PHYSIOLOGY

PARTICIPATION OF ACETYLCHOLINE IN THE PROCESS OF ACCOMMODATION AND PARABIOSIS OF THE NERVE TRUNK

L.N. Zefirov and O.S. Kochnev

Department of Normal Physiology (Director – Dr. I.N. Volkova), Kazan Medical Institute

(Received April 23, 1957. Presented by Active Member Acad. Med. Sci. USSR V.N. Chernigovskii)

Our previous communications [7-10] showed that under natural conditions acetylcholine appeared to act not as a stimulating factor but rather as a factor which predominantly determined the reaction of tissue to stimulation. Such tissue reaction is known to be dependent to a considerable degree on the process of accommodation. This led us to investigate the part played by acetylcholine in the accommodation process of the nerve trunk. Taking into account the close connection between accommodation phenomena and parabiosis [3, 4, 14, 17], a simultaneous attempt was made to elucidate the significance of acetylcholine in the development of the parabiotic process.

Literature data on participation of acetylcholine in the development of nerve parabiosis are contradictory. A.A. Zubkov [11] and O.V. Zeidlits [6] postulated that the direct cause of development of parabiosis in nerve was the depolarizing action of acetylcholine; they based this view on data concerning inhibition of nerve cholinesterase activity by narcotics and data on accumulation of acetylcholine in the narcotized area during stimulation.

Conflicting findings are reported by D.A. Lapitskii [13] and L.L. Vasil'ev [3] who established that acetylcholine acted on the altered nerve in a "deparabiotizing" fashion. Recentlyone of us [7] has shown that increase in the lability of the altered area of nerve under the influence of incoming impulses is connected with the formation and action of acetylcholine.

EXPERIMENTAL METHOD

Experiments were performed on the usual frog nerve-muscle preparation (Rana ridibunda). The preparation was put in a moist chamber and the nerve was placed on silver electrodes which had been exposed to chloride before the experiment; the interelectrode distance was 4 mm.

Accommodation was measured by apparatus constructed on the basis of a condenser chronaxiemeter [15, 18] by selection of condensers of appropriate capacity with current strength of 1, 2, 3, etc. rheobase. 5-6 points were usually determined and an accommodation curve was plotted. λ was calculated for current strength of two rheobase according to the formula $\lambda = RC$ [14], where R is the summated resistance of the circuit equal in our installation to 200,000 ohms.

Development of parabiosis in an area of the sciatic nerve was elicited by a DC cathode of definite intensity; complete loss of conduction occurred after 15-20 minutes from the beginning of this treatment. The rate of development of parabiosis (in terms of onset of the inhibitory phase) was noted, as well as the presence and prominence of the different phases, their duration and interrelations. The nerve was stimulated by tetanizing induction current.

Investigations were carried out on normal frogs and on frogs which had been subjected to preliminary removal of the pancreas under sterile conditions. This operation led to impairment of acetylcholine formation in the organism (after varying periods of time) [12], apparently as the result of disturbances of phospholipid metabolism [16]. In the case of control experiments the operated animals received 0.2-0.3 ml acetylcholine solution (1:10,000) systematically into the posterior lymph sac. In part of the experiments accommodation was tested after administration of acetylcholine (1 ml of 1:10,000 solution) or of eserine (1 ml of 1:10,000 solution) to normal animals; it was also tested when solutions of these substances were allowed to act directly on the nerve trunk.

A total of 270 experiments was carried out.

EXPERIMENTAL RESULTS

Experiments on normal frogs showed fairly considerable fluctuations in the rate of accommodation. The accommodation constant (the reciprocal of the velocity of the accommodation process) had the average value of 25 milliseconds. The rate of accommodation was lower in winter frogs than in autumn frogs (the accommodation constant increasing to an average of 40 milliseconds). The accommodation curve was usually a straight line (Figure 1, Curve 1).

Preliminary (1-2 hours prior to experiment) administration of acetylcholine to the frogs (1 ml 1:10,000 solution) caused a definite decrease in the rate of accommodation. The accommodation constant λ extended to 100 milliseconds on the average, i.e., showed a 3-4-fold increase as compared with the normal. The accommodation curves maintained their straight line character (Figure 1, Curve 2). Analogous results were also obtained in those cases in which acetylcholine was administered 24 hours prior to the experiment.

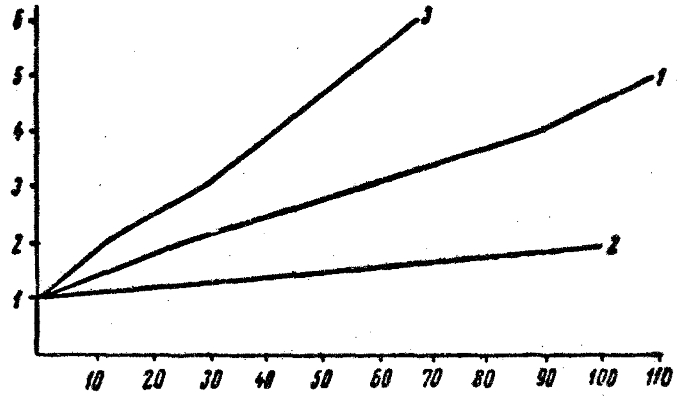

Fig. 1. Accommodation curves for the sciatic nerve (average data) in normal frogs (1), after administration of acetylcholine (2) and on the 8th day after removal of the pancreas (3). Abscissa – rise of stimulating current (RC) in milliseconds; ordinate – threshold strength of stimulus in multiples of rheobase.

Immersion of an area of the sciatic nerve for 15-20 minutes in a 1:50,000-1:100,000 solution of acetylcholine led only to a slight decrease in the rate of accommodation.

Five of the six experiments in which a preliminary administration of eserine was tried showed a definite increase in the rate of accommodation, i.e., an effect opposite to that of acetylcholine. The different influence of acetylcholine and of eserine on the process of accommodation can be explained by the fact that eserine has not only the property of inhibiting cholinesterase with ensuing accumulation of acetylcholine but also, apparently, another property opposed to the action of acetylcholine.

Following removal of the pancreas the excitability of the nerve to DC stimulation underwent a slight and nonuniform change. Thus, on the 7th postoperative day some lowering of excitability was noted. The threshold showed an average rise to 2.2 volts (1.9 volts for normal frogs). Lowering of the threshold could then be observed and by the 10th postoperative day its average value was 1.5 volts.

Figure 2 reflects the dynamics of the changes in the rate of accommodation following removal of the pancreas; it shows that, together with certain fluctuations of the rate of accommodation, there is a perfectly definite and consistent increase in the rate of accommodation on the 6-10th day postoperatively. The changes described were also clearly expressed in the course of the accommodation curve, the most pronounced differences in the rate of accommodation and the course of the curve being observed with a strong stimulating current (5-6 rheobase), i.e., slowly rising currents of low gradient. Figure 1 shows the accommodation curve (3) plotted from average data obtained on the 8th day after removal of the pancreas. It shows that the curve preserves its general straight line character, with a considerably steeper slope than the curve for normal frogs. Systematic administration of small doses of acetylcholine to the operated animals starting from the 3rd-4th day after operation abolished the described deviations and the accommodation values were normal at all periods postoperatively.*

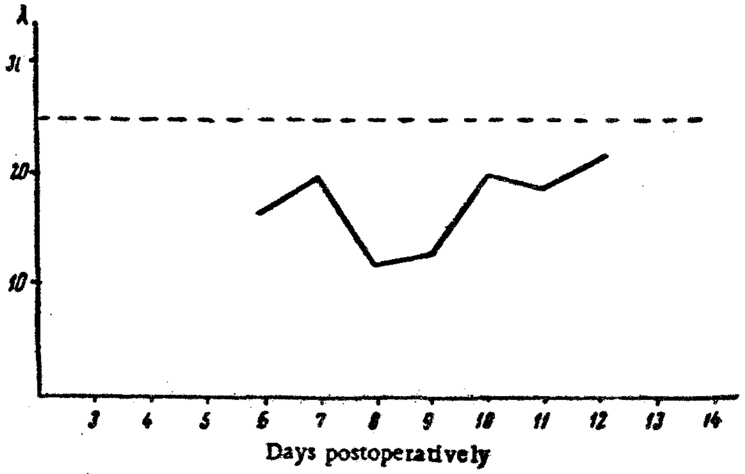

Fig. 2. Change in the accommodation constant of the sciatic nerve in frog following removal of the pancreas. Abscissa – days postoperatively; ordinate – accommodation constant (λ) in milliseconds. Broken line: average value for accommodation constant in normal frogs.

The experimental results described above indicate that acetylcholine given in definite doses elicits quite consistent diminution of accommodation in the nerve trunk. These data were fully confirmed by experiments on removal of the pancreas. Impaired acetylcholine synthesis which occurs under these conditions leads to an opposite change in the accommodation ability of the tissue, viz. its increase.

Since acetylcholine is constantly being formed in the nervous system during its activity, it may be supposed that changes in accommodation occurring under natural conditions in the process of tissue activity are determined to a considerable extent by this chemical agent.

In studying the development of nerve parabiosis, elicited by the action of direct current, it became apparent that following removal of the pancreas in frogs there was considerable reduction in the resistance of the nerve to the change-inducing influence, i.e., the development of the parabiotic process was accelerated with an almost twofold diminution in the strength of effective current necessary to maintain a state of minimal polarization. Figure 3 shows that the change in the rate of development of parabiosis was not uniform on different days postoperatively. Definite acceleration of the development of parabiosis was observed only from the 6th postoperative day and reached a maximum on the 7th-9th day, after which the rate declined and returned to normal along a somewhat fluctuating course.

Removal of the pancreas evoked change in the typical parabiotic phases also. A sharp curtailment and sometimes absence of the paradoxical phase was observed in addition to the disappearance of tonus-like effects described earlier [7]. The typical paradoxical effects were in this case replaced by a number of contractions

*It must be noted that such "compensatory" administration of excessively large doses of acetylcholine (1 ml 1:10,000 solution daily) leads not to a return to normal but to even greater increase in the rate of accommodation.

which decreased progressively and independently of variation in stimulation. The disappearance of such effects and transition to the inhibitory phase occurred rapidly and suddenly. The compensating phase underwent much less marked change. It could, on occasions, be noted from the first few stimulus applications, even without prior alteration.

Systematic administration of acetylcholine to operated animals smoothed out the described changes to a considerable extent and normalized the functional state of the nerve (Figure 3, Curve 3).

The obtained results conflict with the concept of acetylcholine as a factor which directly determines the development of parabiosis in the nerve trunk [6, 11] and indicate that acetylcholine raises the resistance of the nerve to the alteration by stimulating the restorative processes in the tissue.

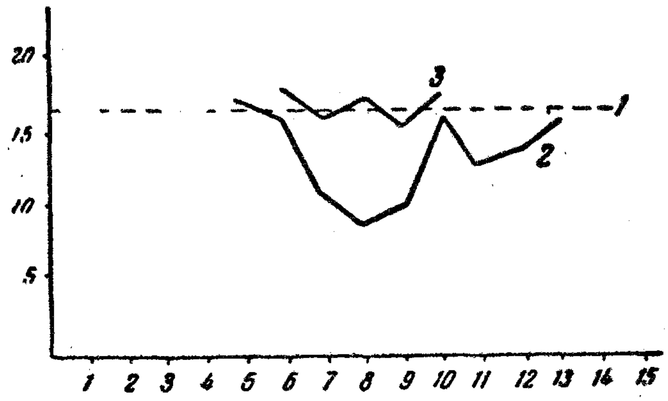

Fig. 3. Rate of development of parabiosis in the sciatic nerve of normal frogs (1), after removal of the pancreas (2) and on compensatory administration of acetylcholine to the operated animals (3). Abscissa – days postoperatively; ordinate – time of onset of inhibitory phase in minutes.

Comparison of results obtained on investigation of accommodation and the rate of development of parabiosis after removal of the pancreas reveals that depression of the functional state of the nerve corresponds to a high rate of the accommodation process. A similar relationship directly confirming the interrelation of accommodation and development of stationary excitation, was described by E.K. Zhukov [5] in the case of preliminary application of a DC cathode to the nerve and by I.A. Arshavskii and co-workers [1] in the course of studying accommodation in the process of ontogenesis.

In contrast to this, L.L. Vasil'ev [2] and L.V. Latmanizova [14] found that a high rate of accommodation was observed when the functional state of the tissue was at a high level and when it showed high resistance to change-inducing activity, and vice versa.

At the present time this contradictory and dual character of accommodation finds explanation in the dynamics of the parabiotic process [3, 4, 14]. It has been established that increase in the rate of accommodation occurs both during the initial, first stage of parabiosis and during the final stage of this process, whereas the transitional phase of parabiosis is characterized by a reduction in the rate of accommodation.

The experimental and literature data cited permit the suggestion that accommodation is a manifestation of the development of local excitation in the tissue elicited by the test stimulus and following the laws of parabiosis. The change in excitability associated with this finds expression in the form of the accommodation process.

SUMMARY

Disturbance of production of acetylcholine in the organism following removal of the pancreas brings about increased speed of accommodation and of development of parabiosis in the sciatic nerve in frog.

Administration of small doses of acetylcholine to operated and normal frogs results in decreased speed of accommodation and of development of parabiosis.

The correlated changes of accommodation and parabiosis demonstrate that these processes are related and allow us to consider the process of accommodation as a manifestation of the development of local excitation due to the effect of stimulation.

LITERATURE CITED

[1] I.A. Arshavskii, Uspekhi Sovremennoi Biol. 32, 1 (4), 18-43 (1951).

[2] L.L. Vasil'ev, Uchenye Zapiski Leningrad. Gos. Universiteta No. 123, 56-72 (1950).

[3] L.L. Vasil'ev, The Significance of the Physiologic Teachings of N.E. Vvedenskii for Neuropathology,* (Leningrad, 1953).

[4] N.V. Golikov, Physiologic Lability and its Utilization in the Main Nervous Processes* (Leningrad, 1950).

[5] E.K.Zhukov, Trudy Leningrad. Ob-va Estestvoispyt. 68, 53-81 (Leningrad, 1940).

[6] O.V. Zeidlits, Biull. Ekspt. Biol. i Med. 7, No. 6, 514-517 (1939); 9, No. 6, 405-406 (1940).

[7] L.N. Zefirov and A.V. Kibiakov, Fiziol. Zhur. SSSR No. 2, 183-190 (1954).

[8] L.N. Zefirov and A.V. Kibiakov, ibid. No. 6, 470-476 (1956).

[9] L.N. Zefirov, A.V. Kibiakov and R.S. Orlov, ibid. 971-976.

[10] L.N. Zefirov and I.G. Shapiro, Biull. Ekspt. Biol. i Med. 43, No. 1, 23-28 (1957).**

[11] A.A. Zubkov, ibid. 6, No. 5, 595-598 (1938).

[12] A.V. Kibiakov and A.A. Uzbekov, ibid. 29, No. 3, 202-205 (1950).

[13] D.A. Lapitskii, in the book: Communications Presented at the Conference in Memory of N.E. Vvedenskii* (Moscow, 1949), page 56-72.

[14] L.V. Latmanizova, Fiziol. Zhur. SSSR No. 3, 342-353 (1950).

[15] L.V. Latmanizova, in the book: Textbook of Practical Human and Animal Physiology* (Moscow, 1954), pages 333-373.

[16] L.I. Leites, Uspekhi Sovremennoi Biol. 18, 2, 214-224 (1944).

[17] A.N. Magnitskii, Biull. Ekspt. Biol. i Med. 5, No. 5-6, 466-470 (1938).

[18] D.I. Solandt, Fiziol. Zhur. SSSR 19, 1, 129-132 (1935).

*In Russian.
**Original Russian pagination. See C.B. translation.