DYNAMICS OF THE DIURNAL RHYTHM OF MITOTIC ACTIVITY IN THE PANCREATIC ACINAR CELLS AFTER DISTURBANCE OF THEIR INNERVATION

Yu. K. Eletskii and L. K. Lindenberg

UDC 612.34.014.3:612.6"52"

The diurnal mitotic activity of the acinar cells of the rat pancreas was studied under normal conditions and after bilateral subdiaphragmatic vagotomy (7 days after the operation). The diurnal rhythm of mitotic activity in the control animals was represented by a bimodal curve with a maximum of the number of mitoses at 7 A.M. (1.5%) and 10 P.M. (2.3%) and a minimum from 3 to 6 P.M. (0.2%). The mean diurnal mitotic activity of the pancreatic acinar cells was considerably increased (by 3.5 times) in the vagotomized rats. The biphasic character of the diurnal rhythm persisted but the maximum was shifted to a different time and the amplitude of the fluctuations of mitotic activity was reduced.

When studying the state of the pancreas after disturbance of its innervation (removal of the ganglia of the solar plexus or spinal ganglia) the writers previously observed the appearance of mitoses among the acinar cells [4], whereas normally they are relatively rare [8]. It has also been stated that subdiaphragmatic vagotomy leads to an increase in mitotic activity in the rat pancreas [7]. However, these solitary observations did not take into account the diurnal dynamics of mitotic rhythms. Yet the mitotic activity of the organ is known to differ at different times of day [1-3, 5, 6]. Without allowing for these differences it is therefore impossible to estimate the true change in proliferative activity in the organ. Meanwhile,such investigations on glands with disturbance of their innervation are of definite interest because, first, they broaden our ideas of the development of compensatory and adaptive processes in denervated organs and, second, they deepen our knowledge of the role of the nervous system in the regulation of mitosis.

The object of this investigation was to study the effect of subdiaphragmatic vagotomy on the diurnal rhythm of mitotic activity of the pancreatic acinar cells.

EXPERIMENTAL METHOD

Experiments were carried out in February on noninbred albino rats weighing 150-170 g. Colcemid (3 μg/100 g body weight) was injected into the animals 7 days after bilateral subdiaphragmatic vagotomy and 4 h before sacrifice.* The same dose of colcemid was injected into rats of the control group. The experimental and control animals were decapitated simultaneously at 3, 7, and 10 A.M. and 3, 6, and 10 P.M. Six pairs of rats (72 altogether) were taken at each time. The number of dividing acinar cells in 300 fields of vision (objective 90, ocular 10) was counted in serial sections 7 μ in thickness and the mitotic index was calculated per 1000 cells. In each case from 8000 to 10,000 cells were counted. Statistical analysis of the results was carried out by the Fisher–Student method.

*The largest increase in mitotic activity of the pancreatic acinar cells is observed at this time after vagotomy.

Department of Histology and Embryology, Faculty of Internal Medicine, N. I. Pirogov Second Moscow Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR Yu. M. Lopukhin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 3, pp. 93-95, March, 1974. Original article submitted July 5, 1973.

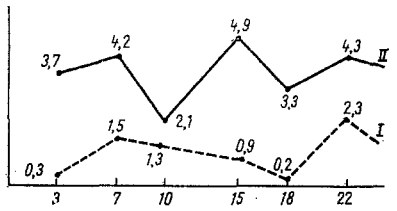

Fig. 1. Changes in mean diurnal mitotic activity (in ‰) of acinar cells of the rat pancreas under normal conditions (I) and after bilateral subdiaphragmatic vagotomy (II). Abscissa, time (in h); ordinate, mitotic index (in ‰).

EXPERIMENTAL RESULTS

The diurnal rhythm of mitotic activity of the pancreatic acinar cells of normal albino rats is represented by a bimodal curve (Fig. 1) with maxima of the number of mitoses at 7 A.M. (1.5%) and 10 P.M. (2.3%). Minimal mitotic activity was observed between 3 and 6 P.M. (0.2%). From 3 to 7 A.M. there was a significant increase in the number of mitoses, from 0.3 to 1.5% ($P < 0.01$), and this was followed by a gradual decrease until 6 P.M. from 1.5 to 0.2% ($P < 0.05$). A significant increase in mitotic activity was observed between 6 and 10 P.M., from 0.2 to 2.3% ($P < 0.001$), and this was followed by an equally rapid fall to 0.3% by 3 P.M. ($P < 0.001$).

It is interesting to note that between 6 P.M. and 3 A.M. there was a marked increase in mitotic activity (maximum 2.3%) and that the subsequent fall occurred within relatively short times, so that the maximum in this phase was clearly defined whereas during the rest of the day the increase in mitotic activity was smaller (maximum 1.5%) and the decrease more gradual (over 11 h), so that the second maximum was not so well marked.

Investigation of the pancreas of the vagotomized rats revealed a marked increase in the mean diurnal mitotic activity of its acinar cells (3.75% compared with 1.08% in the control).

Mitotic activity in the experimental animals at 7 A.M. was higher than in the controls at the same time (4.2%). By 10 A.M. a significant decrease was observed in this index, from 4.2 to 2.1% ($P < 0.01$). An increase in mitotic activity of the acinar cells from 2.1 to 4.9% ($P < 0.01$) was observed from 10 A.M. to 3 P.M., after which, as in the normal animals, the number of mitoses fell until 6 P.M., to 3.3% ($P < 0.02$). A small increase in the number of dividing cells also took place from 6 to 10 P.M., from 3.3 to 4.3% ($p < 0.05$).

Clearly, therefore, the diurnal rhythm of mitosis of the acinar cells is modified in vagotomized animals. The biphasic character of the changes in the diurnal rhythm was still maintained but the maxima were shifted to different times and the amplitude of the fluctuations in mitotic activity was reduced.

These observations thus show that subdiaphragmatic vagotomy leads to a marked increase in the general level of mitotic activity of the pancreatic acinar cells (on the average by 3.5 times) and that it alters the dynamics of the mitotic rhythm during the 24-hour period.

The fact that the mitotic rhythms remain biphasic in character shows that this feature is essentially conservative. The decrease in amplitude of the fluctuations, however, indicates that after vagotomy synchronization of the entry of the acinar cells into the phase of mitosis is disturbed.

No final conclusion regarding the character of the influence of the nervous system on the regulation of mitosis can be drawn from the results of this investigation. Meanwhile, the experimental evidence for a gradual increase in mitotic activity of the acinar cells of the denervated pancreas (during the first week after the operation), preceded by an increase in the number of dying cells, suggests that it plays an essential role through its indirect action in regulating the level of general metabolism in the tissues of the organ.

LITERATURE CITED

1. I. A. Alov and N. V. Krasil'nikova, Dokl. Akad. Nauk SSSR, 142, No. 4, 933 (1962).
2. G. N. Voronin, Annual Report of the Institute of Experimental Medicine, Academy of Medical Sciences of the USSR [in Russian], Vol. 9, No. 2, Leningrad (1966), p. 26.
3. N. V. Krasil'nikova, Byull. Éksperim. Biol. i Med., No. 4, 100 (1962).
4. L. K. Lindenberg, General Histological Changes in the Exocrine Part of the Pancreas after its Denervation, Candidate's Dissertation, Moscow (1963).
5. I. V. Markelova, Byull. Éksperim. Biol. i Med., No. 6, 74 (1962).
6. G. I. Podderyugina and V. N. Dobrokhotov, in: Current Problems in Biology and Medicine [in Russian], Moscow (1968), p. 162.
7. A. B. Stroganova and Yu. K. Eletskii, in: Proceedings of the 4th Conference on the Results of Recent Research into Regeneration and Cell Division [in Russian], Moscow (1971), p. 173.
8. J. L. Cameron, Texas Rep. Biol. Med., 28, 203 (1970).