

shock. These disturbances are accompanied by impairment of the circulation in the pulmonary capillary system and they play an important role in the pathogenesis of "shock lung" in pancreatic necrosis.

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CATECHOLAMINE CONTENT IN THE STRIATUM, HYPOTHALAMUS, AND ADRENALS OF RATS GENETICALLY PREDISPOSED TO EPILEPSY

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The results of previous experiments on rats genetically predisposed to epileptiform convulsions (KM rats, bred by L. V. Krushinskii and L. A. Molodkina) led to the hypothesis that correlation exists between genetic predisposition to epilepsy and a generalized defect of catecholamine (CA) metabolism [4, 5]. The following facts served as the basis for this hypothesis: First, it was shown that the dopamine (DA) antagonist bulbo-capnine does not cause catalepsy in KM rats although it invariably arises in audiogenically insensitive Wistar rats (AIWR). Second, it was shown that signs of inadequate sympathetic activation of the cardiovascular system are found in KM rats, compared with AIWR, under conditions of immobilization stress judging from such ECG parameters as the area of the P wave, the P/T ratio, Macruz index, and the area of the T wave [4, 5, 6].

Investigation of the tyrosine hydroxylase kinetics in the striatum and hypothalamus showed that values of K_m and V_{max} in KM rats are significantly lower than in AIWR. These observations suggested hyperproduction of DA in both structures in KM rats. However, the "sympathetic activation deficiency" under conditions of immobilization stress and the low thresholds of the avoidance reaction in response to electrical stimulation of the ventromedial hypothalamus in KM rats suggested that the CA content in their hypothalamic structures is lower than in AIWR.

The object of the present investigation was, accordingly, the direct determination of the content of DA, noradrenalin (NA), and of DA metabolites in the striatum and hypothalamus, and also the CA content in the adrenals of KM rats and AIWR differing in their predisposition to seizures.

EXPERIMENTAL METHOD

Experiments were carried out on 16 male rats weighing 180-270 g (9 KM rats, 7 AIWR, selected by triple testing with a bell with an intensity of 105 dB*).

*It should be pointed out that at the present time at least 60-80% of Wistar rats are audiogenically sensitive, i.e., they react by typical audiogenic epileptiform seizures to the ringing of a bell of the above intensity.

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TABLE 1. Content of CA and Their Metabolites in Striatum and Hypothalamus (in ng/g) of KM Rats and AIWR

Parameter	Striatum		Hypothalamus	
	KM (n=9)	AIWR (n=7)	KM (n=9)	AIWR (n=7)
DA	8335±367	5332±104	1042±36	734±48
DHPAA	980±17	800±19	690±17	504±29
HVA	847±18	736±11	684±49	586±45
NA	405±10	300±13	1887±48	1458±58
NA/DA	0,049	0,056	1,816	2,011
HVA/DA	0,103	0,138	0,662	0,766
DHPAA/DA	0,118	0,151	0,664	0,663
(HVA + DHPAA)/DA	0,223	0,289	1,326	1,429

TABLE 2. CA Content in Adrenals (in µg/g) of KM Rats and AIWR

Parameter	KM (n=9)	AIWR (n=7)
DA	17±1,0	10±1,6
NA	354±10	264±14
A	975±25	809±32
NA/DA	20,82	26,4
A/DA	57,35	80,9
A/NA	2,75	3,06

Decapitation was carried out under open ether anesthesia, the hypothalamus and adrenals were quickly removed, and after the animal had cooled for a few minutes, the striatum also was removed. Samples were immediately frozen on dry ice, DA, NA, and dihydroxyphenylacetic and homovanillic acids (DHPAA and HVA respectively) were determined by the method of Westerling and Korf [16], and CA in the adrenals were determined by the method of Kogan and Nechaev [8]. The numerical results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS AND DISCUSSION

It will be clear from Tables 1 and 2 that the CA content was higher in KM rats than in AIWR in all the structures tested. The greatest differences between the two groups compared were found in respect to the DA content: in KM rats it was 58% higher in the striatum, 43% higher in the hypothalamus, and 70% higher in the adrenals than in AIWR.

The increase in the DA concentration found in the striatum and hypothalamus of KM rats correlates fully with the change in the kinetic characteristics of tyrosine hydroxylase found previously in these structures. It is evidently the result of an increase in the activity of this enzyme.

However, analysis of the data reveals the following relationships: Despite the absolute increase in the content of DA metabolites in the striatum of KM rats, the HVA/DA and DHPAA/DA ratios, and also the (HVA + DHPAA)/DA ratio were lower in these rats than in AIWR, indirect evidence of the delayed destruction of DA in the striatal system of KM rats. The NA/DA ratio in the striatum also was lower in KM rats than in AIWR. These values are evidence that there is a relative excess of DA in the striatal system of rats predisposed to seizures, for it is slowly metabolized and converted into NA insufficiently rapidly.

The excess of DA, inhibiting neurons of the caudate nucleus indirectly [2, 10-12, 14, 15] or by excitation of interneurons inhibiting cells of the caudate nucleus [13], can evidently be the cause of the insufficient inhibitory function of the caudate nucleus in KM rats: These animals are characterized by increased excitability of the motor cortex, the facilitated spread of excitation over the motor structures of the brain, a low seizure threshold, and the severity of convulsive states [3]. The absence of any clearly defined blocking effect following administration of the DA antagonist bulbocapnine can also be satisfactorily explained by excess of the mediator.

The NA concentration in the hypothalamus of KM rats was 22.5% higher, but their NA/DA

ratio was lower than in AIWR, evidence of the relative deficiency of the NA concentration in the hypothalamus of KM rats. The DA excess in this case also was probably due to delay of its metabolism: The HVA/DA and also (HVA + DHPAA)/DA ratio in KM rats also is lower in the hypothalamus than in AIWR.

Similar changes in the quantitative ratios between conversion products of DA were also found in the adrenals: a much higher level of DA (70% higher than in AIWR) results in an adrenalin level in KM rats that is higher by only 20.5%.

Considering that DA in the hypothalamus is the precursor of NA only, whereas in the adrenals it is the precursor of both NA and adrenalin, it was logical to compare this relative deficit of the end products of the reaction (NA in the hypothalamus, NA and adrenalin in the adrenals) both with the low threshold of the avoidance reaction to direct stimulation of the ventromedial hypothalamus and with the signs of deficient sympathetic activation under conditions of immobilization stress and with the increased "autonomic vulnerability" of KM rats.

The results of the present experiments, together with those obtained by other workers [1, 9], indicate a relationship between the degree of sensitivity to stressors and the initial level of CA metabolism and, in particular, the CA concentration in the hypothalamus and adrenals.

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