DYNAMICS OF MITOCHONDRIAL MONOAMINE OXIDASE ACTIVITY IN THE LIVER DURING ALLERGIC REACTIONS OF THE DIRECT TYPE

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During sensitization of guinea pigs by horse serum, a marked decrease in mitochondrial monoamine oxidase activity is observed in the liver. Acute anaphylactic shock is characterized by a sharp rise in the activity of this enzyme.

The development of immunopathological processes is accompanied by marked changes in the activity of several enzymes with responsibility for the genesis and metabolism of some biogenic amines [5, 8, 12]. The object of the present investigation was to study the activity of mitochondrial monoamine oxidase (MAO; monoamine: deaminating O_2-oxidoreductase; 1.4.3.4) in hypersensitivity tests.

Because of the marked allergic alteration of the liver mitochondria in the course of immunologic conflict and because of the lack of information in the accessible literature regarding changes in mitochondrial monoamine oxidase activity under these conditions, it was decided to study the dynamics of MAO activity in guinea pig liver during sensitization and acute anaphylactic shock [6, 7, 9, 10].

EXPERIMENTAL METHOD

Acute anaphylactic shock was chosen as the experimental model of an allergic reaction of direct type. The work was done on guinea pigs weighing 250-350 g. Group 1 (control) and group 2 (experimental) each consisted of 20 animals. The guinea pigs were sensitized by a single subcutaneous injection of normal horse serum (NHS) in a dose of 0.8 mg protein/100 g body weight. The control animals received parallel subcutaneous injections of physiological saline. The reacting dose of antigen (8 mg/100 g body weight) was injected into the heart of the experimental and control animals 21 days later, at the end of the incubation period. A special feature of the investigation, due to the use of ultramicromethods of biochemical analysis [3], was that samples were taken at successive periods from the same animals. In this way, individual variations in enzyme activity were reduced and the reliability of the results was increased. To estimate mitochondrial MAO activity, the writers' micromodification of the colorimetric method [2] was used. Since the method was not developed with guinea pigs, the necessary corrections were introduced to allow for species differences in enzyme activity. MAO activity was expressed in millimicromoles ammonia liberated during oxidation of p-nitrophenylethylamine per gram fresh liver tissue or per milligram protein during incubation for 1 min.

EXPERIMENTAL RESULTS

These experiments revealed a significant decrease in mitochondrial MAO activity in the liver of the guinea pigs during sensitization. The mean MAO activity in the control animals was 19 ± 1.18 μmoles/mg protein (or 233 μmoles/g tissue), whereas in the sensitized guinea pigs it was 5 ± 0.44 μmoles/mg protein or 63 μmoles/g tissue.

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TABLE 1. Effect of Reacting Dose of Antigen on Level of MAO Activity in Sensitized and Control Animals

Group of animals	No. of animals	MAO activity in mμmoles/mg protein/min			
		before injection of antigen	after injection of antigen		
			1 min	2 min	5 min
Unsensitized	10	17,1± 1,11	18,7± 0,94	18,5± 1,20	20,2± 1,18
Sensitized	20	5,0± 0,44	11,0± 0,63	10,7± 0,58	13,0± 0,73

Variations in mitochondrial MAO activity in the control guinea pigs after intracardiac injection of NHS did not significantly exceed the level of its activity before the reacting dose was given (Table 1). In the sensitized animals, after the reacting injection of antigen, a classical picture of severe anaphylactic shock developed, terminating in death of the animals by asphyxia after 4-6 min. In the first minute of development of acute anaphylactic shock the MAO activity was higher than in the sensitized animals, but in the terminal phase of shock a further increase in activity of the enzyme was observed. The development of acute anaphylactic shock was thus accompanied by a rapid and sharp increase in MAO activity over its level in the sensitized animals.

The depression of activity of membrane-bound mitochondrial MAO discovered in this investigation during sensitization can be compared with the results indicating selective absorption of antigens on the mitochondrial membranes and the possible fixation of antibodies synthesized by the organism by these membranes [1, 4, 11, 13]. The antigen is probably capable of forming complexes with the protein components of the mitochondrial membrane. This can evidently lead to blocking of active groups of the MAO. Acceptance of this hypothesis thus to some extent explains how the marked depression of MAO activity can take place.

The molecules of antigen injected with the reacting dose react extremely rapidly with antibodies fixed by the cell, and probably free the outer mitochondrial membranes from these antibodies. The rapid rise in activity which was observed can perhaps be connected with partial manifestation of free MAO activity. The following conclusions can be drawn from these results. Sensitization sharply reduces mitochondrial MAO activity in the liver of of guinea pigs, while acute anaphylactic shock is accompanied by an increase in MAO activity by 220-260% compared with the level of its activity in the tissues of sensitized animals.

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