

# SOME DATA ON ESERINE'S EFFECT ON THE CEREBRAL CORTEX OF WHITE RATS

## COMMUNICATION 1. THE EFFECT OF ESERINE ON CONDITIONED REFLEX ACTIVITY

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Eserine's effect on the functional activity of the cerebral cortex has not been adequately investigated [6, 9, 14, 18, 19, et al.], and the data obtained with the help of the conditioned reflex method do not concern the effect of eserine itself on the conditioned reflex activity of animals so much as the antagonism between eserine's effect and that of various cholinolytic substances [10, 16]. As for morphological research, the only relevant data we could find in the literature were those of S. A. Sarkisov and T. M. Mokhova [11] regarding the structural changes in the neurons and interneuronal synapses of rats given eserine. This work demonstrated that the change in the electrical activity of the cortices (motor and visual) effected by convulsant doses of eserine is attended by pathological changes in the nerve cells and their processes. This brings up the question of whether eserine only affects the condition of neurons and interneuronal synapses when used in convulsant doses, or whether smaller doses of the drug can have a similar effect; the question of histochemical changes is also interesting, and has not been studied at all.

The important role of ribonucleic acid (RNA) in the functional activity of the nerve cells is becoming more and more apparent. Most authors espouse the opinion of Caspersen regarding the participation of RNA in the synthesis of proteins. Many investigations have demonstrated the link between the functional condition of neurons and their RNA content [2, 3, 4, 7, 8, 12, 13, 15, 16, 18, et al.].

The above formed the basis for our study of how different doses of eserine affect the dynamics of conditioned reflex activity in rats and the condition of the neurons (their morphology and RNA content) and structure of the interneuronal synapses in the cerebral cortex of rats.

### EXPERIMENTAL METHOD

The investigation was performed on 35 male white rats weighing 200-300 g each, kept in a vivarium and fed the usual diet. Stable positive motor-food reflexes were developed in the animals over a period of 1½ months by L. I. Kotlyarevskii's method [5]. The conditioned stimulus used was a bell of average force, the total effect of which lasted ten seconds. Seven combinations were given daily at intervals of 30-40 seconds. The conditioned reflex was considered to be developed if the rat responded correctly to the conditioned stimulus without reinforcement in every case or in five out of seven cases. Our purpose in this work did not require us to determine

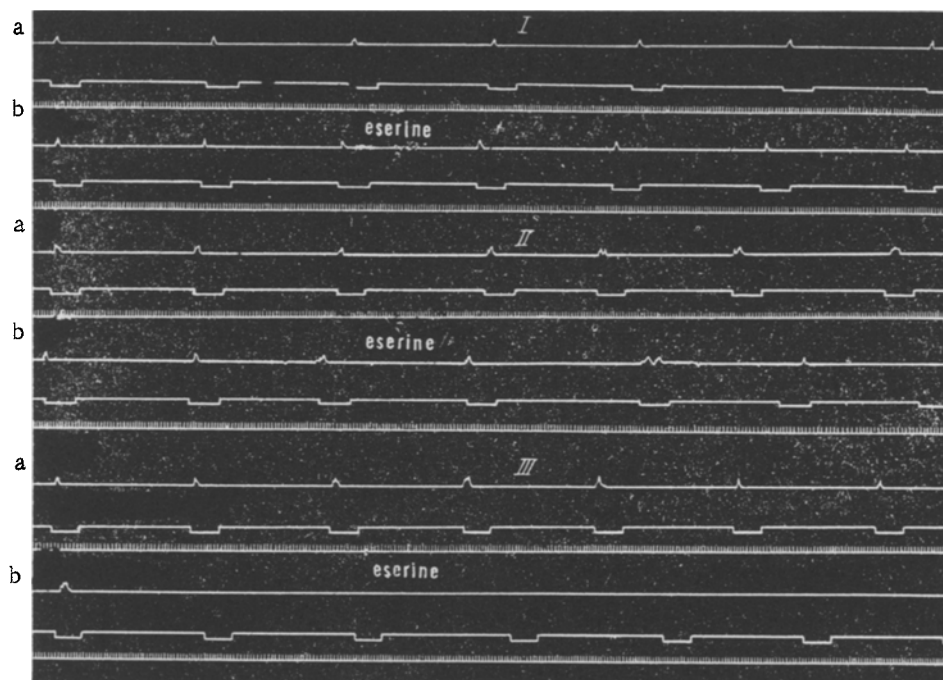
the animals' type of higher nervous activity, but the animals chosen for the experiments were those in which conditioned reflexes were developed by approximately equal numbers of combinations. Conditioned reflex activity was evaluated according to the duration of the latent period of the reflexes and to the force of the motor reaction.

The experimental animals were divided into three series. Eserine was subcutaneously injected 50-60 minutes before the animal was put into the chamber in a dose of 0.01 mg per 100 g body weight in the first series of animals, in a dose of 0.02 mg per 100 g body weight in the second and in a dose of 0.1 mg per 100 g body weight in the third series. The control animals were injected at the same times with the same doses of a saline solution.

## EXPERIMENTAL RESULTS

The investigation showed that the administration of salt did not, as a rule, change the conditioned reflex activity of the rats.

In a dose of 0.01 mg per 100 g (see figure, I, *b* and Table 1), eserine shortened the latent period of the conditioned reflexes and caused some increase in the force of the motor reaction (rats No. 2 and 9). In several cases, single (rats No. 23 and 25) or repeated (rat No. 28) intersignal runs could be observed, although, in these cases, the administration of eserine did not cause change in the force of the motor reaction. The duration of the latent period and the force of the motor reaction were normal on the days following the injection of this dose of eserine.



Change in conditioned reflex activity of white rats effected by eserine. a) Before eserine injection; I, b) eserine injected in a dose of 0.01 mg per 100 g animal weight; II, b) eserine injected in a dose of 0.02 mg per 100 g weight; III, b) eserine injected in a dose of 0.1 mg per 100 mg weight.

When eserine was administered in a dose of 0.02 mg per 100g weight (see figure, II, *b* and Table 2), a stable change in the length of the latent period was observed in most of the animals; the latent period was usually shorter at the beginning of the experiment than it was before the eserine injection, but became longer at the end of the experiment. In some of the animals (rats No. 6 and 16), the force of the motor reaction was greater during the first 1-4 combinations in the experiment than before the eserine injection, but gradually decreased towards the end of the experiment; in other animals, however, the eserine injection either did not change

TABLE 1

Effect of Eserine Administered in a Dose of 0.01 mg per 100 g Weight on the Conditioned Reflex Activity of White Rats

Rat No.	Body wt. (in g)	Experiment date	Experimental conditions	Combina- tion No.	Duration of latent period (in seconds)	Force of motor reac- tion(in mm)	Remarks
9	260	Aug. 18, 1958	Eserine not ad- ministered	237	2	6	Food eaten
				238	2	6	" "
				239	2	6	" "
				240	2	6	" "
				241	2.5	5	" "
				242	2	6	" "
				243	1.5	7	" "
9		Aug. 19, 1958	Eserine injected 50 minutes be- fore experiment	244	1.5	6.5	Food eaten
				245	1	6.5	" "
				246	1	6.5	" "
				247	1	6.5	" "
				248	1.5	6	" "
				249	2	5.5	" "
				250	1.5	6	" "
25	280	March 11, 1959	Eserine not ad- ministered	210	2.5	7	Food eaten
				211	2	7	" "
				212	2.5	7	" "
				213	2.5	7	" "
				214	2	7.5	" "
				215	2.5	7	" "
				216	2.5	6	" "
25		March 12, 1959	Eserine injected 60 minutes be- fore experiment	217	2 intersignal	7	Food eaten
				218	2	7	" "
				219	1.5	7	" "
				220	2	7	" "
				221	1.5	7	" "
				222	2	7	" "
				223	2	7	" "
28	250	March 24, 1959	Eserine not ad- ministered	230	2.5	5.5	Food eaten
				231	2.5	5.5	" "
				232	2.5	5	" "
				233	2.5	5.5	" "
				234	2.5	5.5	" "
				235	2.5	5.5	" "
				236	2	6	" "
28		March 25, 1959	Eserine injected 50 minutes be- fore experiment	237	2 intersignal	5.5	Food eaten
				238	2 intersignal	5.5	" "
				239	2 intersignal	5.5	" "
				240	3 intersignal	6	" "
				241	2 intersignal	6	" "
				242	1.5 intersignal	5.5	" "
				243	1.5	6	" "

TABLE 2

Effect of Eserine Administered in a Dose of 0.02 mg per 100 g Weight on the Conditioned Reflex Activity of White Rats

Rat No.	Body wt. (in g)	Experiment date	Experimental conditions	Combination No.	Duration of latent period (in seconds)	Force of motor reaction (in mm)	Remarks
16	240	Aug. 22, 1958	Eserine not administered	229	2	6	Food eaten
				230	2	6	" "
				231	1.5	6	" "
				232	2	6.5	" "
				233	2	6	" "
				234	2	6	" "
				235	2.5	5	" "
16		Aug. 23, 1958	Eserine injected 50 minutes before experiment	236	0.5	7.5	Food eaten
				237	1.5	7	" "
				238	1.5	7	" "
				239	0.5	7	" "
				240	6	6	" "
				241	8	5	" "
				242	no reaction	—	Did not approach
24	260	Mar. 11, 1959	Eserine not administered	202	3.5	8	Food eaten
				203	2	8	" "
				204	2	8	" "
				205	2	8	" "
				206	1	8	" "
				207	2	7	" "
				208	2	7	" "
24		Mar. 12, 1959	Eserine injected 60 minutes before experiment	209	1	7	Food eaten
				210	3	6	" "
				211	3	6.5	" "
				212	3.5	6	" "
				213	4	6	" "
				214	5	6	" "
				215	4.5	6	Not eaten
29	260	Mar. 24, 1959	Eserine not administered	190	2	5.5	Food eaten
				191	2	5	" "
				192	2	5.5	" "
				193	1	6	" "
				194	2	5.5	" "
				195	2	5.5	" "
				196	3.5	5.5	" "
29		Mar. 25, 1959	Eserine injected 50 minutes before experiment	197	1 intersignal	6	Food eaten
				198	2	5	" "
				199	2	5	" "
				200	1.5	5	" "
				201	2.5	5.5	" "
				202	4	5	" "
				203	5	5	" "

(rats No. 14 and 26) or reduced (rats No. 24 and 29) the force of the motor reaction. The motor reaction to the positive conditioned stimulus was sometimes observed to disappear at the end of the experiment (rats No. 6 and 26). The duration of the latent period and the force of the motor reaction were, as a rule, restored on the days following the experiments with eserine. The repeated administration of eserine caused a more acute disturbance of the rats' conditioned reflex activity; the latent period of the conditioned reflexes increased to such an extent

TABLE 3

Effect of Eserine Administered in a Dose of 0.1 mg per 100 g Weight on the Conditioned Reflex Activity of White Rats

Rat No.	Body wt. (in g)	Experiment date	Experimental conditions	Combina- tion No.	Duration of latent period (in seconds)	Force of motor reac- tion (in mm)	Remarks
21	240	Aug. 22, 1958	Eserine not ad- ministered	233	2	7	Food eaten
				234	2	7	" "
				235	2	6	" "
				236	2	7	" "
				237	2	7	" "
				238	2	7	" "
				239	2	6	" "
21		Aug. 23, 1958	Eserine injected	240	4	6	Abandoned the food
				241	no reaction	—	Did not approach
				242	" "	—	" " "
				243	" "	—	" " "
				244	" "	—	" " "
				245	" "	—	" " "
				246	" "	—	—
27	300	Mar. 11, 1959	Eserine not ad- ministered	215	2 intersignal	8	Food eaten
				216	1 intersignal	7	" "
				217	2	7	" "
				218	2	7	" "
				219	2	7	" "
				220	2.5	7	" "
				221	2	7	" "
27		Mar. 12, 1959	Eserine injected 60 minutes be- fore experiment	222	2.5	5.5	Food eaten
				223	4	7	" "
				224	8	6	" "
				225	jerkings	—	Did not open door
				226	7	6	Food eaten
				227	8	4	" "
				228	8.5	4.5	Did not eat
30	240	Mar. 24, 1959	Eserine not ad- ministered	199	1.5	6	Food eaten
				200	3	6	" "
				201	2	6	" "
				202	2	5	" "
				203	2	5.5	" "
				204	2	6	" "
				205	2	6	" "
30		Mar. 25, 1959	Eserine injected 50 minutes be- fore experiment	206	4	5	Did not take the food
				207	no reaction	—	Did not approach
				208	23	4.5	Did not take the food
				209	10	5	Food eaten
				210	no reaction	—	Did not approach
				211	the same	—	" " "
				212	" "	—	" " "

that the motor reaction to the positive conditioned stimulus often disappeared. The unconditioned food reflex was retained, however; if food were placed on the floor of the chamber, the rat would eat it.

In a dose of 0.1 mg per 100 g body weight, eserine induced the development of a convulsive attack 13-18 minutes after the subcutaneous injection of the preparation. After the attack (see figure, III, *b* and Table 3), we observed the animals' conditioned reflex activity to be acutely disturbed; the latent period of the conditioned reflexes was so prolonged (rat No. 27) that the motor reaction to the positive conditioned stimulus often disappeared (rats No. 21 and 23). Although there was a considerable increase in the duration of the latent period, the force of the motor reaction varied; it either decreased (rats No. 21, 27 and 30), remained as before the eserine injection (rat No. 8) or even increased (rat No. 7).

Repeated administration of eserine in convulsant doses usually caused a more acute disturbance of the conditioned reflexes.

The type of change in the duration of the conditioned reflex latent period induced by the administration of the different doses of eserine to rats indicates that, in a dose as low as 0.01 mg per 100 g body weight, eserine affects the interneuron transmission of impulses, as shown by the shortening of the latent period of food-motor conditioned reflexes. When the dose is increased, eserine's effect disturbs the transmission of nerve impulses in the interneuronal synapses, as indirectly expressed by prolongation of the latent period of the reflexes up to the complete disappearance of the motor reaction.

The facilitating effect of eserine in small doses may be associated with the exaltation phase of this substance's effect discovered by L. S. Lanskaya [6] in experiments with mice given physiological doses of eserine (0.08-0.1  $\gamma$  per 1 g weight).

#### SUMMARY

The study of the effect of eserine on the conditioned reflexes of white rats has demonstrated that its various doses exert a different effect on the conditioned reflex activity. In a dose of 0.01 mg per 100 g of body weight eserine reduces the latent period of the food-motor conditioned reflexes. Higher doses of eserine disturb the nerve impulse transmission in the interneuronal synapses; this is manifested in a considerable prolongation of the reflex latent period up to complete disappearance of the motor reaction to the positive conditioned stimulus.

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