THE EFFECT OF ANTICHOLINESTERASE PREPARATIONS ON THE DARK ADAPTATION OF THE EYE

G. N. Sorokhtin, M. S. Trusov and M. L. Raev

From the Department of Physiology (Head – Prof. G. N. Sorokhtin) of the Khabarovsk Medical Institute)

(Received September 16, 1956. Submitted by Active Member of the Acad. Med. Sci. SSSR V.N. Chernigovsky)

The present work is a continuation of investigations carried out in this department on the study of the effect of anticholinesterase preparations on varous functions of the body [6,7,8 and 9]. Its object was to investigate the effect of eserine and prostigmin on the dark adaptation of the eye in the healthy human subject.

EXPERIMENTAL METHOD

After a 30 minute period of dark adaptation in a dark room, a 5 minute exposure to light was given. Thereafter, every 5 minutes, the light sensitivity of areas of the retina situated within 15° of the macula was measured with a Nagel adaptometer during adaptation of the eye to darkness.

The light sensitivity of the eye was determined by a Kravkov-Vishnevsky apparatus and a model "AM" Belostotsky-Hoffmann adaptometer in accordance with its operational instructions.

For each subject we determined the rate of dark adaptation and the light sensitivity of the eye before and after the intramuscular injection of physiological saline (0.6 ml) and after intramuscular injection of the preparations. The following preparations were used: eserine (Physostigminum salicylicum [Merck] in a dose of 0.2-0.6 mg, prostigmin (Prostigminum [La Roche]) and proserine* (Proserinum, [NIKhFI]), in doses of 0.15-0.3 mg. To determine the duration of the action of the anticholinesterase preparations, the dark adaptation and light sensitivity of the eye were examined for 2 days.

EXPERIMENTAL RESULTS

The rate of adaptation, measured by Nagel's apparatus, is shown from results of 41 observations (Tables 1 and 2).

In the normal subject with no preparation injected or after injection of physiological saline, dark adaptation of the eye was effected in 25-50 minutes, being complete on the average in 41 minutes. All the experiments of injection of physiological saline gave the same results as without injection. Injection of all the anticholinesterase preparations gave acceleration of adaptation by 2-5 times (average 3) in all experiments without exception.

In the normal subject, without injection and after injection of physiological saline, the threshold of dark

* Prostigmin and proserine are identical preparations (the methyl sulfate of the dimethylcarbamino complex ether of oxyphenyltrimethylammonium).

adaptation of the eye averaged 2400-4000 Nagel adaptometer units, with a mean value of 3200. Injections of anticholinesterase preparations increased the sensitivity of the eye by $1\frac{1}{2}$ - 2 times, with a mean of $1\frac{1}{2}$ times. It was shown by special observations that the action of prostigmin (in a dose of 0.3 mg) lasted 37 hours in subject I. N., after which the rate of dark adaptation and the level of light sensitivity were restored to their original values.

TABLE I

Rate of Dark Adaptation by Nagel's Method in Several Experiments

Subject	O.M.	I.N.	A.D.	A.S.	N.Zh.	Arithmetic mean
Age	46 years	19 years	19 years	26 years	19 years	
With no preparation injection	35. 35. 35. 40	50. 50	35	30	25	41
After injection: of physiological saline	—	50. 50. 50	35. 35. 35 35. 40	25. 30	25. 25	
of eserine	15. 20	10. 10	15. 15. 15	10. 10	10. 10	13.7
of prostigmine	—	10	15. 15	10	—	
of proserine	—	10	20. 20	15. 15	—	
Coefficient of acceleration	2.2—2.0	5	2.3—2.0	3—2	2.5	3

The light sensitivity of the eye was determined in 24 subjects (44 investigations) with the Kravkov-Vishnevsky apparatus and in 44 subjects (50 investigations) with the Belostotsky-Hoffmann adaptometer.

The curves in Fig. 1 demonstrate the changes in the light sensitivity of vision in 24 subjects after intramuscular injection of physiological saline and eserine (taken from mean values). The abscissa represents time after injection in minutes and the ordinate shows the time in seconds during which the subject distinguished the object placed in the apparatus. After injection of eserine the time of distinguishing the object was shortened from 37.8 to 12.4 seconds, i. e. threefold. In some experiments it was reduced to 2-3 seconds.

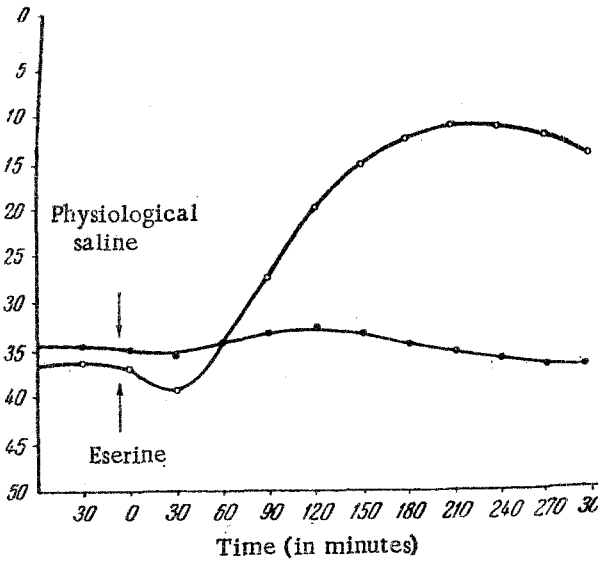

Fig. 1. Effect of eserine on light sensitivity of the normal eye as determined by the Kravkov-Vishnevsky apparatus (mean of 44 observations on 24 subjects).

It must be emphasized that the doses of anticholinesterase preparations which we injected, while increasing the achromatic vision and corresponding to 30-40% of the therapeutic dose given in the Pharmacopeia of the USSR, did not produce any vegetative changes nor influence the subjective state of the experimental subjects.

Investigations with the Belostotsky-Hoffmann adaptometer also showed acceleration of the dark adaptation process and increase in light sensitivity as a result of eserine. The level of dark adaptation corresponding to 40th minute in control experiments was observed at the 20th minute after injection of eserine. The initial light sensitivity (at the 4th minute) was increased on the average from 520 to 1250 relative units to from 30,000 to 54,000 units on the 20th minute and from 68,000 to 110,000 units after 40 minutes. The mean values of the experimental results from 44 subjects are shown in Fig. 2.

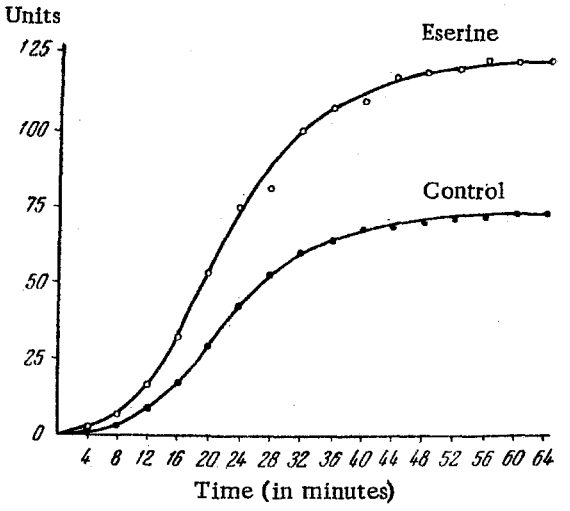

Fig. 2. Effect of eserine on dark adaptation of the normal eye as determined by the Belostotsky-Hoffmann Adaptometer (mean of 50 observations on 44 subjects).

Thus the anticholinesterase preparations described, considerably accelerate dark adaptation (from 2-5 times) and increase by $1\frac{1}{2}$ times the sensitivity of achromatic vision. This testifies to the importance not only of synthesis of visual purple but also of synaptic acetylcholine in the production of dark adaptation to a definite sensitivity of achromatic vision. According to investigations by W. Feldberg [10], the retina contains a large amount of an enzyme synthesizing acetylcholine, while this enzyme is absent from the optic nerve trunk. Bunin [1] showed that in dark adapted retinas of frogs there is a larger acetylcholine content than in light adapted. It must be admitted that perception of light by the subject at the time of dark adaptation depends not only on the state of the acetylcholine mediator of the retina, consisting of a three-membered neuronal chain, but also on the synapses of the external geniculate body and the projection zones of the cerebral cortex, i. e. on mediator exchange in all the links of the optic analysor. A single injection of strychnine in experiments by Kravkov [3,4] also invariably increased the power of discrimination of the eye on the 2nd-3rd day. This effect of strychnine, similar to the action of eserine and proserine, is understandable considering its anticholinesterase properties [11,12,13].

The action of eserine and prostigmin on spinal reflexes, as was first shown by Schweitzer, Stedman and Wright [14] is variable: eserine increases the excitability of the knee reflex, its power and amplitude, while prostigmin shows an inhibitory action on this reflex. In our investigations [8], we demonstrated the great stability of this stimulatory action (not changing into a depressing action) on the motor neuron cell and the respiratory center of the frog, of even massive doses of eserine (100-200 mg/kg), at the same time the biphasic character of the action of considerably smaller doses of proserine (2-10 mg/kg) on the same systems of the frog was shown. The first phase of excitation from the action of proserine usually changed rapidly into a prolonged and stable phase of parabiotic inhibition. Similar differences in the action of eserine and proserine were also noted by us [9] in relation to spinal reflexes in the dog.

TABLE 2

Changes in the Dark Adaptation Threshold (in Nagel Test Units) after Injection of Anticholinesterase Compounds.

Subject	O. M.	I.N.	A.D	A.S.	N.Zh.	Arithmetic mean
Age	46 years	19 years	19 years	26 years	19 years	
No preparation injected	3000 3000 2400 2800	3500 3500	3000	3000	4000	3220
After injection of physiological saline	—	3500 3500	3000 3000 3000 3000 3000	3000 3000	4000 4000	
Eserine	1400 2000	2500 2200	2500 2600 2500	2000 2000	2000 2000	2150
Prostigmin	—	2000 2000	2400 2000	2000	—	
Proserine	—	2000	2300 2500	2000 2000	—	
Coefficient of increase of sensitivity of the eye		1.6	1.6	1.5	2	1.5

The present investigation shows, however, that eserine and proserine act equally and monophasically on the optic analysor. Raev [5] showed the same thing by investigation of the rheobase and chronaxie of the eye. Eserine and proserine lowered the rheobase by 20-25% and lengthened the chronaxie (phosphene) 2.0-6.6 times by comparison with their original state.

The equal – in the type of stable catelectrotonus – action of eserine and proserine on the optic analysor and the different action on the spinal motor neurons of animals and the respiratory center of the frong are the result of the unequal level of lability and functional stability of these particular nerve structures. By the action of eserine and proserine on the foveal sensitivity of the eye, Kravkov [4] and Zaretskaya [2], show that proserine increases the sensitivity of the eye to the whole visible spectrum, while small doses of eserine increase the sensitivity to red and large doses to green light.

SUMMARY

The effect of eserine (Physostigmum salicylicum, Merck) and prostigmin or proserine on the dark adaptation and sensitivity of the eyes to light was studied in healthy adult individuals. Investigations were carried out with the

adaptometer of Nagel, the adaptometer of Belostotsky-Hoffman, as well as with the aid of Kravkov-Vishnevsky apparatus. Intramuscular introduction of small doses of eserine solution (from 0.2 to 0.6 mg) or prostigmin (from 0.15 to 0.3 mg) accelerated the dark adaptation of the eyes and increased the sensitivity of the eye by 1.5-3 times. This effect of eserine and prostigmin is stable and remains for 24 hours or even longer. It is monophasic stimulatory in type. The authors explain the above effect of various anticholinesterase preparations by increased mobilization of the synaptic acetylcholine in the retina, the genu of the internal capsulae and the corresponding projection zone of the brain cortex.

LITERATURE CITED

[1] A. Ya. Bunin, Problemy Fiziol. Opt., 8, 238-246 (1953).

[2] R. B. Zaretskaya, Problemy Fiziol. Opt., 10, 16-22 (1952).

[3] S. V. Kravkov, The Eye and its Work, Izd. AN SSSR (1950)*.

[4] S. V. Kravkov, Problemy Fiziol. Opt., 10, 5-15 (1952).

[5] M. L. Raev, Trudy IV stud. nauchn. sessii Khabarovskogo med. instituta, 99-103 (1950).

[6] G. N. Sorokhtin, Byull. Eksptl. Biol. i Med., 19, 3, 73-77, (1945).

[7] G. N. Sorokhtin and F. E. Poznyakov, Byull. Eksptl. Biol. i med., 25, 33-35 (1948).

[8] G. N. Sorokhtin and M. S. Reizin, Byull. Eksptl. Biol. i Med., 25, 148-151 (1948).

[9] G. N. Sorokhtin and A. S. Suprunenko, Trudy Khabarovskogo med.inst. collection 12, 12-17 (1952).

[10] W. Feldberg and T. Mann, J. Physiol., 104, 411 (1946).

[11] A. C. R. Kaswin, Soc. Biol., 130, 859 (1939).

[12] O. Loewi, Chemical Transmission of Nervous Action Nobel Lect. Stokholm, (1937).

[13] D. Nachmansohn, Bull. Soc. Chim. biol. Paris, 21, 761 (1939).

[14] A. Schweitzer, E. Stedman and S. Wright, J. Physiol., 92, 6, (1938); 96, 302 (1939).

* In Russian.