Histological analysis of the kidneys in the experimental newborn mice of all series revealed marked degeneration of the cells of the tubules, together with considerable karyolysis. The number of lysed nuclei in the experimental newborn mice of series IV was 36%, and of series V, 30%, whereas in the corresponding control newborn mice they numbered only 13%, and in the intact newborn mice only 6%. Thickening of the basement membrane was observed in the renal corpuscles with deposits of granular material in the lumen of the capsule (Fig. 1).

Lymphocytes of syngeneic donors, sensitized to kidney antigen, if injected into female animals at different times of pregnancy and before conception, besides their nonspecific toxic effect, induced changes in the kidneys of the newborn mice (an increase in size of the cells of the convoluted tubules, marked karyolysis). The early stages of embryogenesis, including the period of laying down of the metanephros (10th-12th days), proved to be most vulnerable. However, further investigations are necessary to establish the concrete mechanism of this effect of lymphocyte sensitized to kidney antigen on the fate of the kidneys in the progeny.

LITERATURE CITED

1. R. F. Averkina, Arkh. Patol., No. 3, 56 (1975).
2. R. F. Averkina, O. E. Vyazov, and N. I. Vystavkina, Arkh. Anat., No. 6, 74 (1975).
3. R. F. Averkina and N. I. Suchkova, Ontogenez, No. 5, 490 (1976).
4. R. F. Averkina and E. S. Mashkina, Arkh. Anat., No. 2, 66 (1978).

ROLE OF COATED VESICLES IN SYNAPTOGENESIS IN MAN

A. A. Milokhin and I. V. Chernova

UDC 611.839-013

KEY WORDS: synaptogenesis; coated vesicles; spinal cord; prenatal human development

Despite the ever-increasing number of investigations of the phenomenon, synaptogenesis still remains a largely enigmatic process. This is particularly true of ideas on the mechanisms of the rapid differentiation of postsynaptic membranes, the structural and functional organization of which largely determines the specific features of the maturing synapse.

The complexity of the postsynaptic membrane, which includes a complex of special receptor and enzyme proteins, indicates quite definitely that its growth and differentiation must take place under strict genetic control. However, where and how these membranes are created and mature, and how they or their individual components reach the site of the future synapse also are still unsolved problems, and this naturally gives rise to many hypotheses and conjectures.

The most probable of these suggestions is the hypothesis of the exclusive role of the so-called coated vesicles in the genesis of the postsynaptic membrane and, perhaps, of the whole subsynaptic complex of the nerve cell [1-3], although of course there are other equally probable alternatives to this hypothesis [4, 5].

The object of this investigation was to study the possible role of coated vesicles in processes of synaptogenesis during the period of prenatal development of the nervous system in man.

Laboratory of Development of the Human Nervous System, Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, No. 4, pp. 496-498, April, 1980. Original article submitted January 10, 1979.

0007-4888/80/8904-0540$07.50

EXPERIMENTAL METHOD

An electron-microscopic study was made of the brachial portion of the spinal cord of seven-week human embryos. Their age was determined from a comparison of clinical and morphometric data.

EXPERIMENTAL RESULTS

Our previous investigations [6] and data in the literature [3, 7, 8] indicate that the leading role in the formation of a synaptic junction is played by events taking place in the postsynaptic neurons. It is in this neuron, in the region of the future synapse, that the ordinary plasma membrane of the cell is transformed into a completely special, uniquely constructed postsynaptic membrane, with its characteristic set of receptor and enzyme proteins. However, since these protein structures cannot be synthesized in the membrane itself, but only by the protein-synthesizing systems of the cell under genetic control, it will be evident that all these proteins so essential for differentiation of the postsynaptic membrane must have been transported somehow to their appointed place. There is nothing improbable in the notion that this transport may take place through the participation of what are known as coated vesicles and which, as has been shown, are specially adapted for transporting proteins of intracellular structures [1, 9, 10].

However, in order to confirm this hypothesis, direct participation of coated vesicles in the formation of the subsynaptic membrane had to be demonstrated. Some facts in support of this view were given in publications on synaptogenesis in the cerebellum [1] and olfactory cortex [8] of rats, and also in nerve tissue cultures [3]. The present investigation, conducted on the spinal cord of human embryos, revealed morphological pictures which, in the writers' opinion, clearly demonstrate the direct participation of coated vesicles in the development of the postsynaptic membrane of presumptive synapses.

A dendritic profile, in which two coated vesicles are clearly distinguishable, can be distinctly seen in Fig. 1a, which depicts an area of the marginal zone of the developing spinal cord on the boundary with its ventrolateral nucleus. One of them lies freely in the cytoplasm, between two mitochondria with a dense core, the other is in close interaction with the plasma membrane of the cell. On closer examination (Fig. 1a, b) it will be clear that this vesicle is apparently insinuating into the plasma membrane, fusing with it as in exocytosis.

This developing synaptic junction (Fig. 1a, b), to judge from the morphological features, is passing through the earliest stages of its formation. This is shown both by the structure of its presynaptic membrane, which is almost indistinguishable from the ordinary plasmalemma, and by the presence of only solitary synaptic vesicles, scattered in the axoplasm, in addition to microtubules in the presynaptic terminal; one of these vesicles is adjacent to the presynaptic membrane, apparently opposite the coated vesicle insinuating into the postsynaptic membrane.

A study of static morphological pictures must of course always lead to doubts whether the coated vesicle described is actually fusing with the postsynaptic membrane, and that what we are seeing here is not the ordinary picture of endocytosis. A serious objection to this view, we consider, is the picture in Fig. 1c. Here it will be noted that the membrane of the coated vesicle differs sharply from the plasma membrane with which it interacts. This observation is weighty evidence in support of the view that what is recorded on the electron micrograph is in fact fusion of the membrane of the coated vesicle with the plasma membrane, for otherwise, if it were endocytosis, the two membranes ought to be morphologically identical. Consequently, here we see one of the first stages of synaptogenesis – the initial formation of the postsynaptic membrane.

From where do these distinctive vesicles, which play such an important role in the processes of synaptogenesis, appear and where are they formed? It is not easy to give an unequivocal answer to these questions, for coated vesicles may arise in the most widely different regions of the cell. However, the main sites of their massive genesis are the cisterns of the Golgi lamellar complex. By studying this complex in the same human embryos, it is easy to be convinced of the exceptionally active process of coated vesicle formation (Fig. 1d), and on some electron micrographs all stages of their genesis can be traced – from the appearance of individual regions of "downy" membranes at the edges of the cisterns to complete separation of coated vesicles ready for transportation.

On the basis of these observations it can therefore be suggested that the formation of postsynaptic membranes and, consequently, the development of new synapses takes place as follows. The axon, growing toward a neuroblast, in all probability acts as a specialized inducer, capable of inducing certain differential activity of its genome in the presumptive postsynaptic neuron. It is in this way that the process of synthesis of recep-

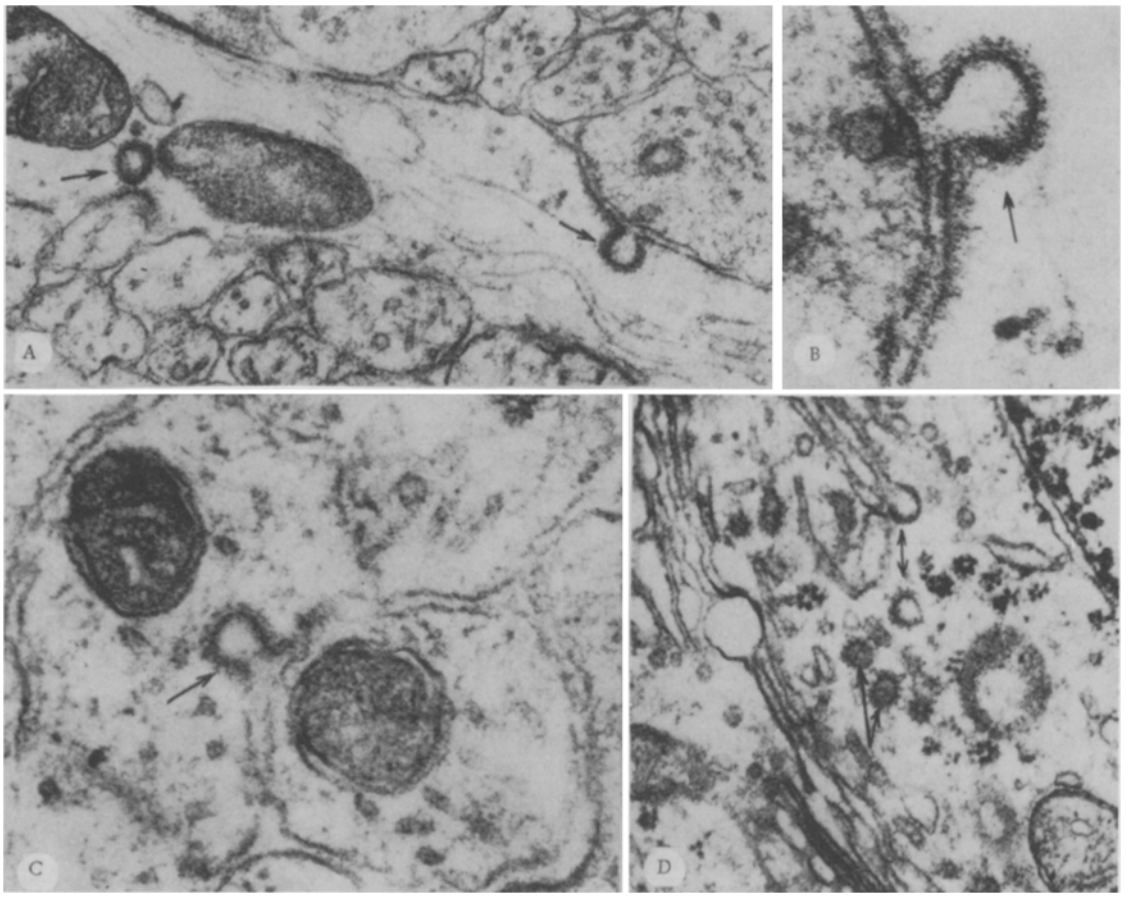

Fig. 1. Coated vesicles (arrows) in developing nerve cells from presumptive anterior horns of brachial portion of spinal cord of 7-week human embryo. Magnification: A) 60,500; B) 170,500; C) 95,000; D) 50,000.

tor and enzyme proteins, strictly specific for the future synapse, is triggered in this nerve cell. These newly synthesized proteins sooner or later enter the Golgi lamellar complex, where they undergo appropriate transformation and are incorporated into the membranes which are being produced there, and which subsequently become what are essentially presumptive postsynaptic membranes. In other words, it is suggested that it is in the Golgi apparatus that an almost ready-made postsynaptic membrane of the future synapse is created, with all its complex system of specific receptor and enzyme protein structures.

Next, this membrane separates from the cisterns of the lamellar complex and proceeds in the form of a coated vesicle to its appointed destination, possibly using microfilamentous and microtubular transport systems of the cell for this purpose. Having reached the region of the plasma membrane of the cell where contact was made with the approaching axon, the coated vesicle stops, becomes firmly apposed to the membrane, and by means of the old-established cytological mechanism of exocytosis, insinuates into it. As a result of this process the until then ordinary plasma membrane is apparently replaced by a special postsynaptic membrane, with its own specific assortment of receptor and enzyme structures. We also consider that it is this process which lies at the basis of growth and differentiation of the postsynaptic membrane of the developing synapse. This is a stepwise process, and each new coated vesicle, insinuating into the membrane, brings with it its own quantum of the specialized postsynaptic membrane which, we must assume, is already capable of performing, although perhaps not fully, its basic functions in the interneuronal synapse. There is every reason to suppose that this mechanism also is widely used in the adult not only during the formation of new synapses, but also during their reconstruction, which is responsible for the plasticity of existing synaptic junctions.

LITERATURE CITED

1. J. Altman, Brain Res., 30, 311 (1971).
2. D. J. Stelzner, A. H. Martin, and G. L. Scott, Z. Zellforsch., 138, 475 (1973).
3. R. P. Ress, M. B. Bunge, and R. P. Bunge, J. Cell Biol., 68, 240 (1976).
4. I. R. Schwartz, Brain Res., 46, 187 (1972).
5. A. A. Milokhin, S. S. Reshetnikov, and I. V. Chernova, Byull. Éksp. Biol. Med., No. 2, 233 (1977).
6. A. Hirano and H. M. Dembitzer, J. Neuropath. Exp. Neurol., 33, 354 (1974).
7. L. E. Westrum, J. Neurocytol., 4, 713 (1975).
8. T. F. Roth and K. R. Porter, Fed. Proc., 22, 178 (1963).
9. D. W. Fawcett, J. Histochem. Cytochem., 13, 75 (1965).

MORPHOLOGICAL CHARACTERISTICS OF THE HEART OF ARGALI LIVING PERMANENTLY AT HIGH ALTITUDES

B. Zhaparov, S. Kh. Khamitov, and M. M. Mirrakhimov

UDC 612.275.1:599.735.5-141.2

Studies of the functional [2, 3, 8] and structural [1, 4-7, 10] bases of long-term adaptation to high-altitude and other extremal conditions have recently been published. Typical representatives of permanent mountain-dwellers are the argali, which live in herds on exposed spaces of mountain plateaus at altitudes of 3800-5000 m above sea level. The specific features of their ecologic environment make special demands on the argali. They have a strong constitution, they have great powers of endurance, and if necessary they can cover great distances over rocky mountains at high speed. No appreciable functional disturbances of the cardiovascular and respiratory systems arise in the argali. Yet no investigations have yet been undertaken to study the particular features of the ultrastructure of the cardiomyocytes in the argali. It was accordingly decided to study the myocardium of these animals by the use of light-optical and electron-microscopic methods of investigation.

EXPERIMENTAL METHOD

Pieces of myocardium from the left and right ventricles of argali were taken 20-30 min after slaughter of the animals. The length of the hearts varied from 11 to 12 cm, the transverse diameter from 9 to 12 cm, and the anteroposterior diameter 6-8 cm. The thickness of the wall of the left ventricle was 1.8-2.2 cm, of the right ventricle 0.5-1 cm, and of the ventricular septum 1.4-1.8 cm, which corresponds to moderate and uniform hypertrophy of the myocardium.

Pieces of myocardium for light microscopy were fixed in 10% neutral formalin solution and embedded in paraffin wax. Sections were stained with hematoxylin and eosin. Material for electron microscopy was fixed in 1% osmium tetroxide solution in veronal-acetate buffer, pH 7.4, for 2 h. The fragments were dehydrated in alcohols of increasing concentration. After appropriate rinsing and processing they were embedded in a mixture of Epon-812 and Araldite. Ultrathin sections were stained with lead citrate by Reynolds' method and examined in the JEM-100B electron microscope. Semithin sections 1 μ thick also were cut from the blocks embedded for electron-microscopy and these were stained with toluidine blue.

EXPERIMENTAL RESULTS

Macroscopically, the heart had the concical shape usual for mammals. The almost complete absence of adipose tissue beneath the epicardium was noted. A very small quantity of adipose tissue was confined to the coronary sulcus. The course of the branches corresponded to the left coronary type of blood supply to the heart. The main branches were straight in their course. On section their intima was smooth. The tissue of

Central Research Laboratory, Department of Forensic Medicine, Kirghiz Medical Institute. Research Institute of Cardiology, Frunze.

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 89, No. 4, pp. 498-501, April, 1980. Original article submitted July 10, 1979.

0007-4888/80/8904-0543$07.50