

CHOLINESTERASE ACTIVITY OF THE CENTRAL NERVOUS SYSTEM AND MUSCLES IN THE COURSE OF EXPERIMENTAL TETANUS

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A number of authors [12-14] have associated the motor disturbances in tetanus with depression of the enzyme cholinesterase in the central nervous system and the muscles. Very few investigations have been devoted to this problem, the methods used have varied, and the conclusions drawn are contradictory. For instance, it has been shown [7, 9] that tetanus toxin depresses the activity of cholinesterase in vitro, while the activity of the enzyme in the spinal cord, the brain, and the muscles is unchanged. An increase in the activity of the enzyme has also been found [8] in the central nervous system. The results of other investigations [6] showed that the changes in neuromuscular transmission arising in tetanus cannot be connected with depression of the cholinesterase activity in the region of the end plate, as was suggested originally [11]. Some workers [13, 14] have reported inhibition of cholinesterase in the spinal cord of animals infected with experimental tetanus.

The object of the present investigation was to study the activity of the enzyme in various parts of the central nervous system in mice in the course of development of tetanus.

EXPERIMENTAL METHOD

To determine the cholinesterase activity the Plattner-Hestrin method [12] was used. The enzymic activity of the tissue was expressed in Qch units (the quantity of acetylcholine split by 1 g tissue per hour). The activity of the enzyme was determined in intact rabbits and in rabbits at different periods of experimental tetanus (incubation period, stage of local tetanus, and stage of general tetanus). The tetanus toxin was injected into the gastrocnemius muscle in an amount equal to 1 lethal dose.

Because of reports in the literature indicating that tetanus toxin spreads mainly along neural pathways, the cholinesterase activity was studied periodically during the development of the disease in the gray matter of the whole spinal cord, the rhomboid fossa of the medulla, the spinal ganglia, and the gastrocnemius muscles. For this purpose the animals were sacrificed by exsanguination, the spinal canal was opened, and the spinal cord as a whole with the spinal ganglia was extracted. By dissection the gray matter was separated from the white throughout the length of the spinal cord. In the medulla the gray matter was isolated in the region of the rhomboid fossa.

Pieces of muscle tissue were excised from the middle third of the gastrocnemius muscle. In each experiment 60 gm of homogenate prepared from all the investigated tissue in a dilution of 1:10 was used. The numerical results obtained were analyzed by statistical methods [1, 2].

RESULTS

The cholinesterase activity of the various parts of the nervous system and of the muscles of the intact and affected animals is shown in the table.

Cholinesterase Activity of Various Tissues of Intact Animals and during the Development of Tetanus (Qch Units, Mean Data)

Tissue	Intact animals			Incubation period			Local tetanus			General tetanus		
	no. of expt.	Qch units	confidence limits	no. of expt.	Qch units	confidence limits	no. of expt.	Qch units	confidence limits	no. of expt.	Qch units	confidence limits
Gray matter of spinal cord	32	72	66,5-77,5	25	56	50,3-61,7	30	65	56,84-73,16	30	64	48,7-69,3
Rhomboid fossa of medulla	27	77	69,3-84,7	16	78	71,6-84,4	18	83	76-80	20	77	68-86
Spinal ganglia	22	49	42,5-55,5	15	38	32-44	17	37	30,6-43,4	17	40,6	33,6-47,6
Muscles	21	6,3	4,3-8,3	16	6,6	5,44-7,76	18	6,3	4,87-7,73	19	6,4	4,9-7,9

As the table shows, the maximal activity of the enzyme in the intact animals was found in the medulla and in the gray matter of the spinal cord. The activity in the spinal ganglia was much less, and in the muscles, where cholinesterase is localized only in the neuromuscular synapses and in the region where the muscle and tendon fibers join, it was very slight. In the course of development of tetanus a statistically significant depression of the enzyme was observed in the gray matter of the spinal cord and in the spinal ganglia. A decrease in the activity of the enzyme by 23% in the gray matter of the spinal cord was observed in the incubation period of the disease. In the stages of local and general tetanus the enzymic activity recovered to a certain extent, but did not regain its original level. Similar changes were found in the tissues of the spinal ganglia: in the incubation period of the disease the cholinesterase activity fell from 49 to 38 units. This lowered level of activity persisted throughout the course of the disease.

The values of the cholinesterase activity of the medulla and muscles at all stages of the disease varied only within normal limits.

The statistically significant results obtained demonstrate that tetanus toxin inhibits cholinesterase only very slightly. However, these results give conclusive evidence against the views of those authors [11, 13, 14] who hold that the motor disturbances in tetanus are the result of inhibition of cholinesterase in the neuromuscular synapses. Recent electrophysiological investigations [5, 10] have established the central genesis of the rigidity and convulsions in tetanus. The present results show that the mechanism of depression of the enzyme does not play the principal role in the central origin of the motor disturbances. The depression of cholinesterase observed in the ganglia and gray matter of the spinal cord cannot, in the authors' opinion, be regarded as the leading factor in the pathogenesis of the disease. Reports in the literature [3] and the authors' earlier investigations [4] have shown that more marked inhibition of cholinesterase need not be accompanied necessarily by pathological manifestations.

At the same time the increased content of acetylcholine in the central nervous system in tetanus [15] means that the mechanism of a disturbance of the cholinergic metabolism cannot be ruled out completely from the pathogenesis of the toxic effects. It is possible that the changes described are associated, not with the depression, but with the redistribution of the enzyme in the central nervous system and muscles.

SUMMARY

A study was carried out on the activity of cholinesterase of the gray matter of the spinal cord, rhomboid fossa of the medulla oblongata, spinal ganglia, and muscles of intact rabbits and rabbits in the incubation period, in the stage of local tetanus, and in the stage of general tetanus. Experiments showed a significant decrease of the activity of cholinesterase of the spinal cord and ganglia in the incubation period of the disease. The pathogenetic significance of this phenomenon is discussed in detail.

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