

EXPERIMENTAL BIOLOGY

REGENERATION OF THE LIVER IN HYPOPHYSECTOMIZED YOUNG AND ADULT RATS

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Irrespective of age, inhibition of regeneration of the liver is observed in hypophysectomized rats after extensive resection. This inhibition is expressed as slowing of the increase in weight of the regenerating liver in the hypophysectomized animals compared with nonhypophysectomized. A more definite inhibition of mitotic activity after resection of the liver is observed in hypophysectomized young rats than in hypophysectomized adult animals.

The role of the pituitary gland and, in particular, of the somatotrophic hormone secreted by it, in regulation of regenerative growth of the internal organs (regenerative and compensatory hypertrophy) is not sufficiently understood. The results of investigations on adult mammals have shown that regenerative growth of the liver and kidneys is not suppressed completely after hypophysectomy, but merely retarded to some extent, whereas the normal postnatal growth of these organs is virtually impossible under such conditions [9, 10, 13-16]. The degree of participation of pituitary somatotrophic hormone in the two types of growth is evidently different, despite the definite similarity between their morphogenetic manifestations [9]. The question thus arises whether the ability of the internal organs to undergo regenerative growth after hypophysectomy is preserved to the same degree at all stages of postnatal ontogenesis. It is conceivable that in the early periods of postnatal development, regenerative processes will be much more dependent upon pituitary hormone.

The object of the present investigation was to compare the character of regenerative growth of the liver (regenerative hypertrophy) in rats of different ages undergoing or not undergoing hypophysectomy.

EXPERIMENTAL METHOD

Noninbred male albino rats of two age groups were used in the experiments: young rats aged 1-1.5 months, weighing 65-80 g and adult rats, aged 4-5 months and weighing 230-245 g.

Hypophysectomy was performed on the animals of both groups by the method of Bagramyan and Sakhatskaya [2].

One month after hypophysectomy, two-thirds of the liver was removed from some experimental animals of both groups by the methods of Higgins and Anderson, for the remaining hypophysectomized rats with an intact liver acted as the control. In a parallel series, partial hepatectomy was performed on rats with an intact pituitary, at ages corresponding to the ages of the animals of the experimental groups. Some rats with intact pituitary and intact liver were left as a control in order to compare the degree of increase in mass of the regenerating liver during its recovery.

The criteria of regenerative growth of the liver in the hypophysectomized rats and the animals with an intact pituitary were the degree of increase in weight of the organ and the level of mitotic activity of the hepatocytes 25 h (for young animals), 28 h (for adult rats), 48 h, and 7 days after the operation. At each

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TABLE 1. Changes in Indices of Regenerative Growth of Liver in Hypophysectomized and Nonhypophysectomized Rats of Different Ages after Partial Hepatectomy

Age of animals	Group of animals	Indices of regenerative growth of the liver	Time after partial hepatectomy			
			25 h	28 h	48 h	7 days
Young	Hypophysectomized	Weight of liver (in % of control)	43		52	78
		Mitotic activity (in ‰)	1.2		19.5	0.1
	Nonhypophysectomized	Weight of liver (in % of control)	55		66	85
		Mitotic activity (in ‰)	18.4		6.9	0.3
Adult	Hypophysectomized	Weight of liver (in % of control)		45	43	65
		Mitotic activity (in ‰)		2.5	18.7	0.5
	Nonhypophysectomized	Weight of liver (in % of control)		54	68	80
		Mitotic activity (in ‰)		15.3	20.5	2.9

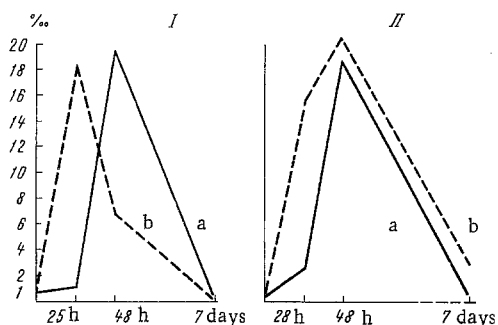


Fig. 1. Mitotic activity of hepatocytes in regenerating liver of hypophysectomized (a) and nonhypophysectomized (b) young (I) and adult (II) rats. Ordinate, mitotic index (in promille).

period of investigation 6-10 rats from the experimental and control groups were sacrificed. The degree of increase in weight of the liver during regeneration at various times after the operation was expressed as a percentage of the weight of the organ in the corresponding control.

Hypophysectomized rats with an intact liver acted as the control for the hypophysectomized animals with a regenerating liver. The control for animals with a regenerating liver and intact pituitary consisted of rats with an intact pituitary and intact liver. Mitotic activity was expressed in promille, and the number of mitoses in 6000 hepatocytes was counted in each animal. Statistical analysis of the numerical results was carried out by the Fisher-Student method.

EXPERIMENTAL RESULTS

Analysis of the results (Table 1) shows that regeneration of the liver after hypophysectomy takes place independently of the age at which hypophysectomy was performed. At the same time, in both young and adult hypophysectomized rats, definite inhibition of regenerative growth of the liver was observed by comparison of the rats with an intact pituitary.

A slower gain in weight of the regenerating liver in the hypophysectomized rats than in animals with an intact pituitary was observed even in the earliest observations, 25-28 h after the operation. Nor had equality been reached by the 7th day after partial hepatectomy ($P = 0.001$), especially in the adult animals.

Inhibition of regenerative growth of the liver after hypophysectomy was due primarily to delay in the proliferation of the hepatocytes. This is shown by the results of counting mitotic activity of the hepatocytes in the regenerating liver of hypophysectomized and nonhypophysectomized animals. The mitotic activity in animals with an intact pituitary 25-28 h after partial hepatectomy was 18.4‰ in young animals and 15.3‰ in adult rats, while the corresponding figures for the hypophysectomized animals at the same time were only 1.2 and 2.5‰. Later, absence of the pituitary had a more distinct effect on proliferation of the hepatocytes in the young animals than in the adults. On the second day after the operation (after 48 h) for instance, the wave of increase of mitotic activity in the nonhypophysectomized young rats had already started to decline (6.9‰), whereas in the hypophysectomized animals it had only just reached its maximum (19.5‰).

Mitotic activity in the adult hypophysectomized and nonhypophysectomized rats was similar at this time: 18.7 and 20.5‰; $P = 0.4$ (Fig. 1).

The slower regeneration of the liver in the hypophysectomized rats than in nonhypophysectomized animals demonstrates that the pituitary is undoubtedly concerned in the regulation of regenerative growth

of the internal organs. This is confirmed by published data [9, 13, 16]. However, the nature of its participation is not yet clear. Other workers and the present authors [3, 4, 6-8] have recently demonstrated that pituitary somatotrophic hormone is concerned in the regulation of mitotic activity of cells, especially in certain periods of their mitotic cycle, in some systems of the alimentary tract. In the absence of growth hormone, some stages of the cycle (S and G₂) may be considerably prolonged. Administration of exogenous somatotropin normalizes these disturbances [3, 4]. The role of the pituitary in regenerative growth of the internal organs is, of course, not limited to the regulation of mitotic activity of the cells. Its role is much more complex, for the work of several systems also participating in the regulation of regeneration is also intimately connected with its function; other endocrine glands, the lymphatic and nervous systems [1, 5, 9, 11, 12].

All that can be postulated on the basis of the results of this investigation is that the pituitary may participate to different degrees in the regulation of regeneration of the internal organs at different stages of postnatal ontogenesis. Evidence in support of this hypothesis is given by the different character of the change in proliferative activity of the hepatocytes in the early stages of regeneration of the liver in hypophysectomized young and adult rats.

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