HISTOCHEMICAL AND IMMUNOHISTOCHEMICAL IDENTIFICATION OF ENDOCRINE CELLS IN THE INNER EAR

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The concept of neuroendocrine cellular organization (the APUD system) is a fundamental problem in biology and medicine. Since the appearance of the first publication on this question [7] the attention of research workers has been drawn mainly to problems connected with the study of the functional morphology of the APUD system, whose cells (apudocytes) produce highly active chemical substances — biogenic amines and peptide hormones which play an important role in the maintence of homeostasis [2, 7]. More than 40 types of apudocytes, forming the diffuse endocrine system, have been described. They have been identified in various parts of the brain, glands of internal secretion, gastrointestinal tract, lungs, trachea, larynx, and other organs. Information on the presence of cells of the diffuse endocrine system in the human or animal inner ear, and on the possible synthesis of biogenic amines and peptide hormones in cells of the spiral organ or other parts of the labyrinth cannot be found in the Soviet or other literature. Nevertheless the complexity of the structure of the peripheral part of the auditory and vestibular analyzers, and also the characteristics of their function suggests a possible role of hormonally active substances (biogenic amines and peptide hormones) in the realization of cochleovestibular reception. Accordingly, we have undertaken a histochemical and immunohistochemical study of the aural labyrinth of animals to determine whether any hormone-producing cells could be identified in it.

EXPERIMENTAL METHOD

The material for study consisted of preparations of decalcified temporal bones of rabbits and of the isolated membranous cochlea of guinea pigs, dissected by the usual method [1, 5]. The material was fixed in 10% neutral formalin and Bouin's fluid and embedded in paraffin wax. Dewaxed sections were stained with hematoxylin and eosin and by the argyrophilic method of Grimelius. Serial sections were cut from pieces of tissue fixed in Bouin's fluid by an immunohistochemical method, using specific antisera against serotonin, melatonin, insulin, ACTH, STH, and C-peptide. Luminescent donkey sera against rabbit and guinea pig globulins, labeled with fluorescein isothiocyanate, were used as the label. The sections were examined in the LYUMAM I-3 luminescence microscope (1-2, SZS 7-2 filters).

EXPERIMENTAL RESULTS

Apudocytes, characterized by a positive Grimelius' argyrophilic reaction, were found in preparations of decalcified rabbit cochlea and membranous guinea pigs cochlea. They were identified in various formations of the inner ear: the basilar membrane, receptor elements of the spiral organ, and the spiral ligament. The last structure mentioned was richest in argyrophilic cells, which were arranged in groups of 5-8 cells, most frequently around blood vessels (Fig. 1a, b). They were less frequent in other parts of the inner ear. On immunohistochemical analysis of serial sections these cells reacted positively with antisera against serotonin and melatonin (Fig. 1c, d). The number of endocrine cells, their size, and the intensity of their staining differed in different preparations, possibly due to different levels of functional activity of the apudocytes in each concrete case. No species-specific differences in the endocrine function of these cells could be found in rabbits and guinea pigs.

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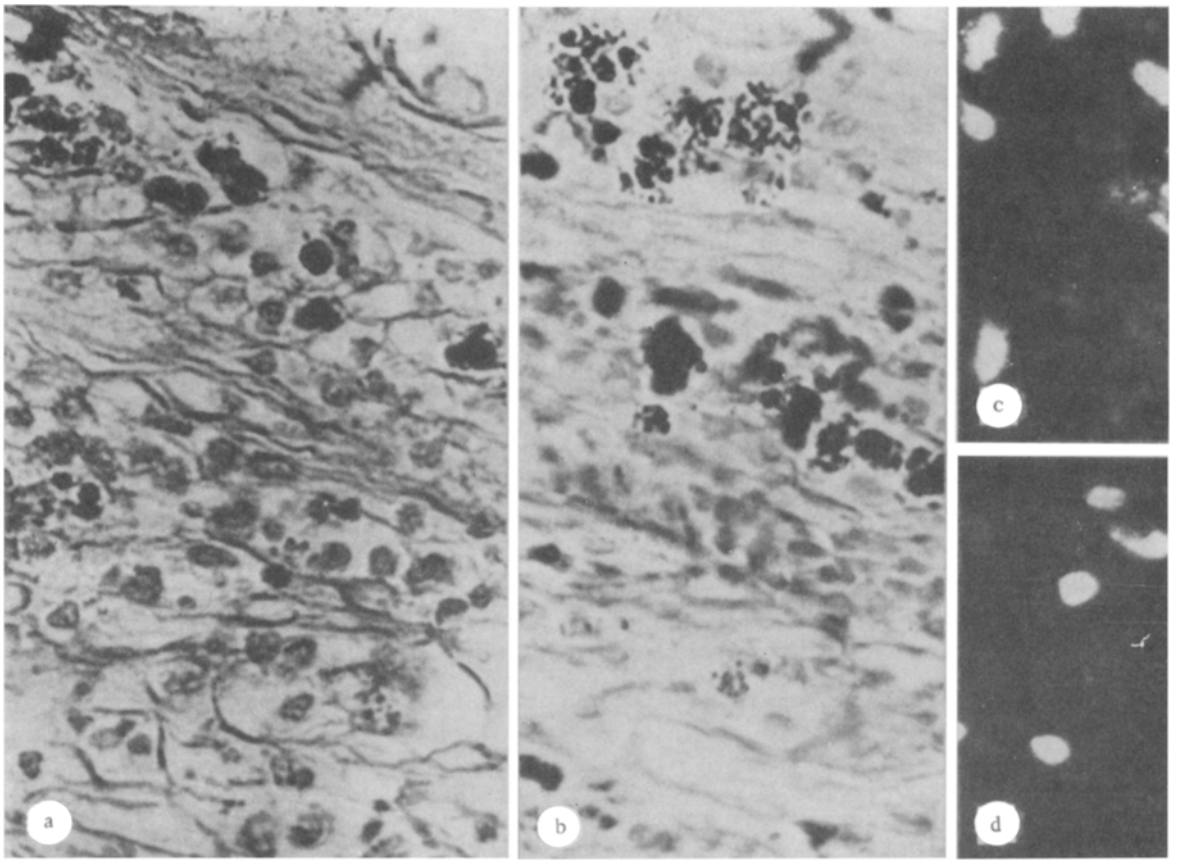

Fig. 1. Endocrine cells (apudocytes) in inner ear of rabbit and guinea pig. a, b) Apudocytes in spiral ligament of membranous cochlea of rabbit. Positive argyrophilic reaction. Grimelius' method, 240 ×; c, d) positive immunohistochemical reaction of apudocytes of spiral ligament of membranous cochlea of guinea pig with antisera aginst serotonin (c) and melatonin (d), 240 ×.

Many of the functional and morphological features distinguishing the inner ear cannot yet be completely and definitively interpreted. The marked ability of the aural labyrinth to regulate its own complex biochemical processes, ensuring normal functioning of the receptor formations located in the anatomically closed spaces of the membranous cochlea and semicircular canals remain an enigma. The fact that individual structures of the inner ear (the vestibular and basilar membranes, the stria acustica) are semipermeable formations and perform the role of blood labyrinth barrier cannot fully explain the many processes observed in the normal and pathologically changed labyrinth. In particular, it is not clear how the trophic function of the endolymph is controlled, so as to ensure constancy of the internal medium of the endolymphatic space, or what lies at the basis of the mechanism disturbing this space and, as a result, causing the development of labyrinthine hydrops. The explanation of this last situation is particularly important because hydrops of the inner ear is the morphological substrate of diseases such as Meniere's disease [4, 5], the early syphilitic lesion of the inner ear [3, 9], and serious labyrinthitis of varied etiology [8]. Cells of the APUD system discovered by the writers in various parts of the membranous cochlea and the identification of biogenic amines with an almost universal functional spectrum, namely serotonin and melatonin in them may provide a basis for the explanation of the unique characteristics of function of the oral labyrinth under normal conditions, and also, most important of all, they may provide a new insight into the development of various pathological states and, in particular, the development of endolymphatic hydrops. A detailed study of the morphology and topography of the cochlea apudocytes and also the changes in their functional activity in diseases of the inner ear will be subjects for futher research by the writers.

The histochemical and immunohistochemical investigations thus revealed for the first time the presence of endocrine cells (apudocytes) in various formations of the cochlea. Identification of synthesis of such highly active chemical products as serotonin and melatonin in them may provide a theoretical basis for a fundamentally new approach to the study of the functional role of particular parts of the labyrinth under normal and pathological conditions.

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HETEROPHILIC ANTIBODIES AGAINST ANTIGENS OF MYOCARDIAL INTERSTITIAL CONNECTIVE TISSUE AND ERYTHROCYTES OF ANIMALS OF DIFFERENT SPECIES

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Heterophilic antibodies, i.e., antibodies reacting with antigens of other species, are found in the sera of patients with various diseases. In most cases these antibodies are discovered in tests with heterologous erythrocytes. For instance, in infectious mononucleosis antibodies are found against erythrocytes of animals of various species. Determination of heterophilic agglutinins against sheep's erythrocytes is used for the diagnosis of this disease [8]. Antibodies of the H–D (Hanganutziu–Deutscher) type, active against a ganglioside located on the ovine and bovine erythrocyte membrane, were first described in serum sickness [7]. These antibodies have also been found in diseases of the liver, kidneys, and intestine [9]. Heterophilic reactions playing a role in kidney transplantation in man have been described. Elevation of the antibody titer against rat erythrocytes, carrying the so-called heterophil transplantation antigen (HTA), frequently correlates in patients with acute graft rejection [10, 11, 14].

In previous investigations the writers found heterophilic antibodies reacting with heterophilic antibodies reacting with cells of the interstitial connective tissue (ICT) of bovine myocardium in the sera of patients with rheumatic fever and other diseases (myocarditis, myocardial infarction, diseases of connective tissue). The frequency of their discovery and the intensity of the reaction were shown to increase considerably in patients with rheumatic fever in the active phase of the disease [2, 5]. Antibody titers were particularly high in patients after heart valve replacement [1]. The corresponding heterophilic antigen has been shown to be a tissue-specific bovine antigen which is found in all animals in cardiac ICT and on erythrocytes. With the aid of antibodies isolated from the sera of patients on erythrocyte stroma and immunosorbent prepared from antigens of bovine connective tissue, the antigen was shown to be located in the cytoplasm and cytoplasmic membrane of connective-tissue cells of various bovine organs. Reactions of the antibodies with myocardial ICT cells were shown to be inhibited by D-galactose [3].

Heterophilic antibodies against rat myocardial ICT antigens have also been described [13] in various heart diseases, but the authors cited did not undertake a detailed study of these antibodies.

The aim of this investigation was to compare reactions of heterophilic antibodies with bovine myocardial ICT with reactions to heart tissues of animals of other species. The dis-

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