CHOLINERGIC SUBSTANCES OF THE CENTRAL NERVOUS SYSTEM IN THE ACUTE STAGE OF EXPERIMENTAL HEAD INJURY

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The total acetylcholine concentration and the cholinesterase activity were determined in different parts of the brain, the liver, and the blood in experiments on 91 rabbits in the acute stage of experimental head injury. During the first minutes after injury the total acetylcholine concentration in the brain is increased while the cholinesterase activity is lowered. Normal levels of cholinergic substances are restored 24 h after injury.

The basis of the pathogenesis of head injury is considered to be "functional asynapsia" [1, 2]. Having regard to the chemical nature of nervous excitation, investigation of the primary components of neurohumoral changes would appear to be an adequate method for studying the functional state of an organism. These components include the mediator systems and among them the acetylcholine– cholinesterase system. Most workers have studied cholinergic processes in acute head injuries and have based their conclusions purely on the dynamics of cholinesterase activity. Some investigators have studied the relationship between acetylcholine and cholinesterase in head injury purely in the cerebrospinal fluid and blood. It is only in a paper by Kamenetskaya [3] that a parallel is drawn between the degree of accumulation of acetylcholine in the brain and the permeability of the blood-brain barrier in brain injury.

The object of the present investigation was to study the dynamics of cholinergic processes (from the acetylcholine concentration and cholinesterase activity) in the brain substance, the liver, and blood in the acute stage of head injury.

TABLE 1. Acetylcholine Concentration (in μg/g) in Brain after Head Injury (M ± m)

Cause and time of death of animals	Number of animals	Test object			
		cerebral cortex	anterior hypothalamus	posterior hypothalamus	medulla
Decapitation (control)	6	1.75 ± 0.48	2.6 ± 0.45	3.3 ± 0.49	1.84 ± 0.32
Death 1-5 min after injury	6	3.4 ± 0.76 P < 0.2	4.1 ± 0.55 P < 0.1	6.37 ± 0.8 P < 0.2	4.74 ± 0.71 P < 0.02
Decapitation 30 min after injury .	6	6.5 ± 1.1 P < 0.01	8.2 ± 1.35 P < 0.01	10.5 ± 1.5 P < 0.01	7.45 ± 0.75 P < 0.01
Decapitation 3 h after injury. . . .	6	7.9 ± 0.5 P < 0.001	9.0 ± 1.04 P < 0.01	8.46 ± 0.9 P < 0.01	6.43 ± 0.49 P < 0.001
Decapitation 24 h after injury. . .	6	3.05 ± 1.5 P > 0.05	2.5 ± 0.9 P > 0.05	3.9 ± 1.3 P > 0.05	2.7 ± 0.98 P > 0.05

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TABLE 2. Cholinesterase Activity (in mg/g/h) in the Brain in the Acute Stage of Head Injury (M ± m)

Cause and time of death of animals	No. of animals	Test object						
		cerebral cortex	anterior hypothalamus	posterior hypothalamus	medulla	liver	blood
Decapitation (control)	10	44,3 ± 2,45	78,16 ± 6,36	79,01 ± 2,84	69,56 ± 5,4	17,2 ± 2,03	5,6 ± 0,4
Death 1-5 min after injury	19	35,0 ± 2,24	58,2 ± 4,7	60,37 ± 4,1	55,97 ± 2,7	9,72 ± 1,17	—
		$P < 0,01$	$P < 0,02$	$P < 0,001$	$P < 0,05$	$P < 0,001$	
Decapitation 30 min after injury	10	33,1 ± 3,24	57,3 ± 6,5	58,3 ± 4,95	53,3 ± 6,62	11,1 ± 1,35	3,7 ± 2,08
		$P < 0,02$	$P < 0,05$	$P < 0,01$	$P > 0,05$	$P < 0,01$	$P < 0,05$
Decapitation 3 h after injury	8	34,6 ± 1,55	58,7 ± 4,7	59,1 ± 4,58	57,2 ± 2,63	18,0 ± 2,1	4,1 ± 0,39
		$P < 0,01$	$P < 0,05$	$P < 0,01$	$P < 0,01$	—	$P < 0,01$
Decapitation 6 h after injury	8	36,4 ± 1,73	56,1 ± 3,92	64,6 ± 3,95	60,3 ± 4,92	14,0 ± 1,16	4,3 ± 0,37
		$P < 0,05$	$P < 0,01$	$P < 0,01$	$P > 0,05$	$P < 0,1$	$P < 0,01$
Decapitation 24 h after injury	6	37,9 ± 0,91	71,0 ± 5,55	64,8 ± 4,25	62,0 ± 6,33	10,5 ± 2,6	4,0 ± 0,17
						$P < 0,01$	$P < 0,01$

EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on 91 noninbred rabbits, 16 of which formed the control group (killed instantaneously by decapitation). Head injury was caused by allowing a weight of 3.5-4 kg to fall from a height of 2 m on to the parieto-occipital region of the head of the animal while fixed to a frame. Microscopic and macroscopic studies of the internal organs were made.

The dynamics of the cholinergic substances were studied in the cerebral cortex, anterior and posterior hypothalamus, and medulla, and also in the liver and blood. Cholinesterase activity was determined by Hestrin's method [4], and the total acetylcholine concentration by a biological method on the eserinized rectus abdominis muscle of a frog.

When the animals died quickly after head injury (1-5 min), the total acetylcholine concentration in the parts of the brain tested showed a marked increase of 180-257%, while cholinesterase activity was reduced by 20-25% (Tables 1 and 2). During the first hours after closed head injury, a steady increase in the total acetylcholine concentration was observed to reach a maximum after 30 min-3 h (in some parts the concentration increased by 4 times or more), followed by a decrease toward the end of the first day. Meanwhile the cholinesterase activity 30 min-3 h after injury was lowered by 25-30%, and this was followed (after 6 h) by recovery. However, the initial level had not been restored by the end of the first day.

The changes discovered in the acetylcholine concentration concern the total acetylcholine, most of which is in a bound state, while the excess of free acetylcholine enters the blood stream. This is clear from the results of a study of the dynamics of the free acetylcholine fraction in the blood. The free acetylcholine concentration 5 and 10 min after injury was the same as initially (before injury). The first considerable liberation of the free fraction into the blood (10-20 times above its initial level) was observed 30 min after injury; by 1-2 h the concentration showed a sharp increase (80 times) and this was followed by a gradual decrease until 3 h. However, the free acetylcholine concentration was still high 3 and 24 h after injury. Consequently, free acetylcholine accumulates in the blood because of an increase in the total acetylcholine concentration in the brain, following it after a delay of 30-60 min.

The reaction of the cholinergic structures to head injury thus develops immediately after the action of the traumatic agent and reaches a maximum 30 min-3 h after injury. Although some return to normal is observed 24 h after brain injury, nevertheless at this time a state of humoral subcompensation is observed. These changes are due not only to functional changes in the diencephalon and brain stem, but also to the presence of foci of softening and to microscopic and macroscopic hemorrhages.

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