ACETYLCHOLINESTERASE AND BIOELECTRIC ACTIVITY OF THE BRAIN UNDER THE ACTION OF ESERINE AND GALANTHAMINE IN ANIMALS WITH PREMESENCEPHALIC SECTION OF THE BRAIN

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In our previous investigations [1], under the action of anticholinesterase substances (galanthamine and eserine), a definite parallelism was noted between the degree of inhibition of acetylcholinesterase in various portions of the brain and the changes in the EEG and behavior. It was hypothesized that inhibition of the acetylcholinesterase activity in the mesencephalon plays a great role in the mechanism of the activating action of anticholinesterase substances.

With this as a background, there is special interest in a comparative study of the effect of anticholinesterase substances with respect to the bioelectric and acetylcholinesterase activity of the brain in animals with premesencephalic section, when the anatomical connections of the mesencephalic reticular formation with the higher-lying divisions of the brain are disrupted. The detection of such relationships during premesencephalic section and a comparison of them with the effect of the action of anticholinesterase substances in the case of cerveau isolé may aid in elucidating the role of inhibition of the acetylcholinesterase activity in the mesencephalic reticular formation in the mechanism of cholinergic EEG activation. This is possible, since there is a difference in the central effect of anticholinesterase substances during cerveau isolé, i.e., when the connections of the rostral portion of the reticular formation with the higher lying divisions of the brain are preserved, and in the case of premesencephalic section, when they are disrupted [2-4].

EXPERIMENTAL

The experiments were performed on 37 cats. The acetylcholinesterase activity was determined photoelectricolorimetrically according to the procedure of G. A. Panosyan [5]. The biocurrents of the brain were drawn off bipolarly, using steel needles implanted in the bone in portions corresponding to the projections of the sensomotor and optical regions of the cortex, and were recorded on an eight-channel ink-writing electroencephalograph produced by the Kaiser Company. A parallel study of the change in the bioelectric and acetylcholinesterase activities of different portions of the brain was conducted on animals with sections of the brain stem along the planes passing in front of the anterior corpora quadrigemina and emerging at the base of the brain behind the mammillary bodies (premesencephalic section) and between the anterior and posterior corpora quadrigemina (cerveau isolé according to Bremer [6, 7]. The sections were performed both mechanically and electrolytically. The procedure for recording the EEG and section of the brain was described in greater detail earlier [4]. The substances studied—galanthamine and eserine—were injected intravenously.

RESULTS

Our investigations indicated (Table 1) that in the case of total cutoff of the mesencephalon by a premesencephalic section, the acetylcholinesterase activity is inhibited by the injection of galanthamine in all the divisions of the brain studied no less than in animals with an intact brain. In certain divisions of the brain above the section,

TABLE 1. Acetylcholinesterase Activity* of Various Divisions of the Brain in Cats with Premesencephalic Section, During Intravenous Injection of Galanthamine in a Dose of 9 mg/kg

Division of brain	Norm	Intact brain	Premesencephalic section
Cortex	0,34 ± 0,08	0	0,001 ± 0,0001
Thalamus	0,53 ± 0,05	0,014 ± 0,001	0,09 ± 0,03
Hypothalamus	0,56 ± 0,05	0,08 ± 0,01	0,06 ± 0,1
Mesencephalon	9,58 ± 0,02	0,2 ± 0,03	0,16 ± 0,02
Medulla oblongata	0,63 ± 0,03	0,13 ± 0,05	0,62 ± 0,05

*Expressed in 0.001 M acetic acid per 0.2 ml of brain homogenate

TABLE 2. Acetylcholinesterase Activity of Divisions of the Brain in Cats with Premesencephalic Section After Intravenous Injection of Eserine in a Dose of 0.9 mg/kg

Division of brain	Norm	Intact brain	Premesencephalic section
Cortex	0,34 ± 0,08	0,001 ± 0,013	0,04 ± 0,001
Thalamus	0,53 ± 0,05	0,055 ± 0,015	0,12 ± 0,04
Hypothalamus	0,56 ± 0,05	0,08 ± 0,038	0,14 ± 0,05
Midbrain	0,58 ± 0,02	0,12 ± 0,038	0,16 ± 0,04
Medulla oblongata	0,63 ± 0,03	0,1 ± 0,19	0,11 ± 0,04

the acetylcholinesterase activity is even somewhat more inhibited than in animals with an intact brain, which is probably due to disruption of the hematoencephalic barrier. In a parallel study of the bioelectric activity of the brains of these animals, no presence of an EEG activation reaction was detected (Fig. 1), in spite of the almost total inhibition of acetylcholinesterase in the regions lying above the plane of section (in the diencephalic region to 10.7-16.9% of the norm, in the cerebral cortex to 0.03%).

An analogous picture is also noted after the injection of eserine (Table 2). The use of eserine in a dose of 0.9 mg/kg is due to the fact that to obtain the same effect as in the injection of galanthamine (9 mg/kg), the dose ratio of these substances comprises 1:10-12 [5]. In a comparison of the action of anticholinesterase substances in animals with intact brain and with cerveau isolé, it is found that in this case doses of galanthamine and eserine even two to three times lower induce not only inhibition of the acetylcholinesterase activity, but also a distinct change in the bioelectric activity of the brain in the form of EEG activation (Fig. 2).

Thus, the data obtained in experiments with cutting of the brain stem at various levels, in particular when the mesencephalon is cut off, indicated that the EEG activation observed after the injection of galanthamine and eserine cannot be explained by inhibition of the anticholinesterase activity in the diencephalic region and cerebral cortex. The appearance of EEG activation after the injection of anticholinesterase substances depends on the degree of inhibition of the acetylcholinesterase activity precisely in the mesencephalic portion of the brain. Consequently, the final effect of the action of anticholinesterase substances, the presence of cortical EEG activation, is determined not only by the influence on the acetylcholine–cholinesterase system, but also by the need for the presence of association between the cerebral cortex and mesencephalic reticular formation.

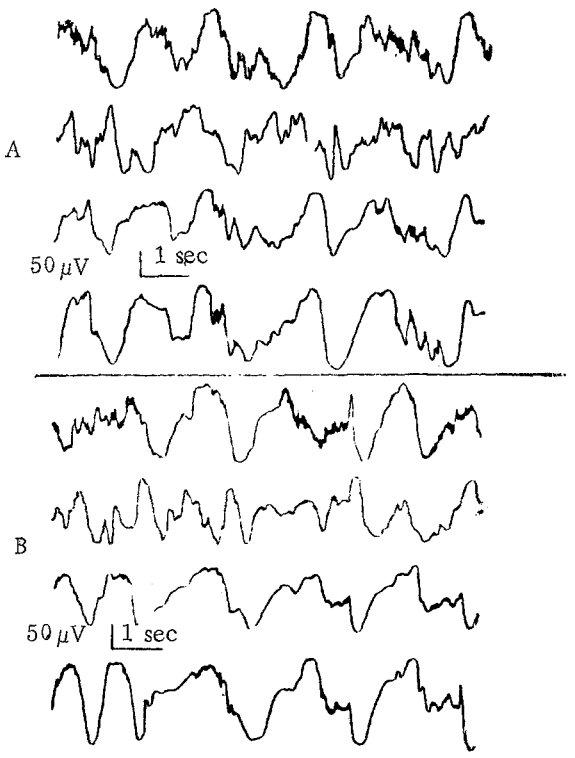

Fig. 1. Effect of galanthamine on the bioelectric activity in cats (premesencephalic section of brain) before (A) and 2 min after its intravenous injection in a dose of 9 mg/kg (B). Significance of the curves (top to bottom): EEG of left and right sensomotor and optical regions of the cerebral cortex.

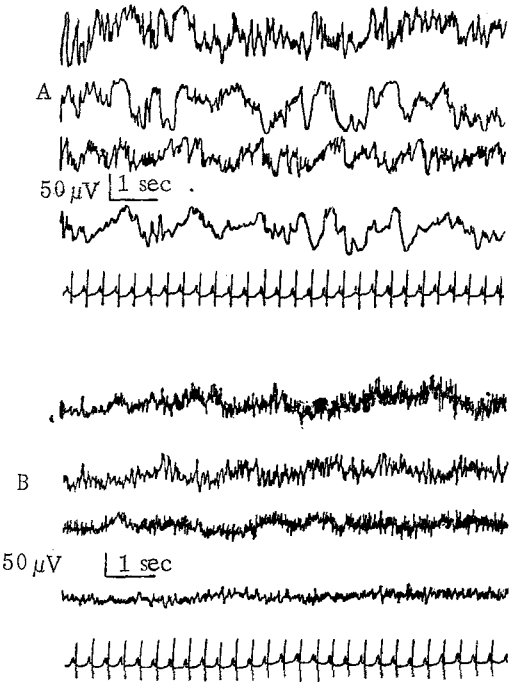

Fig. 2. Effect of galanthamine on the bioelectric activity in cats (intact brain). Significance of curves (top to bottom): EEG of left and right sensomotor and optical regions of the cerebral cortex; EEG: A) before, B) 4 min after intravenous injection of galanthamine (9 mg/kg).

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
