of deprivation had no effect on the RNA content either in neurons or in neuroglia in layer V of the motor cortex (Fig. 2).

The results of cytospectrophotometric determination in the cells of the visual cortex indicate definite compartmentalization of RNA metabolism within the neuron–neuroglia system. The nucleus of neurons is metabolically the most stable part; Neither the DNA content nor the RNA content in it (Fig. 1) was changed under the influence of hyper- or hypofunction of the neurons. The cytoplasm of these neurons, and also their glial satellite cells were characterized by greater functional-metabolic lability; meanwhile functionally determined changes in their RNA content were not identical (Fig. 1). It can be tentatively suggested that the presence of at least three compartments in the neuron–neuroglia system, with different levels of sensitivity of metabolism of their macromolecules to functional loads, makes the whole system more flexible and more adaptable to constantly changing conditions of function.

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STRUCTURAL ORGANIZATION OF SYNAPTIC JUNCTIONS OF DEVELOPING ANTERIOR HORN NEURONS OF THE EARLY HUMAN FETAL SPINAL CORD

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The structural organization of developing synapses, especially in early prenatal ontogeny, continues to attract the attention of neurobiologists of widely different specialties. However, despite the steady increase in the number of investigations in this field, synaptogenesis still largely remains unexplained, more especially in man [1-5].

For these reasons a systematic study of the formation of interneuronal connections during human prenatal ontogeny has been started [4, 5]. In the present investigation an attempt was made to establish the basic principles governing the structural organization of synapses in anterior horns of the human spinal cord in the early fetal period of antenatal development (11th-12th weeks of pregnancy).

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EXPERIMENTAL METHOD

An electron-microscopic study was made of the brachial segments of the human spinal cord in 11- and 12-week fetuses. The age of the fetuses was determined by comparing clinical and morphometric data. Altogether 12 fetuses were studied.

EXPERIMENTAL RESULTS

At the 11th-12th week of intrauterine development of the human fetus examination of the anterior horns of the brachial segments of the spinal cord in sections stained by Nissl's method revealed a concentration of neuroblasts forming two principal presumptive motor nuclei — medial and lateral. Among the cells composing them, which were at different stages of differentiation, several large maturing neurons with a large, pale nucleus, could always be distinguished. These cells had a clear tendency to lie near the marginal zone. In sections impregnated by Golgi's method they appeared as relatively large multipolar cells with a clearly differentiated axon and a distinctive dendritic tree, sending some of its branches into the marginal zone. They differed from mature neurons in their much smaller size and the less well-developed branching of their dendrites. Bundles of thin nerve fibers approached these maturing neurons from the marginal zone of the developing spinal cord and made contact by their terminal branches with the dendrites and bodies of these cells. The nerve fibers running toward the neuroblasts contained many longitudinally oriented microtubules in their axoplasm, along which glycogen granules and vesicles — both large, pale vesicles and others corresponding in size to synaptic vesicles — were arranged.

In some cases, some of these thin nerve fibers could be seen to terminate in a typical cone of growth. At the point where the nerve fiber changed into the cone of growth, characteristic changes took place in the ultrathin structural organization of its cytoplasm. Microtubules collected into bundles in the axoplasm, on penetrating into the cone of growth, became scattered among its cytoplasm, in which they were gradually lost. Only in rare cases could one or two of them reach to its distal pole.

Compared with the nerve fiber, the number of vesicles in the cytoplasm of its growing end was sharply increased. In this situation, they also form two well-distinguished populations: large pale vesicles and small vesicles indistinguishable in size from the synaptic kind, characteristic of synapses of cholinergic type (Fig. 1a, b). This was particularly clear in cases when the cone of growth, having reached the surface of an outgrowth, began to form a synaptosome. Under these circumstances, as a rule it widened considerably, as if spreading out over the surface of the outgrowth. At certain points of this junction the juxtaposed membranes became thickened. Our observations showed that these dense paramembranous thickenings always appeared initially on the postsynaptic membrane, and only after some time on the presynaptic membrane. The developing synapses, from the earliest stages of their formation, thus appeared distinctly asymmetrical on the electron micrographs, i.e., they were strictly polarized structures.

At the same time some synaptic vesicles moved toward sites of thickening of the contacting membranes, where they formed very characteristic concentrations (Fig. 1a, b, c). As regards the large pleomorphic vesicles, they usually were arranged some distance from the active synaptic zones, to form special vesicular groups beneath the plasma membrane that have been called "mound areas" (Fig. 1a, b; arrows). Their presence in the synaptosome definitely indicates that the nerve fiber continues to grow actively even after the formation of a synaptic contact.

During maturation of the synaptosomes the large pleomorphic vesicles gradually disappeared from their cytoplasm and the mainly homogeneous synaptic vesicles that were left showed a definite tendency to form clearly demarcated concentrations in active synaptic zones, the number of which in the synapse could increase in the course of its development. The number of mitochondria in the cytoplasm of the maturing synaptosomes also increased, whereas the glycogen granules gradually disappeared; single granular vesicles also appeared in this region.

Further differentiation of the synapse led to the development of well-marked pre- and postsynaptic paramembranous thickenings and to the formation of a distinct, uniformly widened synaptic cleft, containing so-called cleft material of highly characteristic structure. In the postsynaptic region of the interneuronal junction at this time particular subsynaptic specializations also could appear, evidence that a sufficiently high level of maturity had been reached.

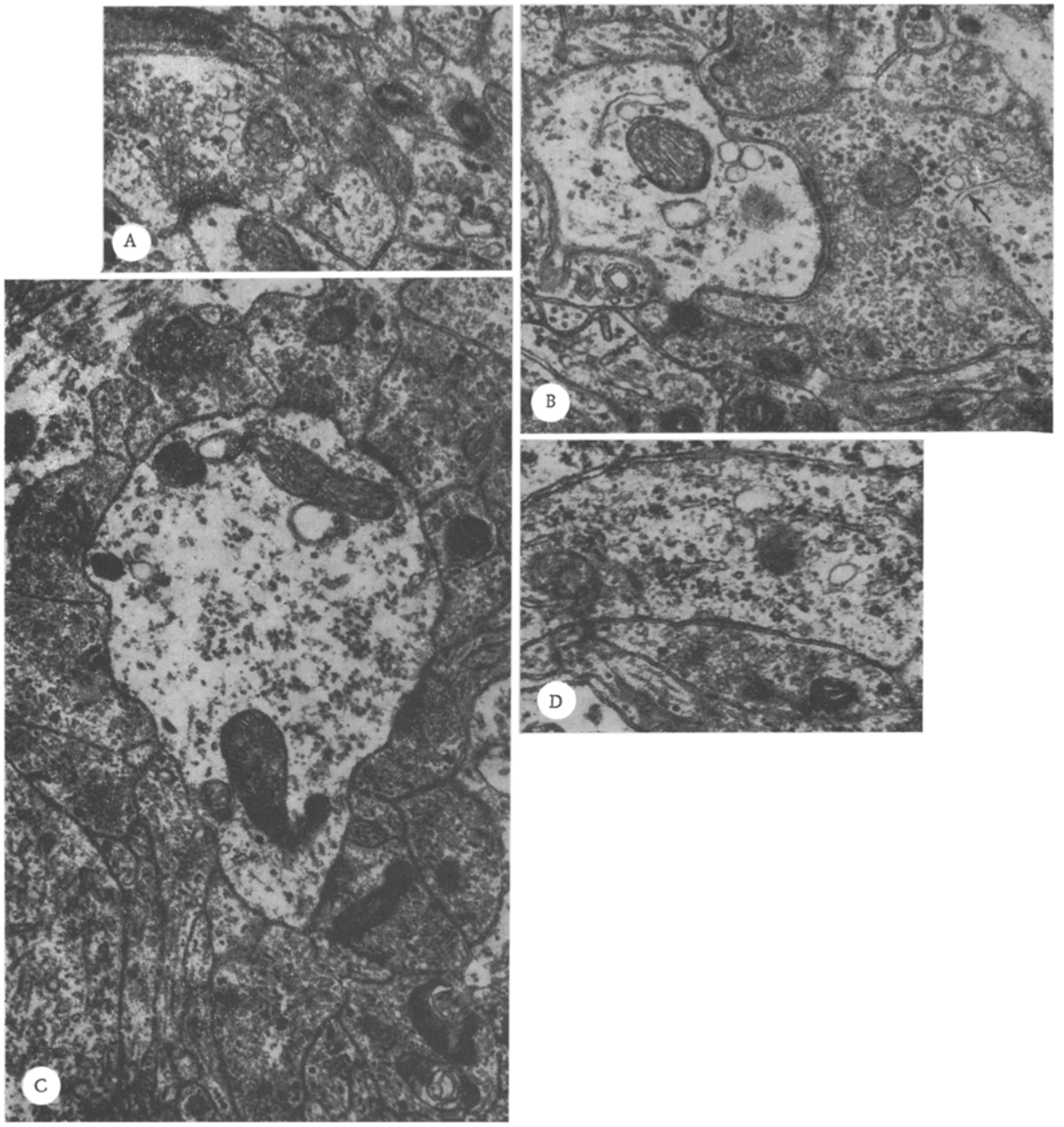

Fig. 1. Developing synaptic junctions on dendrites (a, b, c) and body (d) of neurons from ventral horns of brachial segment of human fetal spinal cord (12th week of pregnancy). Magnification: a) 32,500 ×, b) 35,000 ×, c) 19,000 ×, d) 24,000 ×.

After studying many electron micrographs we were convinced that at the 11th-12th week of intrauterine development of the human fetus not only single, but also multiple synaptic junctions, forming synaptic complexes, appeared on the outgrowths of the maturing neurons in the region of the spinal cord studied. Sometimes there were so many synaptic endings on one outgrowth, and they were so close together, that collectively they appeared to form a distinctive continuous ring around it — a unique kind of synaptic muff (Fig. 1c).

At the 11th-12th week of human fetal development clearly defined axosomatic synapses also were observed. They could arise on the surface of the body of a still poorly differentiated neuron (Fig. 1d), with a small rim of cytoplasm around its nucleus, and an endoplasmic reticulum that had only begun to develop. Such synapses were characterized by less well-developed paramembranous thickenings than axo-dendritic junctions, but in their general structure they were relatively mature and were undoubtedly functionally competent.

The initial phases of the fetal period of human antenatal development are thus characterized, as these observations show, by exceptionally intensive development of synaptogenesis in the presumptive ventral horns of the spinal cord. At this time widely different stages of this process can be identified here — from the time when the cones of growth reach the surface of the neuroblast until morphologically completely mature synapses, which may lie both on cell bodies and on dendrites. On the latter they can already be forming intricate synaptic complexes (of the synaptic muff type), a fact which must indicate a high level of functional specialization of the synaptic apparatus on differentiating ventral horn neurons of the developing human spinal cord.

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