PRINCIPLES OF MORPHOGENESIS OF HIGHER AUTONOMIC CENTERS DURING PATHOLOGIC PREGNANCY

S. A. Kakabadze

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The higher autonomic centers perform mutual regulation of metabolic and morphogenetic processes in the fetus during prenatal development, guaranteeing its resistance to birth stress and adaptation in the neonatal period. On disturbance of development or injury to these centers, autonomic symptoms appear as components of perinatal neurologic disorders, whose interpretation is impossible without information on morphogenesis of the nervous system. The main stages of prenatal ontogeny of the brain stem [1, 7, 9] and spinal cord [6] and the development of these structures during pathologic pregnancy [4] have been established morphologically. The results of most of these investigations are difficult to compare, and it is accordingly necessary to make a systematic approach to the study of the morphogenesis of the higher autonomic centers.

The aim of the present investigation was to determine the principles of morphogenesis and parameters of maturity of the neurosecretory, parasympathetic, and sympathetic centers in full-term fetuses after pathologic pregnancy, allowing for sexual and constitutional factors.

EXPERIMENTAL METHOD

Material was obtained at autopsies on 49 full-term fetuses, divided into four groups: 1) from 2.5 to 3.0 kg (14); 2) over 3.0 to 3.5 kg (15), 3) over 3.5 to 4.0 kg (14), and 4) over 4.0 kg (six). The pathologic conditions of pregnancy for all the groups were the result about equally of toxemias, and the general assessment of the "risk factors" varied from 9.6 to 11.6. The hypothalamus (HT), medulla (M) and superior thoracic segments of the spinal cord (SC) were fixed in formalin, by Bouin's method, and embedded in paraffin wax. Different stains and silver impregnation were used. The area of section of HT, M, and SC and, correspondingly, of the supraoptic nucleus (SON), the posterior nucleus of the vagus nerve (PN), and the lateral horn (LH) was determined. The concentration of neurons, the proportion of neurons with satellites, the dimensions of the neurons and satellites and other parameters were determined in the nuclei. Some material from SON, PN, and LH was fixed with osmium tetroxide by Caulfield's method and embedded in Araldite and Epon. Ultrathin sections were stained by Reynolds' method and examined and photographed in the Tesla BS-500 electron microscope. Numerical results were subjected to statistical analysis by Student's test.

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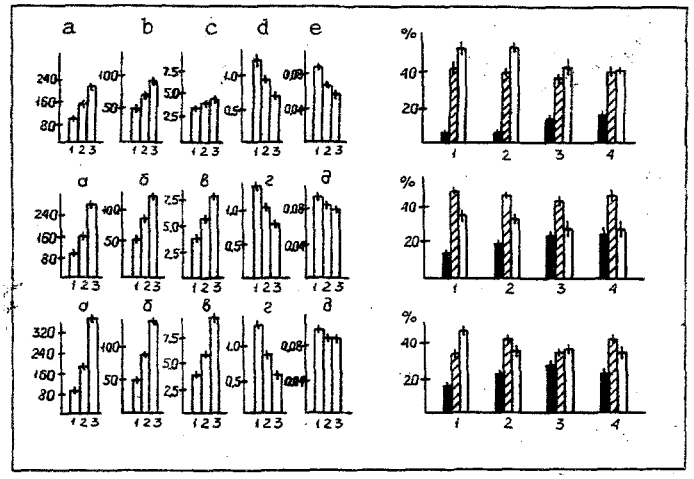

Fig. 1 Fig. 2

Fig. 1. Metric parameters of neurons of autonomic nuclei (averaged data for four groups of fetuses): I) SON, II) PN, III) LH; a) area of neuron, b) area of nucleus, c) area of nucleolus, d) nucleoplasmic ratio, e) nucleolo-karyoplasmatic ratio (areas given in μ^2). 1) Small, 2) medium-sized, 3) large neurons. Differences not significant: Ic, IIe, IIIe.

Fig. 2. Ratio between numbers of neurons by density of nucleic acids in SON (I), PN (II), and LH (III). 1, 2, 3, 4) Groups of fetuses. Black columns – high density, obliquely shaded – average density, unshaded – low density.

EXPERIMENTAL RESULTS

All groups of fetuses were characterized by stability of the relative weight of the brain (10-12%). There was no significant difference between the groups with respect to the dimensions of HT, M, and SC. The area of section of SON, PN, and LH varied, but not significantly, at 0.68 ± 0.057, 0.30 ± 0.011, and 0.060 ± 0.0028 mm^2 respectively. The situation was similar for the concentration of neurons, which was 33.0 ± 0.28, 13.5 ± 0.28, and 10.2 ± 0.25 in SON, PN, and LH respectively. The proportion of neurons with satellites in all groups in SON, PN, and LH was 25.5 ± 0.6, 29.4 ± 1.0, and 30.0 ± 1.1% respectively.

From the total number of neurons in each nucleus, we recorded small (phase of growth), medium-sized (completing differentiation, mature), and large (of definitive type) neurons. In all groups of fetuses in each nucleus the dimensions of neurons of the corresponding categories were the same. A general rule in differentiation is a marked increase in the nucleoplasmic ratio accompanied by a small and not significant decrease in or stability of the nucleolo-karyoplasmatic ratio (Fig. 1). With an increase in the degree of differentiation the frequency of discovery of neurons with low density of nucleic acids and proteins was reduced and the proportion of high-density neurons was increased. A characteristic feature of all nuclei from group 1 to group 4 was accumulation of nucleic acids and proteins (Fig. 2).

All groups of fetuses possessed the same relative numbers of neurons in different phases of the neurosecretory cycle, with predominance of the phase of secretion release. At the ultrastructural level, an increase in the degree of differentiation of the neurons was accompanied by rearrangement of the nuclear chromatin and accumulation of

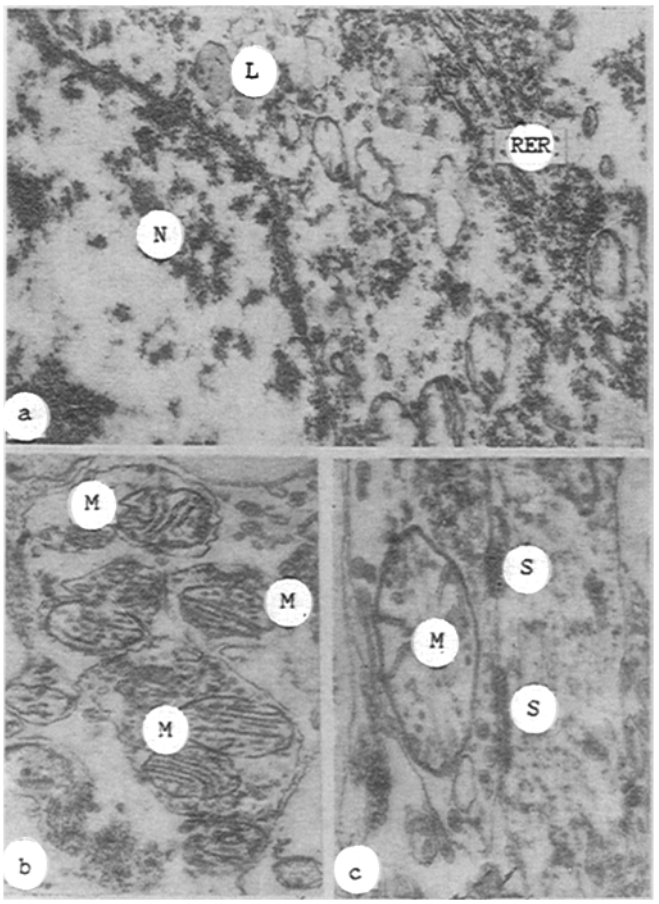

Fig. 3. Fragment of maturing neuron from lateral horn of spinal cord (a) and part of neuropil in region of posterior nucleus of vagus nerve (b) and supraoptic nucleus (c) in full-term fetuses: N) nucleus, M) mitochondria, L) lysosome, RER) rough endoplasmic reticulm, S) synapse. Magnification: a) 12,000, b) 18,000, c) 20,000×.

a rough endoplasmic reticulum, free ribosomes, mitochondria, and lysosomes (Fig. 3a). A characteristic feature of the interneuronal neuropil was a looser structure, but with the presence of large mitochondria in the outgrowths of the neurons, evidence of intensification of metabolism during the formation of the synaptic system (Fig. 3b, c).

The distance from the satellite nucleus to the perikaryon of the neuron in SON, PN, and LH of all groups of fetuses was 1.07 ± 0.06, 1.59 ± 0.08, and 1.51 ± 0.9 μ respectively. Nuclei with a low density of nucleoproteins were the largest, those with a high density the smallest in size. The fraction of low-density satellite nuclei in SON and PN decreased from fetuses of group 1 to those of group 4, whereas the fraction with high density increased. In LH this parameter was stable. The number of neighboring neurons was reduced in the microenvironment of all groups of neurons and all groups of fetuses, with an increase in the degree of differentiation, but the number of gliocytes remained stable.

Levels (high, average, low) of morphologic and functional maturity of the autonomic nuclei were determined from all the metric and cytochemical parameters of the neurons taken together. From all cases these levels of development were found in SON with a frequency of 40.0, 31.4, and 28.6%, and in PN and LH with values of 28.5, 54.2, and 17.3, and 14.3, 60.0, and 25.7% respectively. Levels (high, average, low) of morphological and functional

development of the whole central component of the autonomic regulatory apparatus were determined from all the parameters of maturity of the nuclei in each case, taken together. The general level of development of this apparatus appreciably rose from fetuses of group 1 to those of group 4, where only cases with high (50.0%) and average (50.0%) levels of development were found. An equal level of development of all parts was found in only 22.8% of cases. Uneven development with predominance of one or other part was observed more frequently. Comparative analysis in groups distinguished by sex revealed no significant differences in all parameters studied.

The conditions of gestation and birth could have a marked effect on the development and state of different parts of the nervous system [4, 10]. The absence of antenatal changes and the presence only of acute changes, due to intranatal asphyxia, in the parts studied indicates that the principles discovered reflect processes of morphogenesis and differentiation of the autonomic centers during "medium to high risk pregnancy." These conditions of gestation and birth have a smaller effect on formation of the metric parameters of these parts and of cellular formations, and a lesser effect on the cytological parameters of morphogenetic processes. The parameters of neurosecretion indicate activation of the function of SON, characteristic of pathologic pregnancy [4].

A characteristic feature of early neuro-ontogeny is heterochromia, manifested as the earlier formation of quantitative parameters of elements of the morphologic system compared with its size [2]. This rule was exhibited at the nuclear level in the material studied. The aggregate of these principles discovered for the majority of parameters indicates a general rule expressed as relative independence of formation of bulbar and spinal morphologic systems and their nuclei of the type of general nutrition of the organism and mass of the brain. The degree of this independence grows strongly in the caudal direction. The results are evidence of the high adaptive powers of the autonomic nervous regulatory apparatus of the large fetus. Nevertheless, these possibilities are not realized because of the imbalance and insufficiency of the hormonal mechanisms of adaptation characteristic of macrosomes [3, 8].

Heterochronia also is manifested in the development of morphologically and functionally homogeneous and heterogeneous structures of the diencephalon [1, 7], and also of M and SC [5, 6]. Despite the identity of the general principles of morphogenesis, a higher level of development of the neurosecretory part and the lowest level of the sympathetic part was established, although each of them was still far from the definitive state. The rostrocaudal gradient in development of autonomic centers was not always observed because of delay or accelerated development of certain centers. Dyschronia of development, along with other factors, lies at the basis of disturbance of integrated and coordinated activity of the autonomic nervous regulatory apparatus. The latter weakens the adaptive powers of the fetus toward birth stress, and in the extreme form it is responsible for death in the intranatal period. The principles of morphogenesis and parameters of maturity of the autonomic centers we have discovered can provide a reference point for the study of postnatal adaptive and pathological processes in the autonomic nervous system in cases with similar conditions of gestation and similar conditions of birth.

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