EFFECT OF DISTURBANCE OF NERVOUS INTEGRATION ON RELATIONS BETWEEN AURICULAR GRANULES AND OTHER COMPONENTS OF THE MYOCYTES

V. G. Tsyplenkova

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The morphology of the specific auricular granules and their connection with the cell organelles of the cardiomyocytes were studied by electron microscopy in normal rats and after division of the right vagus nerve. The results suggest that the muscle cells of the mamalian auricles have a secretory function. The secretory activity of the cardiomyocytes is considerably altered after division of the vagus nerve.

In a few investigations into the ultrastructure of the myocytes of the mamalian auricles the presence of electron-dense granules not found in the muscle cells of the ventricles has been described [1, 2, 5, 6, 9]. According to Palade [9], the number of auricular granules decreases in the myocardial cells after administration of reserpine. This suggested that the granules are an intracellular reservoir of catecholamines.

Investigations were carried out later to study the functional significance of the granules. However, the chemical composition and role of these inclusions have not yet been established.

The study of the morphology of these granules and their connection with the cell organelles would evidently shed some light on their functional role. In addition, because the nervous system exerts its regulatory action on the heart through mediators of the acetylcholine and catecholamine series, it would be interesting to study the fate of the granules, hypothetically containing catecholamines, after a disturbance of the innervation of the heart and, in particular, after the blocking of parasympathetic influences.

The object of the investigation described below was to study the fine organization of the specific auricular granules, their intracellular distribution, and their relations with the other components of the cell under normal conditions and after division of the right vagus nerve.

EXPERIMENTAL METHOD

Noninbred male albino rats weighing 180-220 g were used. The hearts of intact animals and of 15 rats in which the right vagus nerve had been divided below the ganglion nodosum were investigated. A mock operation was performed on 8 animals of the control group: the skin and subcutaneous fascia were divided, the neurovascular bundle was isolated, but the nerves were not divided and the wound was sutured. Material was taken from all three groups of animals at the same time of day, between 11 a.m. and 2 p.m.: from the vagotomized animals 12 h and 1, 3, 7, and 28 days after the operation and from the control animals 12 h and 1, 3, and 7 days after the mock operation.

The rats' hearts were fixed with 2-6.25% glutaraldehyde solution in phosphate buffer by immersion or perfusion [3]. The osmolarity of the perfusion fluids was monitored by a cryoscopic method and was 300-320 mosm. Areas of the right and left auricles and the auricular septum were studied. Blocks of tissue were washed in four portions of buffer and then postfixed in osmic acid [8]; dehydration was carried out in

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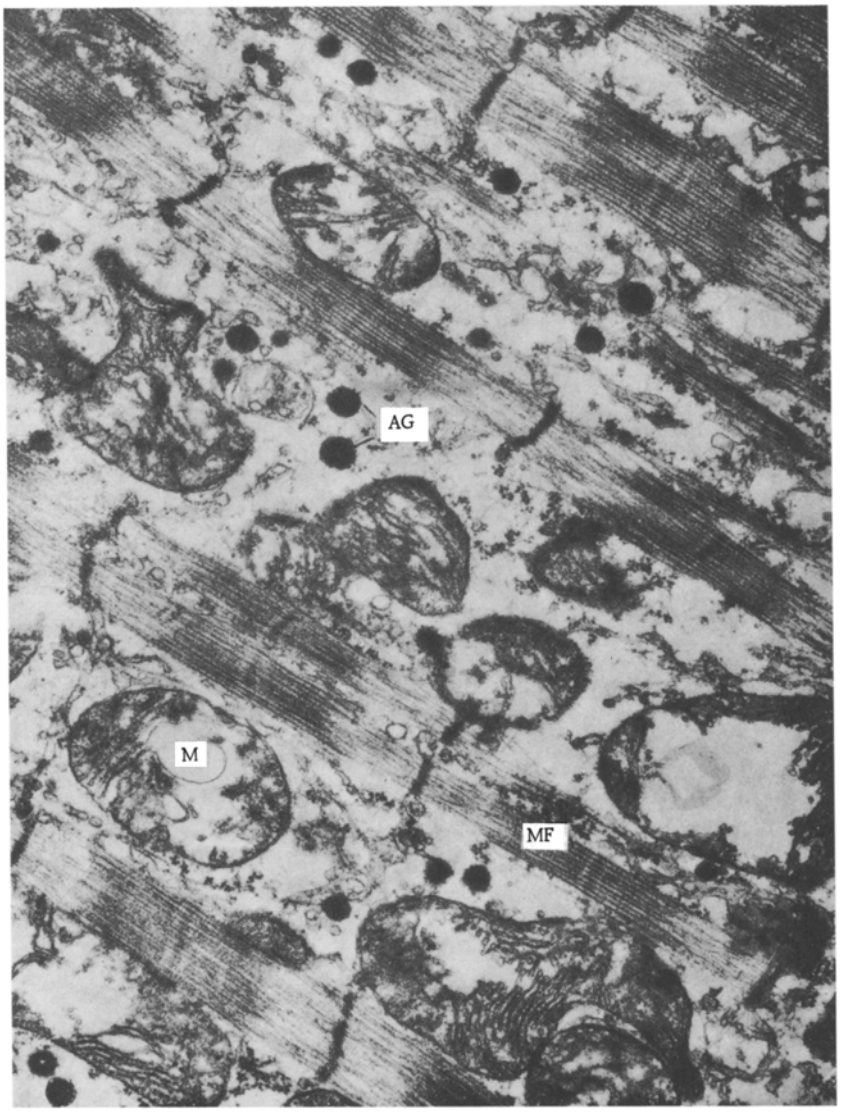

Fig. 1. Muscle cell from myocardium of right auricle (24 h after vagotomy, 26,000 ×): M) mitochondrion; MF) myofilaments; AG) auricular granule.

an increasing concentration of alcohols, after which the material was embedded in Epon-812 [7]. Sections were cut on the LKB-III ultratome, stained with 2-5% uranylacetate [11, 12] and lead citrate [10], and examined in the Hitachi 11-E-2 electron microscope under an accelerating voltage of 75 kV.

EXPERIMENTAL RESULTS

When studied in the electron microscope, the auricular granules appeared as round, dense structures 0.2-0.4 μ in diameter. Their limiting membrane consisted of three layers and was about 80 Å in thickness. Either pores or point ruptures were present in the membrane. The dense homogeneous contents of the granules were separated from the membrane by a narrow, light border 200-300 Å in width. Most of the granules were found in the perinuclear sarcoplasm. There the granules were numerous near the nucleus at one or both poles. Fewer auricular granules were found in other places in the cell: between the myofibrils and also in the subsarcolemmal regions.

The constant juxtaposition of the granules with a well-developed Golgi complex in the auricular muscle cell suggests that the myocyte participates in their formation. Probably the granules are liberated from the cell, as their frequent position by the sarcoplasm and the discovery of similar granules in the endothelium of an adjacent capillary suggest.

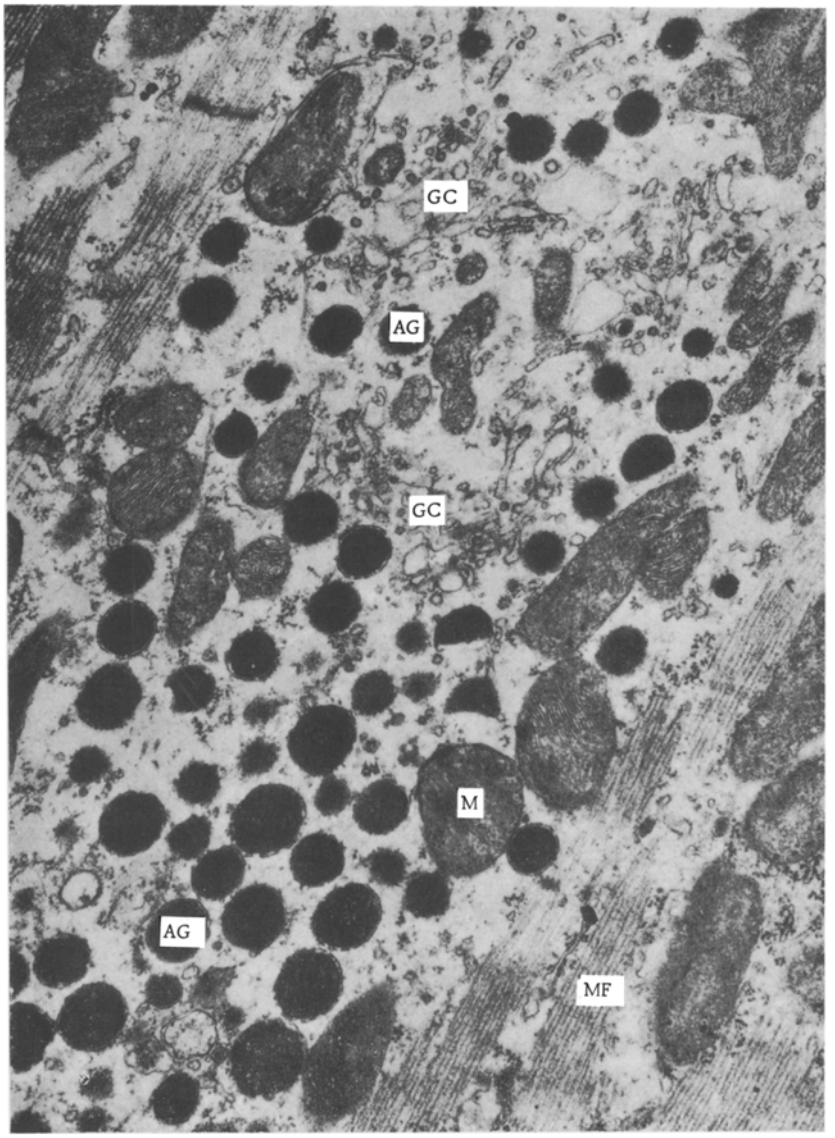

Fig. 2. Muscle cell from myocardium of right auricle (one month after division of right vagus nerve, 26,000 ×): GC) Golgi complex; remainder of legend as in Fig. 1.

Considerable changes in the size, density, and distribution of the granules in the auricular myocyte were observed 12 h after division of the vagus nerve. Their electron density and the number of smaller auricular granules increased. The specific granules appeared to be scattered at random throughout the cell and nowhere was their concentration greater.

The granules 24 h after vagotomy were distributed as before throughout the cell and most of them were smaller (Fig. 1). However, at this period it was possible to detect concentrations of granules chiefly in the subsarcolemmal regions of the sarcoplasm. It must be emphasized that 24 h after the operation the Golgi complex was also located at the periphery of the cardiomyocytes.

An accumulation of many specific granules was observed after 3 days in the myocytes of the right auricle and auricular septum. The Golgi complex at this period was sharply hypertrophied and consisted of dilated cisterns, large vacuoles, and numerous small scattered vesicles.

Large granules were concentrated beneath the sarcolemma seven days after vagotomy. The limiting membrane of the granules appeared swollen and had numerous point ruptures.

In the later stages after vagotomy (one month) the distribution of granules by size was closer to normal but the number of auricular granules was considerably increased. They were concentrated in the central sarcoplasm where the giant Golgi complex occupied a large area (Fig. 2).

In the animals of the control group all the characteristics of the granules were indistinguishable from normal.

The results suggest that besides their contractile function the auricular muscle cells also possess secretory activity. Similar views have previously been expressed in the literature [4]. The secretory activity of the cardiomyocytes is considerably altered after division of the vagus nerve. The parallel between changes in the Golgi complex and in the specific granules after vagotomy suggests that the Golgi complex participates in the formation of these granules in the myocytes of the mammalian auricles.

If results confirming the catecholamine composition of the granules are obtained in the future the dynamics of their changes during an experiment will provide evidence of a disturbance of the mediator balance of the heart after vagal denervation.

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