The ultrastructural changes observed during penicillin-induced seizures differ radically from nonspecific changes described during seizures induced by toxic substances such as cobalt, aluminum, and strychnine [2, 5]. These substances have a harmful effect mainly on the rough endoplasmic reticulum of the neurons, i.e., on the apparatus for protein synthesis. The changes now discovered, however, point to activation of synapses, postsynaptic dendrites, and nerve cells. Each change is nonspecific, but it may be part of a combination of changes characteristic for this particular type of experimental epilepsy.

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HISTOPHYSIOLOGICAL CHARACTERISTICS OF THE SUBCOMMISSURAL ORGAN OF THE BRAIN DURING ISOLATED INHIBITION OF THE ADRENAL ZONA GLOMERULOSA

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KEY WORDS: subcommissural organ of the brain; zona glomerulosa of the adrenal gland; heparin; oxidoreductases.

It is now accepted that the subcommissural organ of the brain (SCO) is one of its neuroendocrine formations [1, 9]. However, the role of SCO in the regulation of particular endocrine functions has not yet been determined. The effect of electrolytic destruction of SCO in depressing the function of the adrenal zona glomerulosa (AZG) was demonstrated previously [3]. These observations suggest that AZG may be a special target for realization of the regulatory effects of SCO. It was therefore decided to study the effect of inhibition of AZG function on the histophysiology of SCO. It is interesting to note that prolonged administration of heparin or heparinoids is accompanied by selective hypofunction of AZG [6, 8].

The object of this investigation was to study the histophysiological characteristics of SCO during isolated inhibition of AZG function.

EXPERIMENTAL METHOD

Experiments were carried out in the fall and winter on 30 male albino rats weighing 180-200 g, divided into two groups. The animals of group 1 (control) were kept on the standard

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TABLE 1. Relative Optical Density of Histochemical Reaction Products in Ependymocytes of SCO and Adrenocorticocytes of AZG in Intact Animals (in parentheses) and during Inhibition of AZG Function by Heparin (M ± m)

Enzyme	SCO	AZG	P
LDH	0,17±0,004 (0,26±0,10)	—	<0,001
GDH	0,10±0,004 (0,22±0,007)	—	<0,001
α-GPDH	0,07±0,003 (0,22±0,013)	—	<0,001
SDH	0,08±0,005 (0,07±0,010)	0,09±0,005 (0,10±0,006)	>0,001
3β-ol	—	0,03±0,002 (0,05±0,003)	<0,001
NAD-diaphorase	—	0,16±0,003 (0,25±0,017)	>0,01

animal house diet. The animals of group 2 were given heparin in a dose of 130 units/100 g body weight by intraperitoneal injection daily for 10 days. The rats were decapitated. Activity of lactate dehydrogenase (LDH), NAD-dependent α-glycerophosphate dehydrogenase (α-GPDH), and glutamate dehydrogenase (GDH) was determined by Rubinstein's method, succinate dehydrogenase (SDH) activity by Nachlas' method in unfixed cryostat sections through SCO, and acid phosphatase activity was revealed by Gomori's method. Activity of SDH, of NAD-diaphorase (by Burstone's method), and of 3β-ol-steroid dehydrogenase (3β-ol) [4] was investigated in the adrenocorticocytes of AZG. RNA was determined by Brachet's method, total protein by Geyer's method, and lipids with Sudan black B by Lyson's method. Aldehyde-fuchsinophilic secretion (AF-secretion) in the ependymocytes of SCO was revealed by Gomori's method. The relative optical density of histochemical reaction products was estimated in conventional units with the aid of a cytospectrophotometer. The area of the scanning probe was 1 μ^2, and of the scanning frame 121 μ^2. The width of AZG was measured by means of an MOV-1-15 screw micrometer (200 measurements each in the control and experiment). Statistical analysis was carried out by Student's t-test.*

EXPERIMENTAL RESULTS

Compared with intact animals (control), significant changes were found in AZG of rats receiving heparin. This was shown by the microstructural features and results of morphometry. In particular, marked deformation of the adenomatous structures took place, the cytoplasm of some of the adrenocorticocytes was filled with vacuoles, some cells were shrunken, and there were fewer rows of cells. The AZG as a whole was considerably narrowed (to 42.7 ± 0.6 compared with 84.0 ± 2.9 μ in the control), but in certain areas this narrowing was extremely irregular. The content of lipids in the adrenocorticocytes of AZG was significantly higher than in the cells of the zona fasciculata and zona reticularis. Degenerative changes of lipoidoses in AZG were combined with changes in their enzyme characteristics. For instance, a reduction in the intensity of staining of the residue during the reaction for NAD-diaphorase took place in practically all cells of the adenomatous structures except the layer next to the adrenal capsule. Activity of 3β-ol was recorded only in isolated cells of AZG. The distribution of SDH was highly irregular, with activity of this enzyme preserved in the subcapsular regions of the adenomatous structures. The enzyme characteristics of cells of zona fasciculata and zona reticularis in the experimental series did not differ significantly from those in the control. The control of RNA and total protein in the adrenocorticocytes of AZG was considerably depressed.

The histophysiological characteristics of SCO showed well-marked changes (Table 1).

A decrease in activity of LDH, GDH, and NAD-dependent α-GPDH was found. Marked irregularity in the distribution of the enzymes was established: they were located chiefly in the apical zones of the ependymocytes of SCO, and were practically absent in the basal zones. SDH activity was low and its localization was similar to that in intact animals (control). The fall in acid phosphatase activity was more clearly defined in the basal zones of the ependymocytes of SCO along the boundary with the hypendyma. Considerable inhibition of the secretory function of SCO was reflected in a decrease in the RNA content and depression of synthesis of AF-secretion, which was observed in the form of single small granules in the apical zones of the ependymocytes and was completely absent in their basal zones (Fig. 1).

*The cytospectrometric investigation was undertaken at the Institute of Human Morphology, Academy of Medical Sciences of the USSR.

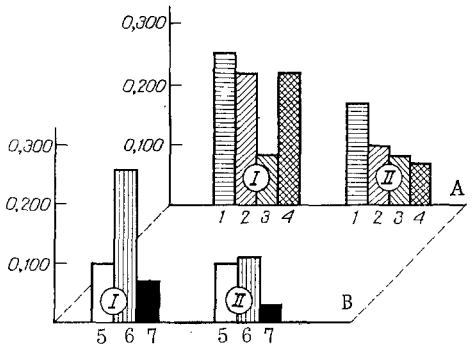

Fig. 1. Comparative characteristics of enzyme activity in SCO (A) and AZG (B) in intact (I) and heparinized (II) animals. 1) LDH; 2) GDH; 3) SDH; 4) α-GPDH; 5) SDH; 6) NAD-diaphorase; 7) 3β-ol. Enzyme activity expressed in optical density units.

Administration of heparin for 10 days was thus followed by considerable reorganization of the functional activity of the adrenocorticocytes of AZG. A marked decrease in the activity of 3β-ol, a key enzyme of steroid formation, indicated depression of synthetic processes. The observed decrease in the RNA and total protein content and also the results of morphometric analysis, indicating a significant (up to 50%) decrease in the thickness of AZG, confirm this hypothesis. The results are in agreement with the isolated antialdosterone effect of heparin observed against the background of a marked decrease in thickness of AZG combined with complete preservation of the width of the zona fasciculata of the adrenal [7, 10].

The histophysiological characteristics of the ependymocytes of SCO during isolated inhibition of AZG function demonstrate inhibition of SCO function also. Reduction of acid phosphatase together with a fall in activity of GDH and NAD-dependent α-GPDH indicates inhibition of the secretory function of SCO. Its enzyme characteristics during isolated inhibition of AZG point to predominance of the glycolytic pathway of oxidation in ependymocyte metabolism. The fall in the secretory function of SCO was combined with a decrease in the content of RNA and AF-secretion, whereas inhibition of enzyme activity in the basal zones of cells of the ependymal layer could indicate inhibition of its internal secretory function.

Parallel changes in SCO and AZG were thus established during selective depression of the mineralocorticoid function of AZG. Similar coordination between responses of SCO and AZG has been found when the sodium content in the diet was changed [2, 5]. The results indicate that the morphological and functional characteristics of these structures are interdependent, and they may be of importance when procedures directed toward SCO and AZG are envisaged with the aim of regulating mineralocorticoid hormone production.

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