ORIGINATION OF NEUROBLASTS DURING POSTEMBRYONIC LIFE

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The question as to whether the intramural ganglions of the gastrointestinal tract possess a finite reserve of neuroblasts, laid down during embryogenesis, from which neurons later develop, or whether this reserve may be supplemented during extrauterine life, remains as yet unanswered.

A. A. Zavarzin and A. V. Rumyantsev [7] and N. G. Khlopin [17] reject the possibility of origination of neuroblasts during postembryonic life. A. I. Bubnova [2], M. I. Vekhova-Shandurova [4], N. M. Zhuk [6], N. G. Kolosov [11], S. I. Kolosova [12], Z. Ya. Tkachenko [16], Z. I. Khoros [18], and others do not mention this problem at all, and merely record the fact that neuroblasts are to be found in the ganglions of the Auerbach plexus of young humans and animals.

Isolated opinions on the division of neuroblasts during postembryonic life (T. A. Koblov [10]) were not supported by any convincing factual evidence.

T. I. Dekanosidze [5] believes that neuroblasts found "in the higher and lower levels of the nervous system" during the whole of the life-time of an individual "cannot represent the remnants of neuroblasts originating during the embryonic stage of life". The author admits the possibility that they may originate from "living matter."

EXPERIMENTAL METHODS

We studied the histological structure of the Auerbach plexus in the small and the large intestines of healthy cats and kittens of different ages, viz., newborn, 4 weeks to $1\frac{1}{2}$ months, 2-3 months, and adults (27 animals in all). Our observations were made on sections of whole preparations, treated by the methods of Bielschowsky-Gross, Avtsyn, and Spielmeyer. We studied the state of the nervous system of the intestine as a whole, and of tis nerve cells, fibers, receptors, and peripheral glia. The present communication deals with the origination of neuroblasts in the Auerbach plexus of young kittens.

EXPERIMENTAL RESULTS

Our studies of the histology of the Auerbach plexus of cats and kittens showed that the myenteric plexus contains, in addition to differentiated nerve cells of Dogel's Types 1 and 2, some nerve cells in the early stages of differentiation. Their morphological features are the same in all age groups. They are oval, round, or triangular cells, often concave on one side, dimensions from 6 × 8 μ, 10 × 8 μ, 12 × 6 μ to 18 × 10 μ, 20 × 22 μ. The nuclei are oval, angular, or crescentic, with 1-2 nucleoli, dimensions 4-6-8 μ, less frequently 10 × 8 μ, 12 × 4 μ, always situated peripherally.

The cytoplasm of these cells is finely granular, staining weakly, and often containing slender neurofibrils. Nerve processes are either absent, or are in the early stages of formation, as short, pointed cytoplasmic processes

(incomplete impregnation of the processes was excluded). These were the least differentiated cells, and we shall hereafter refer to them as neuroblasts.

Other cells of this class were more highly differentiated, and represented transition stages between neuroblasts and mature neurons; their neurofibrillar network is more developed, and is as a general rule concentrated as a ravelled mass at the center of the cell, and they usually possess thin (diameter less than 1μ) processes, which disappear in the stroma of the plexus soon after emergence from the cell. The number of neuroblasts present in the Auerbach plexi is less than of differentiated nerve cells, in all age groups. The number of neuroblasts rises gradually from birth, during the first months of life; more are found in kittens aged from 4 weeks to 3 months than in newborn kittens. Individual ganglions of the plexus of 2-3 months-old kittens consisted exclusively of neuroblasts, which was never encountered in newborn kittens. There are fewer neuroblasts in adult cats than in kittens.

These findings are incompatible with the view that the ganglions of the Auerbach plexus possess a fixed reserve of neuroblasts, laid down during embryogenesis, which is depleted as they undergo differentiation to neurons.

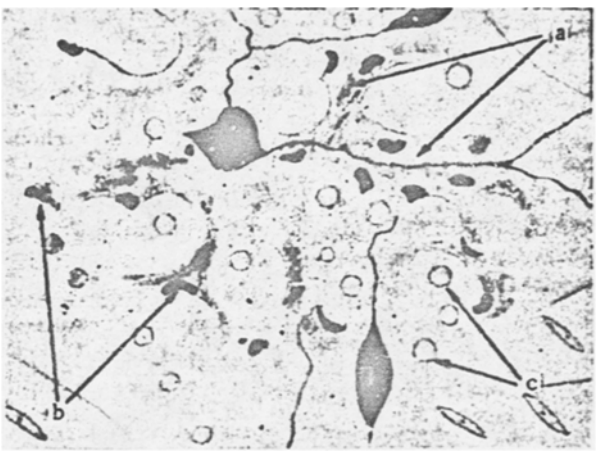

Fig. 1. Myenteric ganglion of the small intestine of a newborn kitten. Semidiagrammatic representation. Whole preparation. Impregnated according to Bielschowsky-Gross. Oil immersion.
a) Regions of differentiation of neuroglial syncytium; b) neuroblasts; c) peripheral glia nuclei.

From what do the neuroblasts originate? From our study of the peripheral glia of the Auerbach plexus we received the impression that they originate from the glial syncytium.

The peripheral glia of the ganglions of the Auerbach plexus of the intestine of cats and kittens is a syncytium, i. e., it consists of numerous nuclei embedded in a protoplasmic mass. The dimensions and the shape of the nuclei are identical in all age groups. With increasing age the number of nuclei rises, by amitotic division, and the protoplasmic mass of the neuroglial syncytium becomes firmer. The syncytial nuclei are, as a general rule, round or oval, and are located compactly. Individual parts of the syncytium differ from the above description in the nature of the nuclei and protoplasmic mass. In these regions, which may be called regions of differentiation of the neuroglial syncytium, the nuclei are more widely spaced, and closely resemble the nuclei of neuroblasts. Similarly to the nuclei of neuroblasts, they are of an irregular oval or angular shape, or are crescentic, and they measure 4-6-8μ. The finely granular, weakly-impregnating syncytial protoplasm forms a complicated pattern around the nuclei, with round vacuoles and narrow channels, i. e., it forms a sort of "nucleo-protoplasmic territory", from which arises the individual cellular element (Fig. 1). Slender neurofibrils can be seen in the cytoplasmic parts of the cells thus segregated (Figs. 2 and 3). Some of the above-described neuroblasts are usually located adjacent to these formations (see Fig. 1).

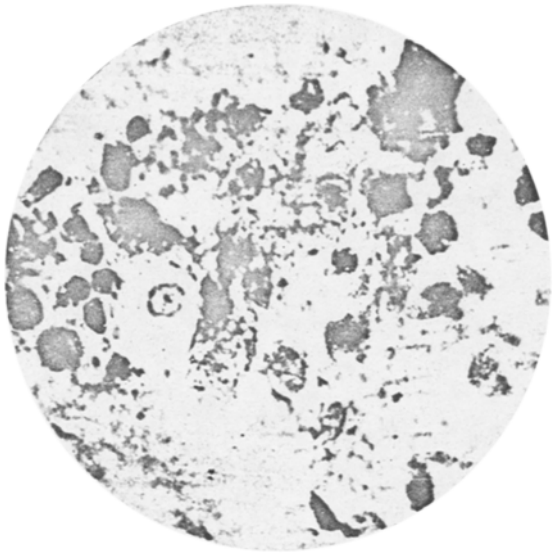

Fig. 2. Myenteric plexus of the small intestine of a newborn kitten. Photomicrograph. Neuroblasts segregated from the neuroglial syncytium. Syncytial continuity between the cells is still preserved, in the form of narrow isthmuses. The fine granular protoplasm of the segregating cells contains slender neurofibrils. Whole preparation. Impregnated according to Bielschowsky-Gross. Oil immersion.

A certain degree of correlation between the number of neuroblasts and the degree of differentiation of the neuroglial syncytium is observed at different ages. Regions of differentiation of neuroglial syncytium are particularly frequently encountered in newborn kittens, in which the number of neuroblasts is small. Individual ganglions of the Auerbach plexus of newborn kittens consist exclusively of differentiating syncytium containing solitary neuroblasts. In kittens aged from 4 weeks to 3 months regions of differentiation are less frequently encountered than in newborn kittens, and the number of neuroblasts in the ganglions rises; individual ganglions consist exclusively of neuroblasts. Regions of differentiation of the syncytium are less frequently seen in adult cats, and the number of neuroblasts in them is smaller than in kittens.

It is of interest, in connection with the above, to consider the embryogenesis of intramural ganglions. Evidence against the migration theory is afforded by certain observations, pointing to the origination of the intramural ganglions in situ, during the process of development of the organ (Remak [15], Veber [3], S. L. Matveeva [13]). Keining [8] showed that the neuroblasts of differentiating intramural ganglions of the esophagus of a 4-day chick embryo are indistinguishable from elements of the mesenchymal syncytium, similarly to which they retain syncytial interconnections. L. I. Belenko [1] remarked that the intramural ganglions of the vascular adventitia of 3-5 months human embryos represent "primitive anlage of syncytial structure".

It may, in the light of these literature references and of our own observations, be supposed that the neuroglial syncytium retains the capacity during postembryonic life of segregating and separating cellular elements, which then undergo differentiation to yield mature neurons.

Fig. 3. The same preparation as in Fig. 2. Magnification x 1200.

The peripheral glia of the ganglions of the Auerbach plexus of newborn kittens appears to possess the greatest potential for differentiation of neuroglial syncytium. Intensive delimitation of neuroblasts is not, however, observed at this stage, which may be related to the presence within the ganglions at the time of birth of a sufficient number of differentiated nerve cells for the proper functioning of the nervous system of the intestine at this age.

In kittens aged from 3 weeks to 3 months, over which period growth and differentiation of the intestinal wall as a whole take place, in relation to the growth of the animal and to its transition to a different mode of nutrition, we observed an increase in the number of neurons in the ganglions of the plexus, due to differentiation of neuroblasts. In turn, the number of neuroblasts rises, owing to an intensive process of their delimitation from the neuroglial syncytium. The number of regions of differentiation of the syncytium must naturally become smaller, and the number of separated neuroblasts must increase, as a result of this process.

In adult animals, which have largely completed the process of growth and differentiation of the intestine, differentiation of the neuroglial syncytium is less frequently encountered, and the number of neuroblasts is smaller than in kittens.

These are our results. They reveal the source and the pathways of origination of neuroblasts in the intramural ganglions of the intestine in the postembryonic period of life of an animal. This finding is of great biological importance, since it elucidates the question of the regeneration of the intramural nervous system of the digestive tract, and provides indirect evidence of regeneration of neurons after their destruction in a number of pathological conditions. It would, in this connection, be of considerable interest to examine the peripheral glia of the Auerbach plexus in such pathological conditions of the gastrointestinal tract as are associated with mass destruction of neurons and with increase in the number of neuroblasts.

SUMMARY

Auerbach's plexus was studied histologically in the intestines of 27 healthy cats and kittens. Besides the differentiated neurons, neuroblasts were revealed in the ganglia of the intermuscular plexuses. In animals the number of these neuroblasts gradually increases during the first several months of life.

Peripheral glia in the plexus ganglia have 2 variations of the neuroglial syncytium. The first is in the form of a protoplasmatic mass with scattered nuclei, while the second is in the form of nuclear-protoplasmic areas with a tendency to separation of the cellular elements. The latter are morphologically similar to neuroblasts. The intensity of the process of separation of neuroblasts from the neuroglial syncytium is connected, in the author's opinion, with the functional activity of the digestive tract.

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