SINGLE MECHANORECEPTORS (PACINIAN CORPUSCLES) STUDIED BY APPLICATION OF COLCHICINE TO THE NERVE

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After application of colchicine to the caudal mesenteric nerve of cats, which contains sensory fibers for single mechanoreceptors (Pacinian corpuscles) the axon of the nerve endings degenerates. The character of the ultrastructural changes in the receptor is virtually identical with that observed during degeneration of axons after division of the nerve, but degeneration takes place much more slowly. The ultrastructural, electrophysiological, and biochemical changes taking place in the Pacinian corpuscles are not the result of the direct effect of the alkaloid, but are realized through the nerve, evidently by the blocking of axoplasmic transport. The results are evidence in support of the view that the structures of the receptor are under neurotrophic control by sensory neurons.

KEY WORDS: duodenum; electrical activity before and after feeding.

To explain the trophic effect of nerve on tissue it has been postulated that certain unidentified substances are synthesized in the neuron bodies, transported along the axons, secreted in the terminals, and exert a trophic influence on the innervated structures [6]. This hypothesis has been confirmed in experiments with colchicine block of axoplasmic transport in the sciatic nerve. Neuromuscular transmission was preserved under these circumstances but typical denervation changes developed in the skeletal muscle [4, 10]. It is considered that the trophic effects of the nerve on primary and secondary sensory receptors [2, 3] can be explained within the framework of this hypothesis [12, 14]. No experimental verification of this hypothesis has been undertaken.

For this purpose experiments were carried out on single mechanoreceptors of Pacinian corpuscles of the cat mesentery during blocking of axoplasmic transport by colchicine in the caudal mesenteric nerve. At different times of the experiments electrical responses of the mechanoreceptors in the Pacinian corpuscles, their ultrastructure, and their alkaline phosphatase activity were studied.

EXPERIMENTAL METHOD

Sexually mature animals were used. After laparotomy the region of the caudal mesenteric ganglion was exposed and colchicine (Fluka) applied to a nerve leaving the ganglion and containing sensory fibers for Pacinian corpuscles. The alkaloid was applied in two different manners. In the experiments of series I, 0.25 mg colchicine polymerized in polyvinyl alcohol was applied to the nerve, and gradual absorption of the alkaloid prolonged its action on the nerve. In the control, the polymer only was applied to the nerve. In the experiments of series II the nerve was painted for 10 min with 1 ml of a 1 mM solution of the alkaloid. In the experiments of series III the caudal mesenteric nerve was divided. The Pacinian corpuscles were studied 12, 24, 48, and 72 h after application of colchicine. For electron-microscopic investigation the receptors were fixed in 2% glutaraldehyde, postfixed in osmium tetroxide, and embedded in Epon-Araldite. The receptor potentials (RP) of the isolated Pacinian corpuscles were studied by the standard method [1]. In some experiments the receptors were perfused with 2.5 and 10 mM solutions of colchicine. Alkaline phosphatase activity was determined in homogenates of receptors by the use of sodium p-nitrophenylphosphate [5] after equalization of the protein concentration. In the control, enzyme activity was studied after incubation (60 min, 37°C) of the homogenates in 1 mM colchicine solution.

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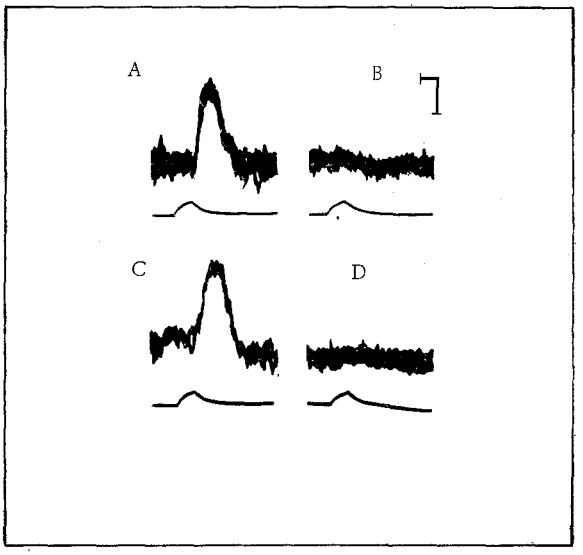

Fig. 1. Changes in RP of Pacinian corpuscles after application of colchicine to nerve. A, B) 24 and 48 h, respectively, after application of colchicine with polymer to nerve; C, D) 12 and 24 h, respectively, after brief application of colchicine solution. Top beam records RP, bottom beam mechanical impulse. Calibration: 50 μV, time marker 2 msec.

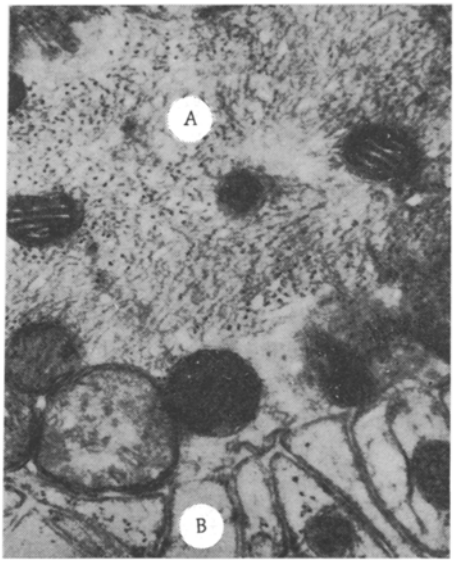

Fig. 2

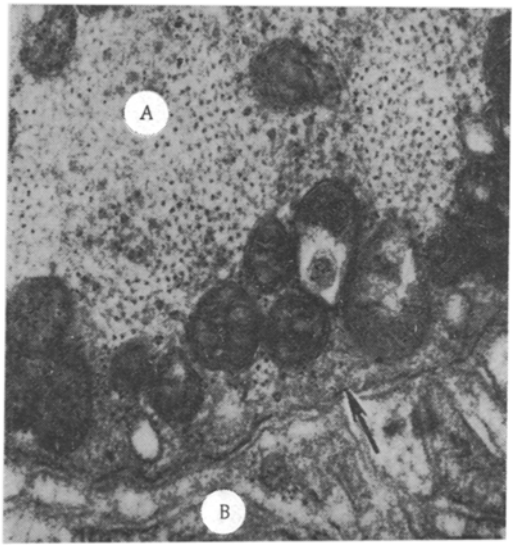

Fig. 3

Fig. 2. Part of axon and inner bulb of Pacinian corpuscle 48 h after application of colchicine with polymer to nerve. A) Axon; B) processes of cells of inner bulb. 33,000×.

Fig. 3. Part of axon and inner bulb of Pacinian corpuscle 24 h after application of colchicine solution to nerve. Arrow indicates axolemma. Remainder of legend as in Fig. 2. 29,000×.

EXPERIMENTAL RESULTS AND DISCUSSION

In the experiments of series I, to examine the prolonged effect of colchicine, no change was observed in the ultrastructure of the receptors or the character of their RP (Fig. 1A) after 12 to 24 h. After 48 h no RP were recorded in the Pacinian corpuscles (Fig. 1B). Changes were found in the ultrastructure of the axon, in the form of opacity of the axoplasm, disappearance of the microtubules, swelling or condensation of the mitochondria, and fragmentation of the axolemma (Fig. 2). In the control (application of polymer without colchicine to the nerve and perfusion of the receptors with colchicine solutions) neither morphological nor electrophysiological changes were found in the sensory nerve endings. In the experiments of series III (division of the nerve) potentials were no longer generated in the receptor after 24 h, and the ultrastructure of the corpuscles was identical with the pattern observed 48 h after application of colchicine to the nerve. It can be concluded from the results of these experiments that the prolonged action of colchicine on the nerve caused degeneration of the axon of the corpuscles, accompanied by disappearance of their electrical activity. The character of degeneration was comparable with the reaction of the Pacinian corpuscles after division of the nerve. However, this process developed more slowly after the application of colchicine to the nerve, in agreement with the results of analogous experiments [8, 9, 11]. The important fact is that the changes observed cannot be explained by the direct effect of the alkaloid on the receptors, as is shown by the results of control experiments in which isolated corpuscles were perfused with colchicine solutions.

In the experiments of series II (brief action of colchicine on the nerve) RP were recorded after 12 h (Fig. 1C) but were absent after 24 h and thereafter (Fig. 1D). However, by contrast with the prolonged effect of colchicine on the nerve, disappearance of RP 24 h after application was not accompanied by any change in receptor ultrastructure: The axon did not degenerate (Fig. 3). Brief application of colchicine to a nerve, unlike the prolonged effect of this alkaloid, is known to block axoplasmic transport [4, 10]. The possibility cannot be ruled out that the disappearance of RP observed in these experiments although the ultrastructure of the receptor remained intact was due to blocking of axoplasmic transport. However, it is evidently too early to regard this phenomenon as confirming the hypothesis of the trophic effect of the neuron on the structures of the receptor [12, 14]. More valuable results from this point of view were obtained by the study of alkaline phosphatase activity localized chiefly in the cells of the inner bulb of the receptors [3, 7]. A decrease of 37.3% in the activity of this enzyme ($P < 0.001$) was observed in homogenates of Pacinian corpuscles 24 h after application of colchicine to the nerve, whereas at this time after division of the nerve alkaline phosphatase activity was increased by 33% ($P < 0.05$). In the control experiments (application of polymer without colchicine to the nerve and incubation of homogenates with colchicine) activity of the enzyme did not differ significantly from that in intact receptors. The results of these investigations thus do not rule out the possibility that primary sensory mechanoreceptors (Pacinian corpuscles) are under neurotrophic control, the mechanism of which may be in accordance with the hypothesis examined above.

LITERATURE CITED

1. O. B. Il'inskii, G. N. Akoev, T. L. Krasnikova, et al., in: Biophysics of Membranes. Proceedings of a Symposium [in Russian], Kaunas (1971), pp. 409-419.
2. O. B. Il'inskii and N. I. Chalisova, Usp. Sovrem. Biol., 80, 441 (1975).
3. E. G. Ulumbekov, in: Tissue Reception [in Russian], Leningrad (1974), pp. 160-168.
4. E. X. Albuquerque, J. E. Warnick, J. R. Tasse, et al., Exp. Neurol., 37, 607 (1972).
5. O. A. Bessey, O. H. Lowry, and M. J. Brock, J. Biol. Chem., 164, 321 (1946).
6. A. J. Buller, J. C. Eccles, and R. M. Eccles, J. Physiol. (London), 150, 417 (1960).
7. H. Chouchkov, Dokl. Bolgarsk. Akad. Nauk, 21, 717 (1968).
8. C. N. Chouchkov, Z. Mikrosk.-Anat. Forsch., 83, 33 (1971).
9. M. Cuenod, P. Marko, E. Niederer, et al., in: Dynamics of Degeneration and Growth in Neurons (Proceedings of the International Symposium), Stockholm (1973), pp. 215-223.
10. W. W. Hofmann and S. Thesleff, Eur. J. Pharmacol., 20, 256 (1972).
11. M. Singer and M. C. Steinberg, Am. J. Anat., 133, 51 (1972).
12. A. A. Zalewski, Ann. New York Acad. Sci., 228, 344 (1974).
13. J. Zelena, Prog. Brain Res., 13, 175 (1964).
14. J. Zelena, Prog. Brain Res., 43, 59 (1976).