

MITOTIC ACTIVITY OF RAT ADRENOCORTICAL CELLS DURING PROLONGED PHYSICAL EXERTION

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After repeated forced swimming by rats for 3 h daily for 30 days the mitotic activity of the adrenocortical cells showed fluctuating changes: the activity at first decreased, then rose considerable above the ordinary level, and finally decreased again.

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Harmful factors acting on the body cause a decrease in the mitotic activity of cells in the adrenal cortex. This phenomenon is observed if rats are stimulated by an electric current for 2 h daily [4], if mice are immersed for 10 min in cold water [1], if formalin is injected into rats [5], if rats are irradiated with radioactive rays [7], or if the skin is incised in the lumbar region [6]. These results were obtained in experiments in which the factors used acted only for short periods. Selye [12], however, considered that if a harmful agent is applied repeatedly and for a long time, the initial decrease in the number of dividing cells is followed by a stage during which the number of mitotically dividing cells rises. Unfortunately, the method of quantitative determination of mitotic activity in different zones of the adrenal cortex has not yet been used, so that this statement can still only be regarded as preliminary. The question of changes in the number of dividing cells in the adrenal cortex during the chronic action of harmful agents is still undecided.

It was therefore decided to study changes in the mitotic activity of the adrenocortical cells in rats compelled to swim for long periods.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats. The animals were selected from the nursery when they reached a weight of 60-70 g, in twice the number required for the experiment, and they were kept on a diet consisting of bread, wheat gruel, milk, bonemeal, salt, and meat. On the subsequent days the animals were twice selected on the basis of weight: individuals with an excessive or an insufficient gain in weight were rejected.

The experiment was started when the majority of the rats had attained a weight of 95-100 g. The animals were divided into two groups: experimental and control. The experimental rats were made to swim in a bath containing water at 28-30° for 3 h daily for 1 month. The control rats were not exposed to this procedure, but were kept in cages together with the experimental animals. Batches of experimental and control rats (5 animals in each group) were sacrificed after swimming 2, 5, 12, 18, 24, and 30 times, on the day following the last exposure. The rats were always killed at 7 A.M., so as to exclude changes depending on diurnal periodicity of adrenal function. The adrenals were fixed in Carnoy's fluid and embedded in paraffin wax. Sections were stained with hematoxylin and eosin. The number of mitoses per 10,000 cells was counted separately for the different zones.

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TABLE 1. Mitotic Index (1:10,000) of Adrenocortical Cells of Control and Experimental Rats (M±m)

Duration of expt. (in days)	Animals	Zona			
		glomerulosa	fasciculata (outer)	fasciculata (inner)	reticularis
2	Control	0,34±0,087	0,12±0,020	0,04±0,023	0,00
	Experimental	0,40±0,089	0,10±0,014	0,00	0,00
	<i>P</i>	0,631	0,447	0,081	—
5	Control	0,40±0,141	0,12±0,020	0,00	0,00
	Experimental	0,00	0,00	0,00	0,00
	<i>P</i>	0,023	0,000	—	—
12	Control	0,42±0,059	0,10±0,038	0,00	0,00
	Experimental	0,04±0,024	0,58±0,105	0,00	0,00
	<i>P</i>	0,000	0,000	—	—
18	Control	0,28±0,037	0,10±0,045	0,04±0,024	0,06±0,40
	Experimental	0,50±0,045	0,60±0,092	0,14±0,060	0,16±0,06
	<i>P</i>	0,009	0,001	0,148	0,199
24	Control	0,36±0,075	0,10±0,032	0,00	0,00
	Experimental	0,32±0,058	0,24±0,024	0,10±0,032	0,04±0,024
	<i>P</i>	0,700	0,005	0,011	0,347
30	Control	0,24±0,04	0,10±0,14	0,00	0,00
	Experimental	0,12±0,03	0,00	0,00	0,00
	<i>P</i>	0,043	0,000	—	—

EXPERIMENTAL RESULTS

The results are given in Table 1.

The general level of mitosis and the distribution of dividing cells by zones in the intact animals (mitoses predominantly in the zone glomerulosa and outer part of the zone fasciculata) were in agreement with data in the literature concerning the adrenocortical mitotic activity during the morning hours [3, 5, 8]. In the swimming rats sacrificed after 2 days of exertion the number of mitoses was normal. After swimming for 5 days cell division ceased in all zones.

Mitotic activity in the zone glomerulosa was resumed after 12 days, but only to a very slight degree. In the outer part of the zona fasciculata, on the other hand, the number of mitoses increased to considerably above the normal level. In the rats which swam for 18 days mitotic activity was sharply intensified both in the outer part of the zona fasciculata (by 6 times) and in the zona glomerulosa (by 1.8 times); mitoses appeared in the inner part of the zona fasciculata and in the zona reticularis.

These events were followed by weakening of mitotic activity. After 24 days it still remained high in the zona fasciculata and zona reticularis, but in the zona glomerulosa it was below the normal level. At the end of the experiment (30 days) the mitotic activity of the cells in the zona glomerulosa was lowered, while in the zona fasciculata and zona reticularis it had ceased altogether.

These experiments showed that under the influence of prolonged and repeated muscular exertion the mitotic activity on the adrenal cortex undergoes fluctuating changes. The number of mitoses at first falls, then rises considerably above the normal level, and finally falls again. Changes take place in all three layers of the adrenal cortex. An essential factor is that during exposure to physical exertion the number of mitoses rises after its preliminary fall not only as a result of resting [5, 7], but also if the exertion is continued.

It is interesting to compare these results with those of experiments in which prolonged stimulation of the adrenal cortex was produced by other factors. During the repeated injection of ACTH the number of mitoses fell only initially, and thereafter it remained above the usual level, despite the fact that the rats continued to receive the hormone [1, 5, 10]. Administration of ACTH in a daily dose of 10 units for 14 days led to an increase in the number of nuclei tagged with thymidine- H^3 in the outer part of the zona fasciculata [9]. An increase in the number of mitoses and nuclei labeled with thymidine- H^3 also was observed after unilateral adrenalectomy [2, 6, 8, 11]. Probably, therefore, the fluctuating changes in mitotic activity observed in rats made to swim for long periods are a reflection of more general rules governing the development of plastic processes during chronic adrenocortical stimulation.

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