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PINEAL GLAND AND THE APUD SYSTEM

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Most research workers include the secretory cells of the pineal gland, or pinealocytes, in the diffuse neuroendocrine system (the APUD system) [2-4, 9]. However, the ultrastructure of the pinealocytes and of the pineal gland as a whole in the adult human has not yet been studied. There have been only solitary electron-microscopic studies, conducted on the human embryonic pineal gland (PG) [11, 12, 14].

The aim of this investigation was a comparative study of cells of the APUD system and adult human and guinea pig pinealocytes.

EXPERIMENTAL METHOD

Altogether 10 PG from persons dying from various cardiovascular diseases (age 40-66 years; five men and five women) and 20 PG from female guinea pigs were studied. Autopsy was carried out 2.5 h after death. The animals (four equal groups) were killed by decapitation under ether anesthesia, at 6 a.m., noon, 6 p.m., and midnight in the course of the 24-h period. The traditional methods of light and electron microscopy were used, with the IEM-100B electron microscope. Stereometric ultrastructural analysis of the guinea pig pinealocytes was carried out on electron micrographs with magnification of 18,000, using a test system with 513 nodal points and a grid with a step of 0.5 cm [1].

EXPERIMENTAL RESULTS

The human and guinea pig PG has an organ-like structure, and in its histoultrastructural parameters it is a neuroendocrine gland, separated from surrounding brain structures by a thin connective-tissue capsule (Fig. 1a). Properties of nerve and endocrine tissues are combined in PG: its neurosecretory cells are closely interconnected with the glial component, blood vessels, and nerve endings (Fig. 1b).

Pinealocytes account for the majority of all cells of the pineal parenchyma (79.9%), whereas gliocytes account for only 15.1%. In other words, in PG there is a kind of quantitative deficit of the glial component compared with brain tissue [5]. Unlike cells of the APUD system, pinealocytes have a neuron-like structure. A perikaryon or trophic center and numerous cytoplasmic processes can be distinguished in their cytoplasm. The cell nuclei, measuring 6.82 ± 0.2 μm, contain delicate chromatin, arranged mainly near the inner membrane of the karyolemma. The nuclear membrane has three or four nuclear pores, through which the ribonucleotide enters the perikaryon. The processes are densely interwoven with each other and they take part in desmosome-like and gap junctions with the neighboring pinealocytes and glial cells (Fig. 2a).

The presence of secretory vesicles with transparent contents or with an electron-dense core in the perikaryon and cytoplasmic processes is morphological evidence of the endocrine

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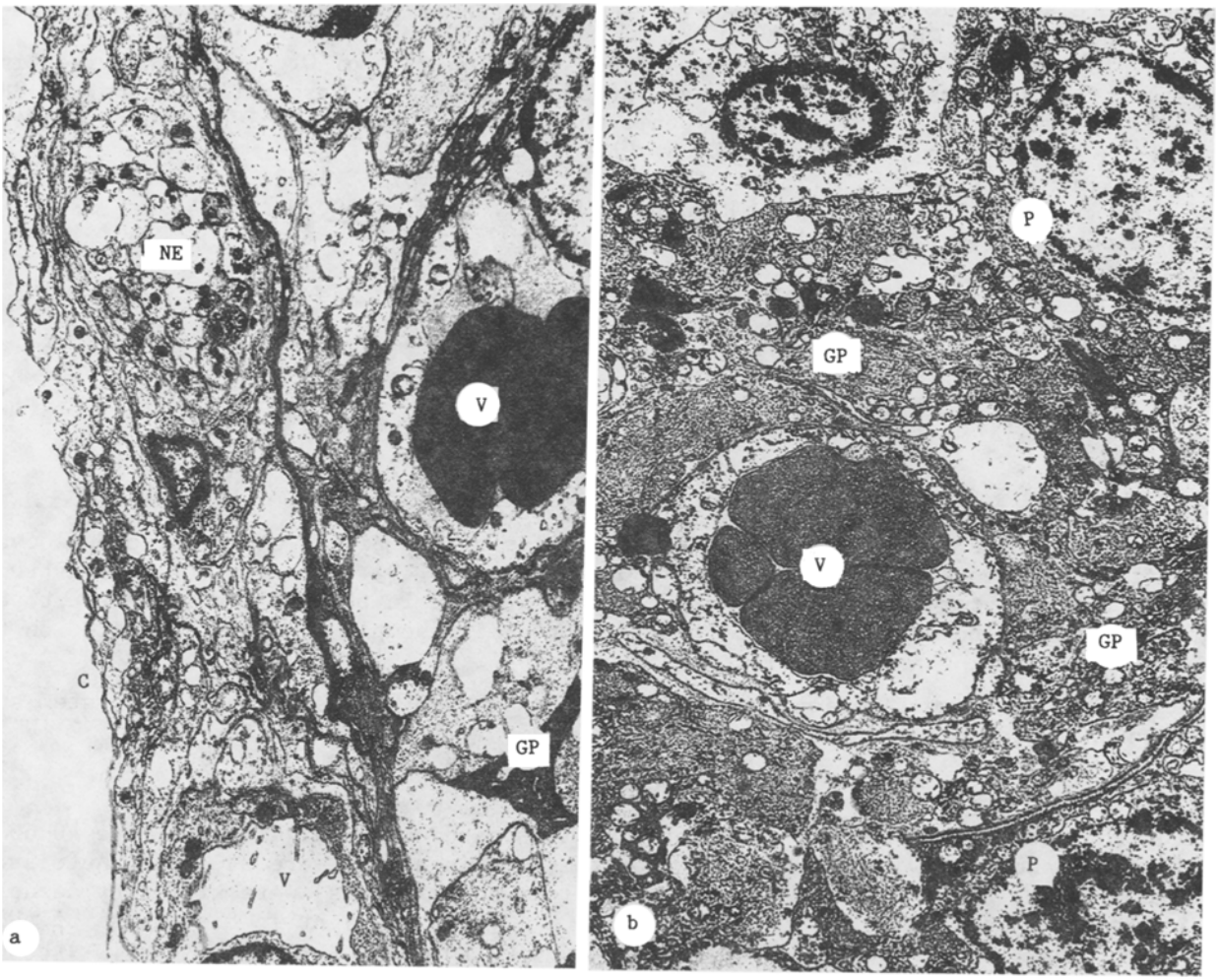

Fig. 1. Ultrastructure of human PG. Magnification 8000. a) Subcapsular zone of gland. Blood vessels (V), capsule (C), glial processes (GP), nerve endings (NE); b) central region of gland. Blood vessel (V) with perivascular barrier zone, consisting of glial processes (GP); pinealocytes (P).

properties of the pinealocytes (Fig. 2b). The dimensions of the vesicles and of the osmiophilic core vary within wide limits: 27-225 and 50-100 nm, respectively. The number of these organelles undergoes considerable fluctuations, and secretory vesicles with a dense core can be found in human pinealocytes only extremely rarely. This does not contradict the generally accepted criteria of cells of the APUD system for in recent investigations the presence of granular and cytosolic pools of neurosecretory material has been demonstrated in pinealocytes [14].

Stereometric analysis of guinea pig pinealocytes, undertaken at different times of the 24-h period, showed that the lowest concentration of secretory vesicles is observed at 6 p.m. and midnight, after which their number begins to rise toward 6 a.m., and reaches a maximum at noon (4, 4, 6.5, and 7.6%, respectively, $p \leq 0.99$). Correlation was thus established between changes in the number of these organelles and the alternation of daylight and darkness. In our opinion, reduction of the number of secretory vesicles at nigh can be explained by the active entry of melatonin into the general circulation, which takes place at night [3, 13, 14].

Similarity between pinealocytes and cells of the APUD system is confirmed by their well developed endoplasmic reticulum, lamellar complex, the abundant mitochondrial component, and the presence of free ribosomes. Moreover, polysomes, lysosomes, phagosomes, lipofuscin granules, and also neurofilaments and neurotubules, i.e., organelles characteristic of nerve and endocrine cells, are visible in the cytoplasm of pinealocytes (Fig. 2c).

Within the context of this article, it is pertinent to distinguish some particular features of the pineal glial component. We found that 77% of all gliocytes are accounted for

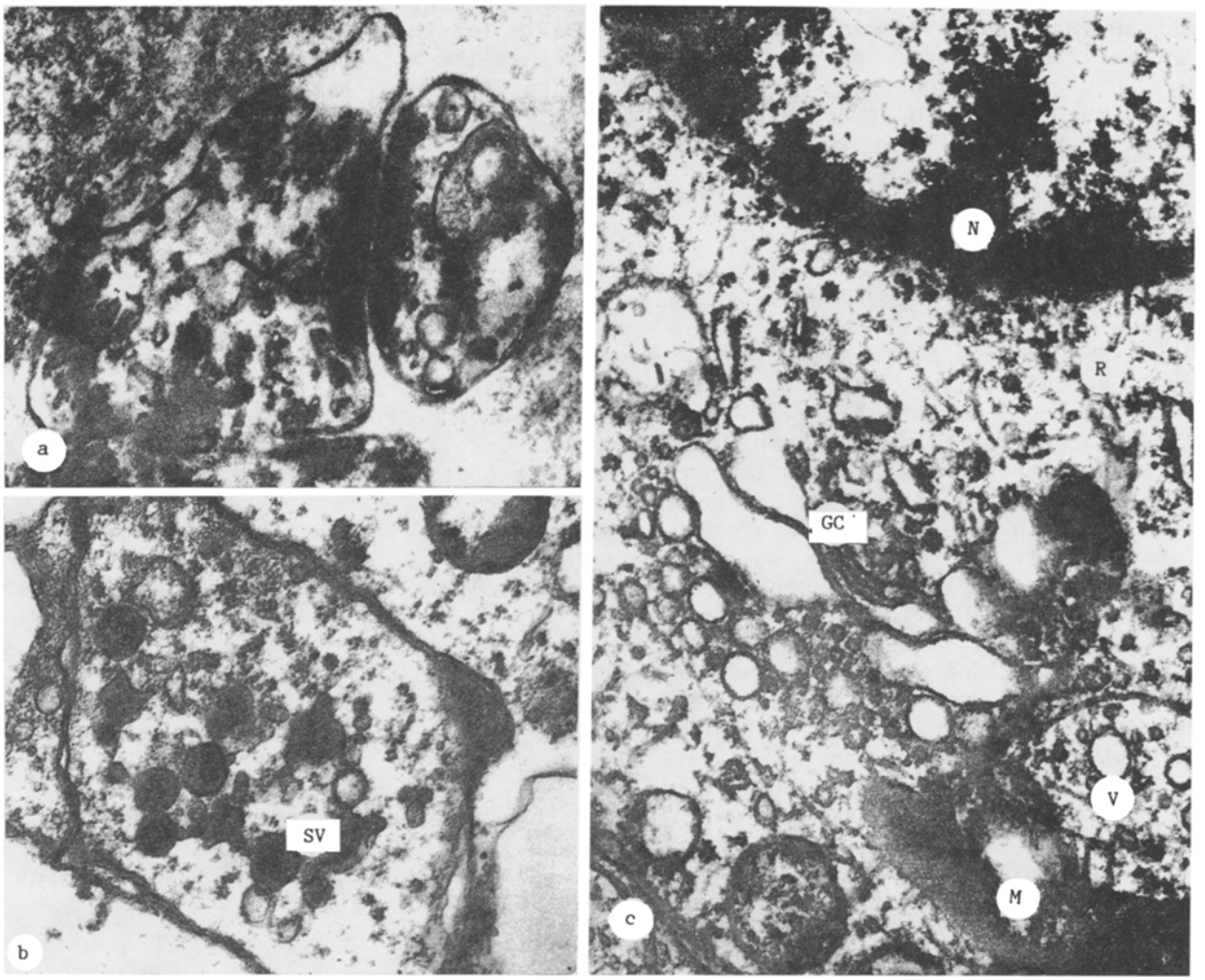

Fig. 2. Characteristics of human pinealocyte. a) Synaptic junction between processes of pinealocytes. 36,000×; b) cytoplasm of process contains secretory vesicles (SV) with transparent and electron-dense core. 36,000×; c) fragment of pinealocyte. Cytoplasm near nucleus (N) contains: mitochondria (M), Golgi complex (GC), ribosomes (R), and transparent vesicles (V). 24,000×.

by fibrillar astrocytes, and that oligodendrogliocytes, protoplasmic astrocytes, and microgliocytes account for 12, 8, and 3%, respectively. Fibrillar astrocytes play a direct role in the formation of perivascular, subcapsular, and subependymal glial barrier zones. The most important metabolic processes in PG are effected through processes of fibrillar astrocytes, for pinealocytes do not make direct contact with the blood stream, the CSF, or the pia mater. The functional role of the glial tissue becomes evident from the fact that it is in that tissue and, in particular, in the perivascular spaces, that the highest concentration is observed of sympathetic endings, which play the key role in the triggering and realization of hormone-producing processes in PG [7, 9, 11-13].

The ultrastructural similarity of human and guinea pig pinealocytes with cells of the APUD system was thus established. However, unlike the latter, pinealocytes are not disconnected cells, but the main part of the pineal parenchyma. Because of differences in evolution, in PG a unique combination of properties of nerve and endocrine tissue takes place. As we know, PG performs the role of organ of adaptation of the body to various external environmental factors [6, 8, 9, 13, 14]. The present investigation has demonstrated how secretory activity of the pinealocytes depends on external lighting conditions, as shown by a statistically significant decrease in the number of secretory vesicles at night compared with the period of daylight.

This analysis of morphological and functional similarity and difference between PG and the APUD system means that PG can be regarded as an APUD organ, forming functional unity with

the diffuse neuroendocrine system. This interpretation of the problem was first adopted by Leong and Matthews [9]. In our opinion, the basis for this hypothesis is the fact that PG maintains central levels of regulation and realizes its effects through the central nervous, autonomic nervous, and endocrine systems [6, 13], and that cells of the diffuse APUD system act on homeostasis at organ and system levels, and are under the control of central mechanisms of regulation, including PG.

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HISTOCHEMICAL ANALYSIS OF OXIDOREDUCTASES IN CARDIOMYOCYTES OF MATURE AND OLD RATS AFTER LOW-DOSE EXTERNAL GAMMA-IRRADIATION

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Investigations of myocardial morphology and functions under the influence of ionizing radiation have been conducted mainly with the use of lethal or sublethal doses [3, 6, 11, 12]. Yet the increase in the external environmental radiation factor at the present time has stimulated interest in the effect of small doses of irradiation and its possible after-effects on heart muscle function. The heart is an organ with intensive energy metabolism. In this connection the study of the state of oxidoreduction processes in the cardiomyocytes after irradiation with small doses is very urgent. It is also necessary to study age-related sensitivity of the myocardium to the action of radiation. These problems have been inadequately dealt with in the literature.

The aim of this investigation was to study changes in the level of activity of the principal oxidoreductases in cardiomyocytes of mature and old rats after total gamma-irradiation in a relatively small dose.

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