EFFECT OF FEEDING TIME AND LIGHTING CONDITIONS ON CIRCADIAN PERIODICITY IN NUMBER OF BINUCLEAR CELLS AND MITOSES IN THE RAT LIVER

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UDC 612.35.014.3:612.6:]612.39+612.014.44

Changes in the feeding time and light conditions influence fluctuations in the number of binuclear cells in the rat liver during the 24 h. An increase in mitotic activity is accompanied by a decrease in number of binuclear cells, and vice versa.

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Mitotic periodicity in the liver is the subject of an extensive literature [1, 3, 5, 8]. Data concerning circadian periodicity of the ratio between the numbers of binuclear cells and mitoses in the liver are few in number and conflicting in nature [4, 6, 9]. One reason for the discrepancy in the results obtained, in our opinion, is failure to pay adequate attention to conditions under which the experimental animals are kept.

In the present investigation the circadian periodicity of mitoses and binuclear cells was studied under normal conditions and during changes in conditions of feeding and lighting.

EXPERIMENTAL METHOD

Three series of experiments were carried out on albino rats aged 2-2.5 months. In the experiments of series I and II the animals were kept under natural conditions of alternation of day and night. For one month the animals of series I received food at 7 A.M. and those of series II at 7 P.M. In the experiments of series III the animals were kept for 3 months in complete darkness during daytime (7 A.M.-7 P.M.), and in artifical lighting at night (7 P.M.-7 A.M.); as in series I the animals were fed at 7 A.M. In all the experiments the animals received the same diet ad lib. Rats were sacrificed in groups of 5 or 6 animals every 4 h (at 3, 7, and 11 A.M. and 3, 7, and 11 P.M.).

Mitoses and binuclear cells were counted in sections (5 μ) under the binocular microscope (ocular 10, objective 90). The indices were calculated in promile. Statistical analysis of the numerical results was carried out by the Fisher-Student method.

EXPERIMENTAL RESULTS

The experimental results showed that both mitotic activity and the number of binuclear cells in the liver varies regularly during the 24-h period (Fig. 1). When the animals were fed at 7 A.M., the curve of circadian periodicity of mitoses was bimodal. Highest mitotic activity was observed at 11 A.M., and somewhat lower at 11 P.M. Solitary mitoses were found in the liver at 7 P.M. At 7 A.M. mitoses were completely absent from the liver. The circadian periodicity of binuclear cells in the liver was also marked by two maxima and two minima. The first maximum was found at 7 A.M. This was followed by a slight decrease in the number of binuclear cells (11 A.M.). The second maximum was observed at 3 P.M. The number of binuclear cells was least at night [11 P.M.-3 A.M. ($P = 0.008$)].

With modifications of the feeding time of the animals (series II) the curve of circadian periodicity of mitoses became unimodal in character. The night maximum (at 11 P.M.) disappeared. The time of the morning maximum was changed from 11 to 7 A.M. At other times of investigation the mitotic activity was very low. The circadian periodicity of the binuclear cells of the liver was also modified. A new maximum appeared at 11 P.M. The number of binuclear cells reached a minimum at 7 A.M. and 7 P.M. Just as in the experiments of series I, the number of binuclear cells was highest during the daytime (at 11 A.M.-

Department of Histology, Khabarovsk Medical Institute (Presented by Active Member of the Academy of Medical Sciences of the USSR N. N. Zhukov-Verezhnikov). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 66, No. 9, pp. 99-101, September, 1968. Original article submitted May 16, 1967.

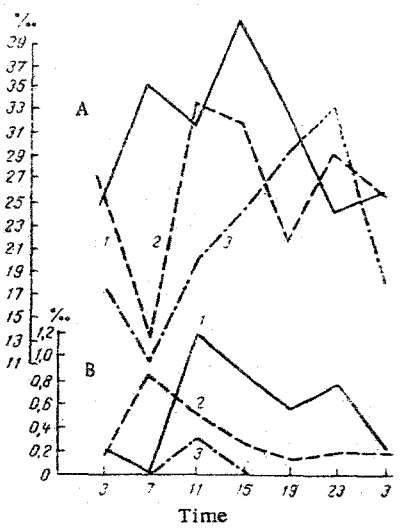

Fig. 1. Circadian periodicity in number of binuclear cells (A) and mitoses (B) in the rat liver. Abscissa, time of day; ordinate, number of binuclear cells and mitoses (in %). 1) feeding at 7 A.M.; 2) feeding at 7 P.M.; 3) feeding at 7 A.M. with reversal of daylight and darkness.

3 P.M.). The differences between maximal and minimal values of the number of binuclear cells in the liver are statistically significant (P = 0.008).

In the experiments with reversal of daylight and darkness, the mitotic activity in the liver was very low. Only during the morning (at 11 A.M.) were solitary mitoses found. The fall in the level of mitotic activity of the liver cells was evidently influenced to some extent by aging of the animals during this long experiment (lasting 3 months). With reversal of daylight and darkness the character of the curve of circadian periodicity of binuclear cells was modified and became unimodal. After the morning minimum (at 7 A.M.), the number of binuclear cells gradually increased to reach a maximum at 11 P.M. followed by a decrease (P = 0.001).

A change in the lighting conditions thus displaced the maximum of the number of binuclear cells from daytime (experiments of series I and II) to nighttime.

The results demonstrate a definite influence of the conditions in which the animals are kept on circadian periodicity in the number of binuclear cells in the liver (Fig. 1). Changing the feeding and lighting conditions almost completely altered the character of the curves for the number of binuclear cells throughout the 24-h period. In this respect the mitotic activity of the liver cells was more resistant. In all our experiments mitotic activity was higher in the morning, as many investigators have observed [1, 3, 5].

The reciprocal relationship between the circadian periodicity of mitoses and number of binuclear cells in the liver is noteworthy, and was most clearly defined in the first half of the day. An increase in mitotic activity was accompanied by a corresponding decrease in the number of binuclear cells. Conversely, minimal indices of mitoses coincide with a high level of binuclear cells in the liver. The increase in number of binuclear cells usually follows a rise of mitotic activity, a large rise being followed by the more intensive formation of binuclear cells (series I).

Our results showing reciprocal relationships between the number of binuclear cells and mitoses during the circadian periodicity are in agreement with existing data: against a background of an experimental increase in mitotic activity in the peritoneal mesothelium of mice produced by blocking the premitotic period by adrenalin, a sharp decrease in the number of mitoses and a parallel increase in the number of binuclear cells were obtained [7]. Binuclear cells are evidently the functional analog of mononuclear polyploid cells [2]. The receiprocal relationships between the number of binuclear cells and mitoses suggest that during the 24 h period the decrease in physiological regeneration, taking place through cell proliferation, is replaced by regeneration of another type, mainly an increase in the number of polyploid (binuclear) cells, on which the increased functional load is thrown.

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