ACTION OF THYROXINE ON CYTOCHROME CONTENT IN BRAIN AND LIVER MITOCHONDRIA IN RATS DURING POSTNATAL DEVELOPMENT

D. Kh. Khamidov*, N. Kh. Ablyaeva, and T. Yu. Koval'

UDC 577.175.444:576.311.347:577.121.7:611.36:611.81

KEY WORDS: thyroxine; brain; liver; mitochondria; cytochromes.

Thyroid hormones affect growth, development, and maturation of the CNS [8]. Thyroid hormones are essential during the so-called critical period, which is characterized by histological and biochemical differentiation of brain tissue [4, 7]. During this period the activity of most respiratory enzymes and the velocity and efficiency of oxidative phosphorylation increase appreciably [10]. No such rise in the level of metabolism is observed in hypothyroid animals. By contrast, an excess of thyroid hormones accelerates many processes of brain development [11].

The writers showed previously [4] that administration of thyroxine (T_4) in the early postnatal period intensifies respiration of brain mitochondria and increases the activity of several enzymes of the respiratory chain, whereas in rats aged 20 days no effect of this hormone was observed. Regulation of energy metabolism of the brain mitochondria by thyroid hormones evidently is confined to the early postnatal period.

In the investigation described below the effect of T_4 on the content of respiratory chain cytochromes in brain and liver mitochondria was studied in rats during postnatal development.

EXPERIMENTAL METHOD

Experiments were carried out on rats aged 6-7 and 20 days, which received daily injections of L-thyroxine in a dose of 0.7 μg/g body weight, dissolved in 0.1 ml of slightly alkalified physiological saline (pH 8.0) for 4 days before sacrifice. Control animals received 0.1 ml of physiological saline. Liver and brain mitochondria were isolated by differential centrifugation. The content of the various cytochromes was determined on a Specord UVVIS dual-beam differential spectrometer by the method in [1]. The isolation medium for brain mitochondria contained sucrose (0.3 M), Tris-HCl (5 mM), EDTA (2 mM), and albumin (0.2 mg/ml), pH 7.4, and for liver mitochondria it contained sucrose (0.25 M), Tris-HCl (10 mM), pH 7.4. To record the spectra, isolation medium for the particular tissue was used and oxidized and reduced media were prepared in accordance with the following scheme (Table 1).

The mitochondrial suspension, in an amount of 10-15 mg measured as protein, was introduced into a 2-ml cuvette. Protein was determined by the biuret method.

EXPERIMENTAL RESULTS

Data on the content of cytochromes $c + c_1$, b, and *a* in liver and brain mitochondria of rats during the first three weeks of life are given in Fig. 1. The cytochrome levels in these tissues reached their adult values [2, 5] in rats by the age of 7 days. This is in agreement with data obtained by other workers [9], who showed that the

*Corresponding Member, Academy of Sciences of the Uzbek SSR.

Laboratory of Cytochemistry and Electron Microscopy, Institute of Biochemistry, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 6, pp. 696-697, June, 1985. Original article submitted May 3, 1984.

 0007-4888/85/9906-0748$09.50

TABLE 1

Medium	
reduced	oxidized
Succinate 5 mM	—
Amytal 2.4 mM	Amytal 4.8 mM
DNP 40 μM	DNP 240 mM
Na cyanide 2 mM	Oxygenated on ice for 2 min
NADH 0.2 mM	NADH 0.2 mM

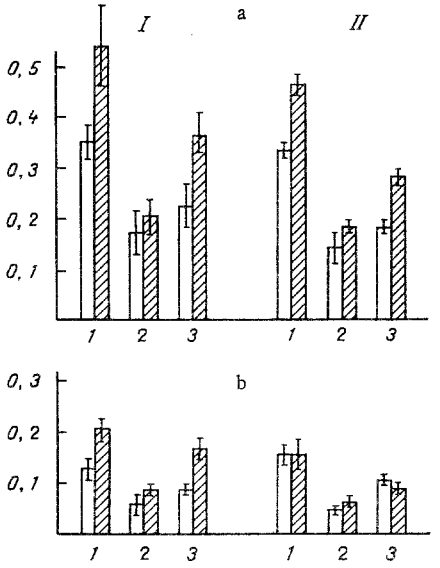

Fig. 1. Effect of L-T_4 on concentrations of cytochromes c + c_1 (1), b (2), and *a* (3) in liver (a) and brain (b) mitochondria of rats aged 7 (I) and 20 days (II). Unshaded columns – control, shaded – experiment. Ordinate, concentrations of cytochromes (in nanomoles/mg protein).

concentrations of enzymes studied in the liver and heart tissues reached their adult levels by the end of the first weak of life, although immediately after birth of the rats the concentrations of the cytochromes were distinctly low. This sharp rise in concentrations of cytochromes of the mitochondrial respiratory chain in tissues of newborn rats is probably connected with an increase in the O_2 concentration in the blood stream immediately after birth [12]. Intensification of oxidative metabolism in the tissues [3], and also activation of the endocrine glands [14].

In the present experiments (Fig. 1) administration of T_4 during the first week of the rats' life caused an increase of 54 and 64% in the concentrations of cytochromes c + c_1 in the liver respectively, and an increase of 60% in the brain mitochondria. The cytochrome b level showed a tendency to rise (the changes were not statistically significant).

Injection of thyroid hormone into 20-day-old rats caused dissimilar effects in the liver and brain tissues. In the liver mitochondria the concentration of cytochromes c + c_1 and *a* increased by 40 and 55% respectively, whereas T_4 had no effect in brain mitochondria. Incidentally, the increase in concentration of cytochromes c + c_1 and *a* correlated with data on intensification of mitochondria respiratory activity, and the increase in cytochrome oxidase activity after injection of T_4 into rats of these same ages [6]. Thus the brain in the early periods of development of rats is sensitive to the action of T_4 and loses this sensitivity by the 20th day of post-

natal development. The liver, which is the target organ for the action of thyroid hormones throughout the animals' life, also reacts on the 20th day.

This difference in the action of thyroid hormone on liver and brain tissues can probably be explained on the grounds that the brain of adult animals is indifferent to the action of thyroid hormones, and it is only during a certain period of postnatal life, namely the first two weeks, that the brain tissue is sensitive to the action of thyroid hormones. Only in the early postnatal period is the rate of protein synthesis in brain tissue increased after injection of T_4 and, in addition, specific binding of T_4 with brain mitochondria is greatest in rats aged 7 and 14 days.

Consequently, T_4 intensifies the synthesis of respiratory chain components in the early postnatal period in mitochondria of the developing brain, and thus causes these organelles to function more rapidly and promotes differentiation of the mitochondria of the developing brain. This is further proof that thyroid hormone is essential in the "critical periods" of maturation of brain cells.

LITERATURE CITED

1. Yu. V. Evtodienko and E. N. Mokhova, in: Mechanisms of Respiration, Photosynthesis, and Nitrogen Fixation [in Russian], Moscow (1967), p. 35.
2. A. L. Lehninger, The Mitochondrion [Russian translation], Moscow (1966).
3. G. M. Maslova, "Characteristics of tissue respiration determining heat production at different stages of ontogeny and during adaptation of adult animals to cold," Author's Abstract of Candidate's Dissertation, Moscow (1971).
4. M. S. Mitskevich, Hormonal Regulation during Animal Development [in Russian], Moscow (1978).
5. Z. D. Pigareva, Biochemistry of the Developing Brain [in Russian], Moscow (1972), p. 122.
6. D. Kh. Khamidov and N. Kh. Ablyaeva, in: Abstracts of Proceedings of the 6th All-Union Conference of Embryologists [in Russian], Moscow (1981), p. 3.
7. J. T. Eayrs, in: Endocrinology and Human Behavior, London (1968), p. 239.
8. D. H. Ford, Drugs Dev. Brain, 8, 451 (1974).
9. M. Hallman, Biochim. Biophys. Acta, 253, 360 (1971).
10. D. Holzman and C. L. Moore, J. Neurochem., 24, 1011 (1975).
11. L. Mela, G. W. Goodwin, and L. D. Miller, Biochem. Biophys. Res. Commun., 64, 384 (1975).
12. N. Myant, in: Hormones in Development, New York (1971), p. 249.
13. R. Sutton and J. K. Pollack, Biochem. J., 186, 361 (1980).