbits with hypertension and in control rabbits

Group	No.	Systolic blood pressure (mm)	Weight					
			Bodyweight at start of experiment (kg)	Bodyweight at autopsy (kg)	Heart (g)	Kidneys (g)	Adrenals (mg)	Pituitary (mg)
Control rabbits	16	103 ± 1.7	2.9 ± 0.09	3.5 ± 0.06	7.8 ± 0.2	15.8 ± 0.6	406 ± 20	32 ± 1.1
Hypertensive rabbits	16	186 ± 5.5	2.9 ± 0.11	3.5 ± 0.05	9.3 ± 0.4	20.7 ± 0.8	556 ± 38	45 ± 1.1
P		<0.001	—	—	<0.001	<0.001	<0.001	<0.001

however, showed an increase in cortical width. Both the cortical and juxtamedullary glomeruli were enlarged in these rabbits compared with the control rabbits, the mean glomerular diameter being increased by 15%. Basal membranes in the glomeruli gave stronger PAS reaction and were somewhat thickened.

The medullary layer of the kidney in rabbits with hypertension was wider, its area being increased by an average of 37% in kidney cross sections, the greatest increase being noted in renal papillary area—62% greater on the average, than in the control rabbits (Table 2).

The renal papillae showed hypertrophy of collecting tubules which were found to contain enlarged epithelium of increased height (Table 2; Fig. 2b and d). Renal papillary interstitium was invariably broadened and swollen, notably in the apical part. The lumen of thin segments of Henle's loop was in most cases open, but no changes in the epithelium were detected by the general study. The lumen of blood capillaries in the papilla was likewise increased.

The outer medulla was enlarged less than the inner medulla as shown by measurement of its area. The general histological study revealed only a slight enlargement of collecting tubules and of the thick segment of the ascending limbs of Henle.

b) Enzymohistochemical Study. The examined dehydrogenases in the epithelium of proximal convoluted tubules of Henle's loop (excepting the thin segment), and of the distal convoluted tubules, all showed enhanced activities in hypertension as judged by the intensity of formazan deposition. The greatest difference between the test and control animals was noted in SDH and IDH, with a lesser difference in LDH and G-6-PDH. In the same portions of the nephron, activities of NADH and NADPH-diaphorases as well as ATP-ase were increased (Fig. 3). In the thin segment of Henle's loop whose epithelium is distinguished by low enzymatic activity no differences were detected between the test and control animals.

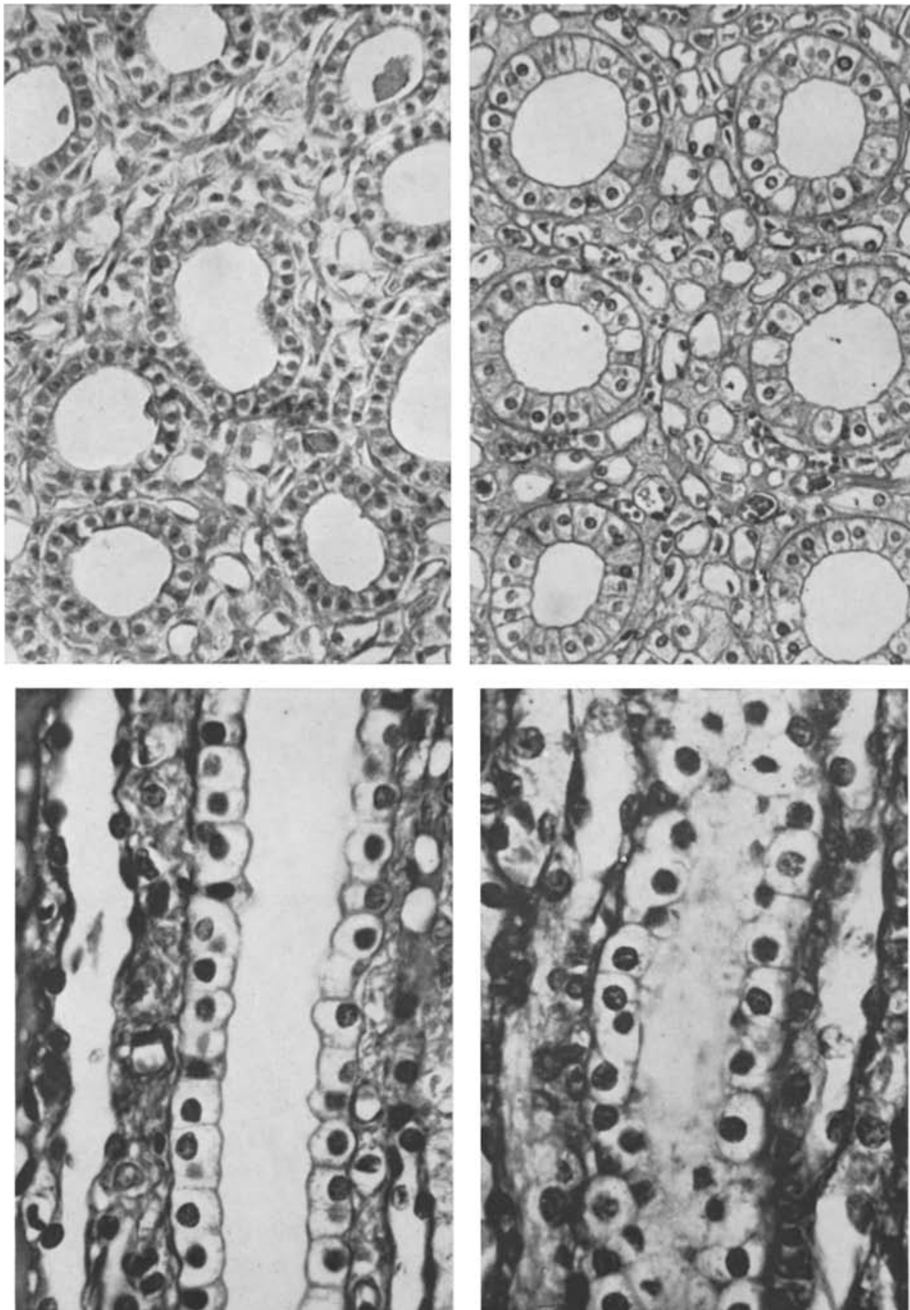
Table 2. Morphometric characteristics of kidneys in rabbits with ischemic cerebral hypertension and in control rabbits

Version I

Group	No. of animals	Systolic blood pressure at sacrifice (mm)	Body-weight by end of experiment (kg)	Kidney weight (g)	Renal cortex				Medulla		Height of collecting tubular epithelium (μ)
					Width (mm)	Area in cross sections (mm²)	Glomerular diameter (μ)		Area in kidney cross sections (mm²)		
							Cortical	Juxtamedullar	Outer medulla	inner meduall	
Control	10	103 ± 2.2	3.5 ± 0.07	15.8 ± 0.8	2.97 ± 0.08	103 ± 4.0	80.9 ± 0.9	92.1 ± 2.1	48.0 ± 3.0	18.1 ± 0.6	16.8 ± 0.3
Hypertensive	10	192 ± 8.0	3.5 ± 0.05	20.5 ± 0.8	3.8 ± 0.15	129 ± 7.0	93.2 ± 1.0	106.5 ± 2.0	65.6 ± 5.5	29.3 ± 1.9	18.9 ± 0.4
P		<0.001	<0.001	<0.001	<0.001	<0.01	<0.001	<0.001	<0.01	<0.001	<0.001

Version II

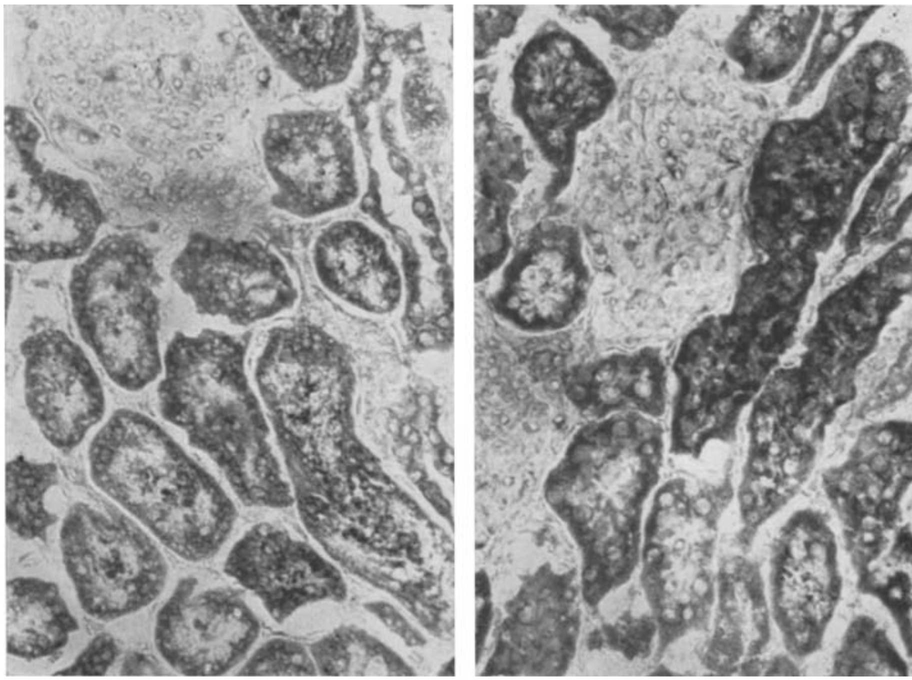
Animal no.	BP	Bodyweight (kg)		Kidney weight (g)	Renal cortex				Medulla		Height of collecting tubular epi-thelium (μ)
		At start of experi-ment	By end of experi-ment		Width (mm)	Area in cross sections (mm^2)	Glomerular diameter (μ)		Area in kidney cross sections (mm^2)		
							Corti-cal	Juxta-medullary	outer medulla	inner meduall	
a) Control rabbits											
4	110	3.2	3.6	17.0	2.86	117.4	81.5	92.4	55.5	15.5	16.1
9	95	3.1	3.5	13.0	2.89	106.3	83.4	92.6	58.3	20.5	16.9
21	95	3.2	3.3	13.5	3.13	85.7	80.4	99.6	41.2	15.7	16.8
22	110	3.2	3.6	14.2	2.41	94.5	80.3	85.6	41.0	17.6	15.3
31	105	2.6	3.4	18.0	2.92	110.0	80.4	87.0	64.0	18.0	15.8
52	110	3.1	3.3	11.6	2.87	132.0	83.1	98.7	30.1	18.3	16.2
57	95	3.4	3.7	19.4	3.22	95.5	83.9	95.6	53.0	20.4	15.8
62	95	3.3	3.8	17.5	3.30	99.0	73.7	84.0	52.5	21.0	16.2
64	110	3.2	3.6	17.5	2.91	102.0	81.7	82.4	43.5	17.6	15.7
67	105	3.3	3.9	16.4	3.20	88.0	81.5	94.8	42.0	16.8	16.0
Mean values	103 ± 2.2	3.1 ± 0.07	3.5 ± 0.07	15.8 ± 0.8	2.97 ± 0.08	103.0 ± 4.0	80.9 ± 0.9	92.1 ± 2.1	48.0 ± 3.0	18.1 ± 0.6	16.8 ± 0.3
b) Hypertensive rabbits											
1	200	2.4	3.4	22.8	3.37	132.1	91.2	104.8	59.5	22.6	16.7
2	170	2.5	3.4	21.5	4.06	149.5	96.6	103.1	73.7	31.3	20.2
13	175	3.2	3.8	23.4	4.00	90.4	94.8	115.5	55.5	27.4	20.0
17	145	3.4	3.8	23.8	4.21	99.9	97.4	106.4	63.5	35.3	18.8
18	175	3.4	3.5	18.6	4.23	115.8	97.2	103.3	41.2	21.0	19.7
19	195	3.1	3.9	18.6	4.00	141.2	87.0	103.3	38.9	26.2	20.0
23	200	3.3	3.6	17.1	4.18	155.6	92.1	104.0	87.6	44.4	18.6
37	220	3.3	3.5	21.7	3.86	120.9	92.4	110.5	76.9	21.0	18.6 *2*
41	225	3.5	3.7	20.0	3.00	138.0	92.4	99.8	78.0	37.5	17.0
47	215	3.2	3.5	18.0	3.13	146.8	96.6	103.1	81.2	26.2	19.0
Mean value	192 ± 8.0	3.1 ± 0.12	3.6 ± 0.05	20.5 ± 0.8	3.80 ± 0.15	129.0 ± 7.0	93.2 ± 1.0	106.5 ± 2.1	65.6 ± 5.5	29.3 ± 1.9	18.9 ± 0.4
P	<0.001			<0.001	<0.001	<0.01	<0.001	<0.001	<0.01	<0.001	<0.001



a b

c d

Fig. 2a—d. Inner medulla of kidney in ischemic cerebral hypertension (right) and in control (left). a and b, Middle third of papilla. Dilatation of interstitium, increased height of epithelium in collecting tubules and enlargement of the epithelium. Increase of lumen of thin limbs of Henle and capillaries. H.E. × 320. c and d, External third of papilla. Enlargement of epithelium in collecting tubule. × 800



a b

Fig. 3a and b. NAD-diaphorase in epithelium of renal tubules. a, Control. b, In a rabbit with cerebral hypertension. ×240

The epithelium of collecting tubules of the renal papilla showed enhanced LDH and NADPH-diaphorase activities. In the papillary capillaries of rabbits with hypertension ATP-ase activity was higher.

Hypothalamic Neurosecretory Nuclei

Volumetric measurements revealed a substantial increase of the nucleus supraopticus of the hypothalamus in hypertension (Table 3; Fig. 4). The size of the neurones of the nucleus was larger and their nuclei were disposed more eccentrically than normally, while the nucleoli were increased in size and the perinuclear spaces were larger (Fig. 5). Most of the neurones contained moderately increased numbers of granules of neurosecretory material in the perikaryon, although neurones also occurred with an expanded and depleted cleared perikaryon. The amount of neurosecretory material was somewhat increased along the course of nerve cell processes. There was slightly less tigroid substance in the neurones. The mean neuronal diameter and the mean diameter of neuronal nuclei in n. supraopticus were $17.6 \pm 0.25\ \mu$ and $10.0 \pm 0.13\ \mu$, respectively, in rabbits with hypertension, against $13.8 \pm 0.2\ \mu$ and $8.8 \pm 0.28\ \mu$ in the control group. The spectra of neuronal nuclear sizes in n. supraopticus for both groups are presented in Fig. 6.

Table 3. Mean diameters of neurons and its nucleus and mean volume of nucleus supraopticus in rabbits with hypertension and in control rabbits

Group	No.	Systolic blood pressure (mm)	Volume of n. supraopticus (mm^3)	Mean diameter of neurone (μ)	Mean diameter of neuronal nucleus (μ)
Control rabbits	10	103 ± 2.2	0.08 ± 0.005	13.8 ± 0.12	8.8 ± 0.28
Hypertensive rabbits	10	192 ± 8.0	0.14 ± 0.002	17.6 ± 0.25	10.0 ± 0.13
P		<0.001	<0.001	<0.001	<0.001

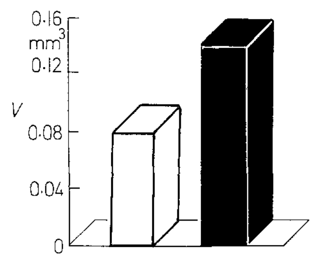


Fig. 4. Volume of supraoptic nucleus in rabbits with cerebral hypertension (black column) and in control rabbits (light column)

The few loosely arranged neurones found in the paraventricular nucleus in rabbits with hypertension, had a somewhat enlarged perikaryon, although no substantial differences were detected in the content of neurosecretory material in them.

Pituitary

The increased pituitary weight in rabbits with hypertension was due to an increase in the size of the adenohypophysis which showed hypertrophia and hyperplasia of cells of the intermediate lobe, with an expansion of the latter and a moderate hyperplasia of chromophobe and basophil cells in the anterior lobe. The neurohypophysis was not enlarged, but contained much less neurosecretory material than in the control.

Adrenals

The adrenal cortex was strongly enlarged in rabbits with hypertension, mainly due to hypertrophy of cells in the fascicular zone whose thickness constantly exceeded that in control animals by a factor of 1.3–1.5. The glomerular zone was also somewhat widened (90.6 ± 1.2 μ in hypertension vs 71.1 ± 1.1 μ in control, at $P < 0.001$). The quantity of lipids in cells of the fascicular zone was greatly increased in hypertension. A moderate increase in lipids was also noted in cells of the reticular zone. No changes were seen in the medullary layer of the adrenals.

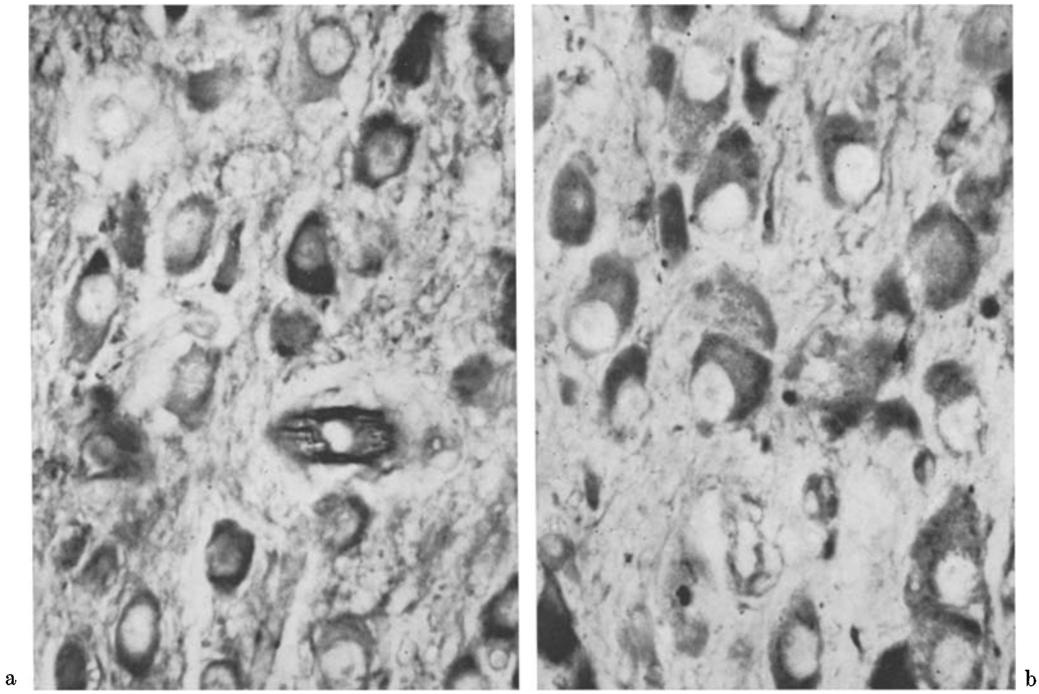


Fig. 5a and b. Supraoptic nucleus of hypothalamus. a, Control. b, In a rabbit with cerebral hypertension. Enlargement of neurones, expansion of perinuclear spaces with increased amount of neurosecretory material. Gomori's stain. × 1280

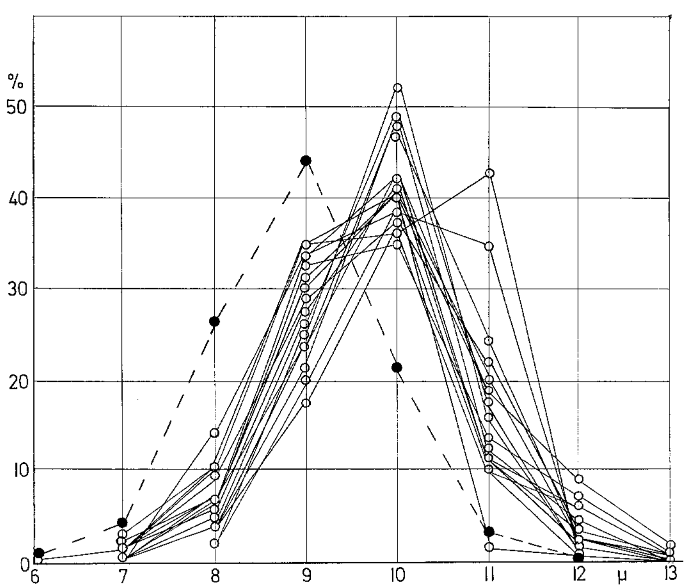


Fig. 6. Spectrum of sizes of neuronal nuclei in supraoptic nucleus of hypothalamus. Solid line—rabbits with hypertension; Dotted line—mean values of nuclear measurements in 16 control rabbits

Discussion

Since the carotid arterial branches were ligated distal to the carotid sinus leaving intact its nervous communications, it is logical to assume that the chronic hypertension that developed in our experiment was not due to an injury of the receptor mechanism of the sinus but mainly resulted from cerebral ischemia (Rosenfeld, 1952). A diminution of blood supply to the brain, particularly to the diencephalic region, has been reported in similar experiments using the method of radiactive indication (Tupikova, 1963) and angiography (Suchkov, 1970).

If the hypertension observed in our experiment is regarded as the end result of an adaptive response permitting compensation of the disturbed cerebral circulation, then one may single out a set of changes which are more likely to be associated with the mechanism providing for long-term maintenance of increased arterial tonus. These changes include the morphological manifestations of activation of the corticosteroid function of the adrenals and the activation of the hypothalamic neurosecretory system producing vasopressin (ADH) and oxytocin.

The hypertrophy of the nucleus supraopticus involving an increase of its total volume and enlargement of the neurones and their nuclei in conjunction with signs of enhanced production of neurosecretory material in neurones and enhanced secretion (low content of neurosecretory material in the neurohypophysis) may well be considered as morphological evidence for a chronic increase of its secretory function, i.e. enhanced production and release of ADH.

Our results suggest that brain ischemia is only a general cause of changes in the adrenals and the hypothalamic secretory system, without any direct indication as to their sequence and interrelationships. It may be supposed, however, that the reduced brain blood supply has a direct effect on the system of the corticotropic releasing factor (CRF) acting on the adenohypophysis and on the output of ACTH by it. The latter may account for the adenohypophyseal hypertrophy and the considerable hypertrophy of the fascicular zone of the adrenal cortex. However, the possibility is not ruled out that the enhanced production of ACTH by the pituitary is due to the potentiating effect of vasopressin on the CRF (Jates *et al.*, 1971) or directly on the adenohypophysis (Dunn and Critchlow, 1971). The effect on the adrenal cortex is probably not restricted to the effect through ACTH, since rabbits with hypertension also showed a strong hypertrophy of the glomerular zone.

Although the method of inducing hypertension used in our experiment leaves the kidneys intact, the latter nevertheless undergo a marked morphological adaptation mainly resulting from a change in the regime of kidney function.

Analysis of the morphological evidence gives an idea of the main features of this regime and makes it possible to distinguish the following characteristics of kidney work in cerebral ischemic hypertension in rabbits:

a) Enlargement of glomeruli which is a sign of their working hypertrophy serves as an indication of a chronic increase in the volume of filtration both in glomerular cortical and juxtamedullary nephrons.

b) The enhanced activity of dehydrogenases of the tricarboxylic acid cycle, glycolysis and the pentose-phosphate cycle, and the increased activity of NADH and NADPH-diaphorases and ATP-ase in the epithelium of proximal and distal tubules in rabbits with hypertension appears to be associated with intensification of cellular metabolism and may indirectly reflect an increase of the main function of those tubules, i.e. tubular reabsorption. This also could be the main reason for a certain enlargement of the cortex as a whole.

Apparently, the above changes may be directly correlated to the effect on cortical tubules of enhanced corticosteroid excretion as suggested by hypertrophy of the adrenal cortex, notably of its fascicular zone, as well as by enhanced lipid production in the cortex; the stimulating effect of corticosteroids on dehydrogenases in nephronal epithelium has been shown in a number of investigations (Bourne and Malaty, 1953; Natochin *et al.*, 1960).

c) The most conspicuous trait of the morphological adaptation of the kidney is a considerable enlargement of the medullary layer (mostly as a result of the enlargement of the renal papilla with its enlarged collecting tubules and their epithelium), and it is a manifestation of working hypertrophy of the renal medulla and reflects a situation of chronic functional overloading. It is indicative of the greater intensity of water resorption by the renal papilla, and this is correlated by the evidence on the morphology of the hypothalamic secretory system producing ADH. This overloading effects not only the mechanism of the resorption of water in the collecting tubules directly, but also exerts an impact on the activity of the counter-current multiplying concentrating system which is closely associated with it. Evidence of this may be found in the hypertrophy of the outer medulla which extensively features the thick ascending limbs of Henle.

If the enhanced activity of enzymes in the epithelium of the nephron is taken as evidence of increased tubular reabsorption, then the functional overloading of the medulla points to a relative inadequacy of the reabsorbtion in respect to the filtration. However, it is not quite clear which part of the nephron is specifically responsible for this change in the glomerulo-tubular balance.

The morphology of the renal papilla in rabbits with hypertension is on the whole similar to changes in the medulla characteristic of antidiuresis (Lapp and Nolte, 1962). It appears that the enhanced ATP-ase activity in papillary capillaries and of LDH and NADPH dehydrogenase activities in the collecting tubular epithelium may also be interpreted in terms of intensification of the resorptive function of the renal papilla.

Thus, our experimental results warrant the conclusion that the kidney function in rabbits with cerebral ischemic hypertension is accompanied with a working overloading of the inner medulla, which is an essential feature of the regime of kidney work.

The change in the regime of kidney functioning reflected in kidney morphology appears to be a manifestation of the adaptive mechanism of escape from the sodium-retaining effect of enhanced corticosteroid release in an animal with ischemic cerebral hypertension. Owing to such enhanced secretion, the tubular reabsorption of sodium increases and a balanced natriureses is attained through an increase in the volume of glomerular filtration and enhanced water resorption in collecting tubules of the renal papilla, which brings about papillary hypertrophy and hypertrophy of the medulla in general. As a matter of fact, analogous changes in the kidney and the hypothalamic secretory system were reported earlier in DOCA-hypertension in rats, where the phenomenon of escape from the salt- and corticosteroid overloading is much more pronounced (Postnov, Fofanova and Fedina, 1970).

The escape from the sodium-retaining effect of corticosteroids in the interests of the whole organism, does not abolish their direct effect on the smooth muscles of the arterial wall. Evidently, this effect should combine with enhanced action of ADH and, possibly, oxytocin which may form the basis for enhancement of their contractile capacity.

Apart from cerebral ischemic hypertension, morphological manifestations of increased function of the hypothalamic secretory system have been previously reported for renal (Aros and Ertl, 1961; Fukushima, 1968), spontaneous (Fukushima, 1968) and DOCA-hypertension (Postnov *et al.*, 1970), in rats and for thyroid hypertension in dogs (Zhukova, 1969).

The very fact that this system becomes more active in different types of experimental hypertension suggests a functional overloading of the renal medulla which is a characteristic sign of arterial hypertension in general. Its role in the pathogenesis of hypertension requires further study.

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