REGULATION OF BRAIN MITOCHONDRIAL MONOAMINE OXIDASE ACTIVITY IN EXPERIMENTAL CLOSED HEAD INJURIES

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Mitochondrial monoamine oxidase (MAO) activity in various parts of the brain (cerebral hemispheres, brain stem, cerebellum) was studied in experiments on rabbits in the normal state and 1.5 h and 1 and 5 days after closed head injury. Serotonin creatinine-sulfate was used as the substrate. Acute closed head injury was shown to cause a sharp decrease in MAO activity in the various parts of the brain of the experimental animals. Stimulation of the activity of the nervous system of the injured animals was shown to restore brain MAO activity.

KEY WORDS: brain monoamine oxidase; head injury; serotonin; amphetamine stimulation.

Monoamine oxidase [monoamine: O_2-oxidoreductase (deaminating), EC 1.4.3.2] was first found in the brain in 1937 by Pugh and Quastel [11].

Inside the cell, in various organs or, at least, in the liver and brain tissue, MAO has been shown to exist exclusively in the mitochondria [1], where it is bound with their outer membrane [9, 12, 14].

The mitochondrial monoamine oxidase (MAO) of the brain catalyzes the oxidative deamination of dopamine (DA), 5-hydroxytryptamine (5-HT), noradrenalin (NA), tyramine, tryptamine, and other monoamines, many of which have a mediator function [2, 13, 15].

The investigation of the brain MAO after head injury is particularly interesting because of associated disturbances to the blood supply of the brain, resulting in some degree of hypoxia.

A previous investigation [6] showed that the coupling of respiration with oxidative phosphorylation in the brain is severely disturbed after head injury. By modifying the functional state of the nervous system of the experimental animals, these processes in the brain can be regulated [7].

It seemed important to investigate the mitochondrial MAO activity of the brain under analogous experimental conditions because one of the functions of this enzyme, located as it is in the outer membrane of the mitochondria, immediately next to mitochondrial polyenzymic complexes catalyzing respiration and oxidative phosphorylation [5], is to regulate these reactions [4].

EXPERIMENTAL METHOD

Experiments were carried out on male chinchilla rabbits weighing 2.2-2.8 kg. A closed head injury was inflicted by a blow from a 500-g weight falling freely from a height of 2.2 m on to the rabbit's head, fixed in a certain position.

In every case the injury was moderately severe and was accompanied by convulsions and by temporary respiratory arrest, followed by more rapid breathing.

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TABLE 1. Effect of Administration of Amphetamine on Brain Mitochondrial MAO Activity of Injured Rabbits

Test object	MAO activity (nmoles NH_3/mg protein/min)					
	normal	head injury			head injury + amphetamine	
		1 1/2 h	1 day	5 days	1 1/2 h	1 day
Cerebral hemispheres	5,62±0,41 n=6	4,66±0,41 n=5	2,27±0,17 n=5	5,78±0,22 n=5	6,60±0,22 n=4	6,09±0,78 n=5
P		<0,1	<0,01	<0,7	<0,2	<0,1
Brain stem	8,93±0,89 n=8	5,85±0,34 n=5	0,00 n=5	5,46±0,29 n=5	7,46±0,38 n=4	6,54±1,13 n=5
P		<0,02		<0,01	<0,2	<0,02
Cerebellum	7,41±0,44 n=7	5,80±0,74 n=5	0,940±0,34 n=5	5,34±0,43 n=5	8,89±0,71 n=3	6,17±0,93 n=5
P		<0,05	<0,01	<0,01	<0,1	<0,1

Mitochondria from different parts of the brain (cerebral hemispheres, brain stem, cerebellum) were isolated by differential centrifugation in 0.25 M sucrose solution by the method of Brody and Bain [8]. The specific mitochondrial MAO activity was determined by the method of Gorkin et al. [3], based on the quantity of ammonia formed by deamination of the substrate during incubation with suspensions of mitochondria in 0.2 M phosphate buffer, pH 7.4, for 45 min in an atmosphere of oxygen at 37.5°C (in a constant-temperature water bath, with shaking). Serotonin creatinine-sulfate added at the rate of 10 μmoles per sample, was used as the substrate. At the end of incubation, samples were fixed by the addition of 50% TCA to a final concentration of 5%.

The ammonia content in protein-free filtrates was determined by Conway's isothermic distillation method followed by Nessler's reaction. MAO activity was expressed as the number of nanomoles ammonia liberated in the course of incubation per milligram protein per minute. The protein content in the samples was determined by Lowry's method [10].

The investigations were carried out at intervals of 1.5 h and 1 and 5 days after head injury. The activity of the nervous system of the injured animals was stimulated 5 min after head injury and again 5 h later by administration of amphetamine in a dose of 0.6 mg/kg body weight.

EXPERIMENTAL RESULTS

The results given in Table 1 show that the mitochondrial MAO activity varies in different parts of the brain of intact rabbits: it was highest in the brain stem, in which it was 1.6 times higher than in the cerebral hemispheres and 1.2 times higher than in the cerebellum.

The MAO activity in all parts of the brain studied was reduced 1.5 h after infliction of the head injury on the animal, and the greatest decrease was observed in the brain stem. The MAO activity 24 h after head injury showed a sharp decrease in all these parts of the brain. The changes were greatest in the brain stem, where MOA activity disappeared completely, and in the cerebellum, where the enzyme activity fell to extremely low values.

In the experiments of series II, the animals were treated with amphetamine after head injury and the MAO activity studied at the same periods as above. The results of these observations (Table 1) demonstrate a marked increase in brain MAO activity both in the tests 1.5 h after head injury and, in particular, in the tests after 24 h.

Stimulation of the activity of the nervous system of animals subjected to head injury thus restored the sharply reduced brain MAO activity.

These results thus provide further confirmation of the view that the active nervous system can compensate for the disturbed biochemical processes in the brain after head injury. This important factor must be taken into account during the treatment of head injuries.

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