EFFECT OF SOME BACTERIAL INTOXICATIONS ON THE CHOLINESTERASE ACTIVITY OF RATS' BRAIN

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Changes in the reactivity of the central nervous system are an important feature of infectious diseases. It may be supposed that such changes in reactivity are a consequence of the action of bacterial toxins or enzyme systems of nerve cells. The elucidation of the mechanism whereby the functional state of the nervous system is affected in infectious diseases may in some cases afford the possibility of modifying enzymatic processes of nerve cells.

Much attention has been paid of recent years to cholinergic reactions, in the study of the pathology of infections. The importance of acetylcholine in modifying the reactivity of the nervous system has been established by a number of authors. To this may be ascribed the interest taken by research workers in changes in cholinesterase activity in infectious diseases.

We have studied cholinesterase activity of the brain of animals suffering from pneumococcal, dysentery, and tetanus intoxications.

We have been unable to trace any literature references to the effects of pneumonia on cholinesterase activity.

A very slight activation of cholinesterase has been reported to result from the direct action of Flexner type dysentery antigen [6]. A fall in cholinesterase activity of the blood serum [11] and of extracts of the brain and spinal cord [10] has been found in experimental dysenteric intoxication of animals. A similar effect has been noted for the serum of dysentery patients [6].

Tetanus toxin exerts an anticholinesterase action in vitro [8, 12, 13, 15]. M. B. Lebedeva and I. L. Chertkov [8] found no change in the cholinesterase activity of extracts of the brain and spinal cord in animals suffering from tetanus intoxication. In similar experiments, N. K. Fruentov [12] found a slight lowering of cholinesterase activity.

As appears from the literature references cited, the effects of the given intoxications on cholinesterase activity were studied using extracts of the whole brain. Bearing in mind the differences in physiological activity of different parts of the brain, we thought it would be more instructive to examine separately the cholinesterase activity of the grey matter of the cerebral cortex, of the part of the brain corresponding to the thalamo-hypothalamic region, and of the cerebellum.

EXPERIMENTAL METHODS

The experimental animals were male and female rats, weighing 100-200 g. Practically healthy rats were taken as controls for each series of sick animals. Pneumococcal intoxication was achieved by giving intradermal inoculations of titrated 18-hour cultures of Type I pneumococcus, which caused death within 2-3 days.

Cholinesterase activity was determined in seriously ill rats. Dysenteric intoxication was effected by intraperitoneal injection of a lethal dose of Flexner type dysentery complete antigen. The animals became seriously ill within 3-4 hours. Tetanus intoxication was achieved by subcutaneous injection into the left hind leg of tetanus toxin, at a dosage of 0.1 mg in 0.1 ml of physiological saline. This was usually followed by localized tetanus, on the 2nd and 3rd day, and the animals died on the 4-5th day, with symptoms of generalized tetanus. Cholinesterase activity was determined in material taken from rats killed shortly before they were expected to die.

The rats were decapitated, and the brain was removed as quickly as possible, cooled, and the requisite samples were removed, weighed, and ground up with cooled buffer solution (1 ml per 50 mg of tissue). Cholinesterase activity was determined manometrically, in a Warburg apparatus, according to D. Nachmanson and M. Rothenberg [14]. The activity was expressed as μl CO_2 evolved per mg of tissue during the first 30 minutes.

EXPERIMENTAL RESULTS

The results are presented in the Table. A tendency towards lowering of cholinesterase activity of the grey matter of the cerebral cortex was evident in pneumococcal intoxication. This decrease was not, however, statistically significant. No change was found in the cholinesterase activity of the thalamo-hypothalamic region.

The cholinesterase activity of the grey matter was raised by 37% in dysenteric intoxication; that of the thalamo-hypothalamic region and of the cerebellum showed no change.

Tetanus toxin raised the cholinesterase activity of cortical grey matter by 40%, and of the thalamo-hypothalamic region by 27%. No change was found in the cerebellum. The rise in cholinesterase activity was in all these cases statistically significant.

TABLE

Cholinesterase Activity of Different Parts of the Brain of Healthy and Sick Rats

Part of brain examined	M—μl CO_2 evolved in 30 min. per mg tissue (mean values; range given in parentheses)	n — number of experiment	m — mean error	Significance of deviations from normal	Percentage of deviations from normal
	Normal				
Cortex	2.7(1.6—3.8)	13	±0.1986	—	—
Thalamo-hypothalamic region	4.7(4.1—5.2)	9	±0.1532	—	—
Cerebellum	2.0(1.2—2.6)	8	—	—	—
	Pneumonia				
Cortex	2.2(1.4—3.1)	7	±0.2560	Not significant	—18
Thalamo-hypothalamic region	4.9(3.5—6.6)	7	—	—	—
	Dysentery				
Cortex	3.7(2.5—4.6)	11	±0.2322	Significant	+37
Thalamo-hypothalamic region	5.1(4.6—5.5)	9	—	—	—
Cerebellum	2.0(1.6—2.3)	7	—	—	—
	Tetanus				
Cortex	3.8(3.2—4.2)	8	±0.1180	Significant	+40
Thalamo-hypothalamic region	5.9(5.2—6.6)	8	±0.2070	Significant	+27
Cerebellum	2.2(1.9—2.7)	7	—	—	—

Our results differ somewhat from those published in the literature. This may be because the changes in cholinesterase activity found by us in particular parts of the brain might not be perceptible when the activity of the whole brain is studied. According to M. B. Aristovskii [2] the enhanced nerve conductivity found in tetanus is a consequence of interference with acetylcholine breakdown, and of its accumulation in the nervous system, owing to the inhibitory effect of tetanus toxin on cholinesterase.

D. E. Al'pern et al., [1] believe that increase in cholinesterase activity of the blood and tissues proceeds, within certain limits, parallel with increase in their acetylcholine content, and may thus be regarded as a compensatory function of the organism. In accordance with this view, G. E. Platonov [9] related the raised cholinesterase activity of the hypothalamic region, found by him in tuberculous intoxications to accumulation of acetylcholine-like substances. Thus our findings also support the view that accumulation of acetylcholine occurs in the grey matter of the cerebral cortex in dysenteric and tetanus intoxications, and in the thalamo-hypothalamic regions in tetanus intoxication; this may explain the raised reactivity of these parts of the brain in these conditions.

The conclusion may be drawn from our results that cholinesterase activity rises in the grey matter of the cerebral cortex and in the thalamo-hypothalamic region, in tetanus intoxication of rats; it does not change in the cerebellum.

Cholinesterase activity of rats suffering from pneumococcal intoxication remains unchanged in the cerebral cortex and in the thalamo-hypothalamic region.

SUMMARY

It was experimentally demonstrated that cholinesterase activity increases in the gray matter of the cerebral hemispheres in tetanus and dysentery intoxications. However, there is no change in its activity in pneumococcal intoxication. The activity of the enzyme does not change in the cerebellum in tetanus and dysentery intoxications. The increase in activity of cholinesterase in all the above cases is proved statistically.

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