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EFFECT OF RESTORATION OF VISUAL IMPULSES ON ENERGY METABOLISM IN THE VISUAL SYSTEM OF THE BRAIN IN DARK-REARED ANIMALS

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Changes in the rate and character of energy metabolism in the mitochondria of the visual system of the brain induced by prolonged visual deprivation (from birth until the age of 2.5 months) were shown to be reversible. The degree of normalization differed for mitochondria of the visual cortex and superior colliculus. During the 2-week recovery period (when the animal was transferred to ordinary conditions of illumination) the rate of these processes increased, when glutamic acid was used as the substrate, and reached the control level or exceeded it somewhat. The rate of electron transport in the cytochrome c–cytochrome oxidase section of the succinate oxidase oxidation chain, which was increased during deprivation, diminished in the recovery period and came close to the control level. The role of specific impulse activity in the formation of mitochondrial energy processes in the brain with age is discussed.

KEY WORDS: mitochondria of rabbit brain; postnatal development; visual deprivation; bioenergetic processes.

Exclusion of visual afferentation before completion of the structural, functional, and biochemical differentiation of the visual system leads to physiological, morphological and biochemical changes in that system at the tissue, cellular, and subcellular levels [1, 2, 6-8]. The writer has shown that mitochondria of the visual system of the brain in animals reared in the dark until the age of 2.5 months differ in several indices of their energy metabolism from controls. The differences are connected with changes in the relative importance of individual substrates in the energy balance and, in particular, an increase in the role of succinic acid and an increase in the efficiency of the final section of the succinate oxidase oxidation chain. The fact that such changes in the mitochondria of the visual system exceed those found in the mitochondria of other parts of the cortex has suggested an important role of visual afferentation in the formation of the energy metabolism of the developing brain [3].

The object of this investigation was to discover whether energy processes in the mitochondria of the visual system (visual cortex, superior colliculus, and, for comparison, the "remaining" cortex), if altered by light deprivation, can be restored to normal.

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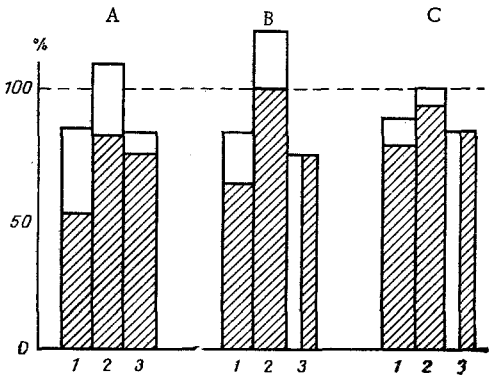

Fig. 1. Oxidation of glutamic acid during deprivation and restoration of visual function: A) visual cortex; B) superior colliculus; C) "remaining" cortex. 1) Oxidative phosphorylation; 2) coupled respiration; 3) ADP/O. Shaded columns represent deprivation, unshaded columns restoration.

TABLE 1. Oxidative Activity of Succinic Acid in Mitochondria of Experimental and Control Rabbits under Different Conditions (effect of rotenone, dinitrophenol, and the ascorbate–tetraphenylenediamine system)

Functional state	Endogenous respiration	Rotenone	Rotenone + succinate	Rotenone + succinate + DNP	Rotenone + succinate + DNP + ascorbate–tetraphenylenediamine
	Visual cortex				
Control	14,2±2,0	12,4±2,2	19,4±2,5	32,7±2,7	86,7±9,7
Per cent of previous level	100	87	156	169	265
Visual deprivation	20,9±0,9	19,7±1,9	30,3±2,9	41,2±2,0	167±7,8
Per cent of previous level	100	94	154	136	405
Recovery	17,9±2,8	18,5±3,6	32,8±6,1	51,4±9,2	109±9,1
Per cent of previous level	100	103	177	157	212
	Superior colliculus				
Control	19,7±2,9	17,3±2,6	24,0±2,5	42,7±3,4	100±9,1
Per cent of previous level	100	88	139	178	234
Visual deprivation	29,7±3,8	27,8±3,7	38,8±3,1	53,3±6,3	189±15,6
Per cent of previous level	100	92	140	137	354
Recovery	19,3±3,8	21,0±3,4	29,3±4,7	40,4±6,1	116±6,6
Per cent of previous level	100	108	140	138	287
	Remaining cortex				
Control	15,7±2,8	10,5±0,9	21,5±4,7	30,0±2,5	77,8±8,4
Per cent of previous level	100	67	205	140	256
Visual deprivation	16,3±1,1	15,0±2,3	24,5±2,8	31,2±2,2	138±5,5
Per cent of previous level	100	92	163	127	442
Recovery	17,9±2,0	21,8±5,3	28,2±2,6	43,0±2,3	129±5,2
Per cent of previous level	100	122	129	153	300

EXPERIMENTAL METHOD

Brain mitochondria from rabbits kept in dark chambers from birth until the age of 2.5 months, and then transferred for 2 weeks into conditions of ordinary alternation of light and darkness, were used in the experiments. Intact rabbits aged 2.5-3 months were used as the control. The results were compared with those obtained on the visually deprived rabbits. The method of isolating the mitochondria and the composition of the incubation medium were published previously [4]. The rate of respiration and of phosphorylation was recorded polarographically.

EXPERIMENTAL RESULTS AND DISCUSSION

After restoration of the flow of visual impulses, the rate of endogenous respiration in the mitochondria studied was reduced compared with the corresponding processes in the mitochondria of the deprived animals (Fig. 1). An increase in the rate of phosphorylation by 35 and 20% respectively was found in the mitochondria of the visual cortex and superior colliculus. A similar tendency also was observed in the mitochondria of the "remaining" cortex.

The rate of respiration when glutamic acid was used as substrate was a little higher than in the control, amounting to 113% in the mitochondria of the visual cortex and 123% in the superior colliculus compared with the control. Under these conditions the rate of respiration in the mitochondria of the "remaining" cortex was the same as in the control. The values of ADP/O in the recovery period became higher than in the deprived animals, but did not reach the control level.

During the study of the brain mitochondria in the recovery period a detailed examination was made of the state of electron transport in the succinate oxidase oxidation chain, for definite changes were found in it in the period of deprivation. As Table 1 shows, in the period of recovery of visual afferentation the addition of succinic acid to the medium with rotenone increased the respiratory activity of the mitochondria of the visual cortex, superior colliculus, and "remaining" cortex compared with the level of that process without the substrate by 77, 40, and 29% respectively. The acceleration of respiration under these conditions in the mitochondria of the control animals was 56, 39, and 105% respectively. The rate of respiration in the mitochondria of the visual cortex of the experimental animals, when succinic acid was used as substrate, was thus higher than in the control, in the mitochondria of the superior colliculus it was the same, and in the mitochondria of the "remaining" cortex it was much smaller still than in the control.

The addition of DNP to the incubation medium containing rotenone and succinic acid led to an increase in the respiration rate of the mitochondria of the animals in the recovery period (Table 1). This increase was less marked for mitochondria of the visual cortex than for the corresponding mitochondria of the control rabbits. In the mitochondria of the "remaining" cortex the degree of uncoupling of respiration was actually somewhat greater than in the mitochondria of the control animals. At the stage of recovery of visual function the uncoupling effect of DNP in the mitochondria of the visual system on oxidation of succinate (in the presence of rotenone) was thus less marked than in the control animals. Compared with the mitochondria of the visually deprived animals, the mitochondria of the visual cortex in the recovery period were more "normalized" than those of the superior colliculus.

The addition of the specific substrate (ascorbate) and a carrier (tetraphenylenediamine) to medium with uncoupled mitochondria and succinate activated electron transport in the cytochrome c–cytochrome oxidase sector. Acceleration of respiration in the mitochondria during the period of recovery of visual function was less marked than during visual deprivation, but it still differed from the control level.

Energy parameters of the brain mitochondria during recovery of visual afferentation thus showed a greater change toward normalization than their state during deprivation. This was reflected in changes in respiratory and phosphorylating activity during utilization of glutamate, and also in corresponding adjustments to the succinate oxidase oxidation chain. The degree of normalization of these processes differed in the brain mitochondria studied, evidently because of the different significance of visual impulses to the different parts of the brain.

The formation of mitochondria in the developing brain is known to be accompanied by regular changes in the properties of the respiratory chain and of the protein-lipid components of the mitochondrial membranes [5]. Possibly under conditions of visual deafferentation the mitochondrial membranes do not reach the level of biochemical differentiation characteristic of control animals of the corresponding age. These features distinguishing the mitochondria of visually deprived animals could account for the greater ability of DNP to pass through the mitochondrial membranes. During recovery of visual function the differences between the effects of DNP on these processes in the mitochondria of the visual and "remaining" cortex became less marked than in the corresponding mitochondria of visually deprived animals. This fact is interpreted as an indication of normalization of the respiratory chain when modified by visual deprivation. The facts described above show that changes in energy processes in the brain mitochondria induced by visual deprivation are reversible.

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