MULTIPLICATION OF CAPILLARIES IN DIFFERENT PARTS OF THE BRAIN IN THE POSTNATAL PERIOD

T. P. Zhukova

Laboratory of the Study of Cerebral Development (Head, Corresponding Member AMN SSSR Prof. B. N. Klosovskii), Institute of Pediatrics (Director, Active Member AMN SSSR O. D. Sokolova-Ponomareva), AMN SSSR, Moscow,
(Presented by Active Member AMN SSSR O. D. Sokolova-Ponomareva)
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The development of the capillary network of the brain in man and many animals is not complete until the postnatal period. There is a vigorous formation of capillaries in various parts of the nervous system for a considerable time after birth, when the capillary network, and particularly its venous portion, become finally differentiated.

The increase in the number of capillaries by branching was discovered by B. N. Klosovskii by using his own method of impregnating the walls of the vessels with silver. He and his co-workers [3,4,7-10,12,13,14] described in detail the different stages in the growth of the cerebral capillaries, and the change in the rate of growth in the cerebral cortex in various animals at various developmental stages. A new capillary is formed from a cell of the adventitia which passes along the vessel, and it passes through a number of stages before a functional capillary is formed. The earliest stage is called the "bud" stage, then as it grows it becomes transformed into a "polyp," and finally forms a "hydroid."

At all stages of the growing capillary, at the free end where the nucleus which formed its cells lies, there are numerous fine protoplasmic outgrowths. As it grows, the newly-formed capillary reaches another functional capillary through which blood is passing and becomes joined to it, usually by one or two protoplasmic outgrowths. Next the remaining outgrowths disappear, and the newly-formed capillary begins to function. Multiplication of the capillaries in the brain is largely complete in cats and dogs by the 4th-5th month, and in rats by the 2nd month of life [5,6,9,12,13,14]. In some cases we observed the appearance of solitary growing capillaries in different parts of the brain of adult rats [2]. The most intensive multiplication of capillaries in the nervous system takes place in the first few days and weeks after birth.

In the investigations referred to above, the growth of the capillaries was studied in some part of the brain either under normal conditions, or when influenced by various means. Nevertheless, no account was taken of the rate of increase of the capillaries in different parts of the nervous system and at different periods, so it is not known whether multiplication of the capillaries takes place simultaneously at the same rate throughout the brain, or whether each part has its own period at which capillary growth is maximal and corresponds to its structure and function. The object of the present investigation has been to solve these problems.

METHOD

A study was made on capillary growth in the brain of rats and cats which ranged from newborn animals to those 2-3 months old. In all, 18 cats and 70 rats of various ages were investigated. The most detailed work was done on the rat brain. The animals were killed by decapitation without anesthesia, and always at the same time of day. The brain was fixed in 10% formalin, and after fixation it was treated by B. N. Klosovskii's method [9]. Frontal serial sections 150 μ thick were made. The capillaries were counted under a magnification of 400 x. The counts were made of the capillaries in different stages of growth, in 100 fields of view. In the rat brain, the growing capillaries were counted in 500-1,500 fields of view, while in the cat brain the number of fields was 1,000-11,000. Capillaries were counted in the frontal, parieto-temporal and occipital regions, in Ammon's horn, the nucleus caudatus, in the thalamus, and in the brain stem and cerebellum.

RESULTS

Table 1 shows the results of a count of newly-formed capillaries in the rat brain at different ages.

TABLE 1. Number of Newly-Formed Capillaries in the Rat Brain at Different Ages

Age of animal	Cortex			Ammon's horn	Nucleus caudatus	Thalamus	Brain stem	Cerebellum
	frontal region	parieto-temporal region	occipital region					
Newborn	126	160	72	305	501	323	184	44
7 days	170	218	162	293	269	174	144	81
10 days	385	443	149	250	212	176	—	—
15 days	288	283	449	171	113	94	—	—
18 days	68	58	53	11	—	5	7	17

It can be seen from Table 1 that in newborn rats the maximum number of growing capillaries is found in Ammon's horn, in the nucleus caudatus, and in the thalamus. In the sensory and motor cortex the number of growing capillaries is at this time much smaller than it is in the subcortical structures, but almost twice as great as in the visual cortex.

In 7-day, and particularly in 10-day, rats the rate of increase of capillaries in the subcortical nuclei and in the thalamus falls; in the cortex of the frontal and parieto-temporal regions it increases by the 10th day by $2\frac{1}{2}$ - 3 times. In the occipital cortex, the number of newly-formed capillaries at this time is also increased, but less than in the regions just mentioned. By the 15th day of life, in the frontal and parieto-temporal regions, there is some reduction in the rate of capillary increase, which is particularly marked in the parieto-temporal region. There is a great increase in the occipital region. As compared with newborn animals, the increase is six times or more. At this age the rats begin to open their eyes, so that the nerve cells of the visual centers become active.

Even by the 18th day after birth, the rate of growth of capillaries in all parts of the brain falls sharply. In the subcortical areas only occasional growing capillaries are found, and in the cortex and cerebellum they are somewhat more numerous. After 20-24 days, the number of capillaries in the cortex is 25-40 per 100 fields of view. At this time most of the newly-formed capillaries are to be found in the cerebral and the cerebellar cortex. In rats older than $1\frac{1}{2}$ - 2 months, new capillary formation has almost ceased in all parts of the brain. In other adult rats, in some cases we have observed the appearance of occasional growing capillaries, but the reason for their presence has not yet been explained.

TABLE 2. Number of Newly-Formed Capillaries in the Brain of Cats at Different Ages

Age of animal	Cortex			Nucleus candatus	Thalamus	Midbrain	Pons	Cerebellum
	frontal region	parietal region	occipital region					
8 days	77	105	82	80	33	—	—	—
23 days	131	79	83	—	34	42	82	32
30 days	149	99	112	—	—	—	—	—
32 days	254	183	156	—	—	—	—	—
35 days	37	47	95	28	33	52	12	29

New capillary formation in different parts of the brain and the occasion for its maximal intensity is closely associated with myelinization of the nerve fibers in the cortex of the different analyzers. Thus, it is known that in the cortex, the nerve fibers of the cutaneous and motor analyzers are the first to become myelinated, and the same applies to the cortical centers of the vestibular receptors. Myelinization occurs later in the visual analyzer [3,15,16]. It should be noted that the increased multiplication of the capillaries heralds the myelinization of the corresponding cortical regions.

There is a similar irregularity in the formation of new capillaries in the different parts of the brain in cats. Table 2 shows a few examples of a count of the number of growing capillaries in different parts.

Not only is there a difference in the number of newly-formed capillaries between widely separated parts of the brain, but there may be differences in a single section between functionally distinct cortical areas, and between different thalamic or midbrain nuclei. For example, in a 30-day-old kitten, in a section passing through the motor cortex, 37 capillaries per 100 fields of view were found around the sulcus cruciatus, while in the posterior sigmoid gyrus there were 30, in the gyrus limbicus anterior there were 59, and in the gyrus sigmoid anterior only 5.

The difference in the number of growing capillaries between neighboring gyri is particularly noticeable in the older animals, and it is better shown in cats.

In rats, the distribution of newly-formed capillaries in the cerebral cortex shows less difference between adjacent areas. But here too there are differences in the rate of increase; for example, between Ammon's horn and the adjacent parieto-temporal region, at certain periods the difference may be two-fold or more. In 10-day rats in the parietal cortex and on the medial surface of the hemispheres (limbic region) 283 growing capillaries per 100 fields of view could be counted, and on the same section on the convex surface of the hemispheres the count was 536, and in the nucleus caudatus it was 207.

The number of newly-formed capillaries per 100 fields of view varies greatly from one animal to another. Thus, in one newborn rat there might be 158 capillaries per 100 fields of view, and in another 271. However, as a rule, the changes occurred in all parts of the brain, and the increase was not confined to particular regions.

In healthy rats and cats there is a more or less definite and characteristic relationship between different kinds of growing capillaries. Usually the "hydroid" forms preponderate, and next in order are the "buds"; the least frequent type is the "polyp." The capillaries which are least frequently found are those which are joined to others which are already functional. A small percentage are atypical,having atrophic protoplasmic autgrowths, or a greatly constricted or twisted foot. The distribution of the growing capillaries in stages is illustrated by the following figures which applied to the brain of a newborn rat and a 30-day-old cat. Figures represent counts per 100 fields of view.

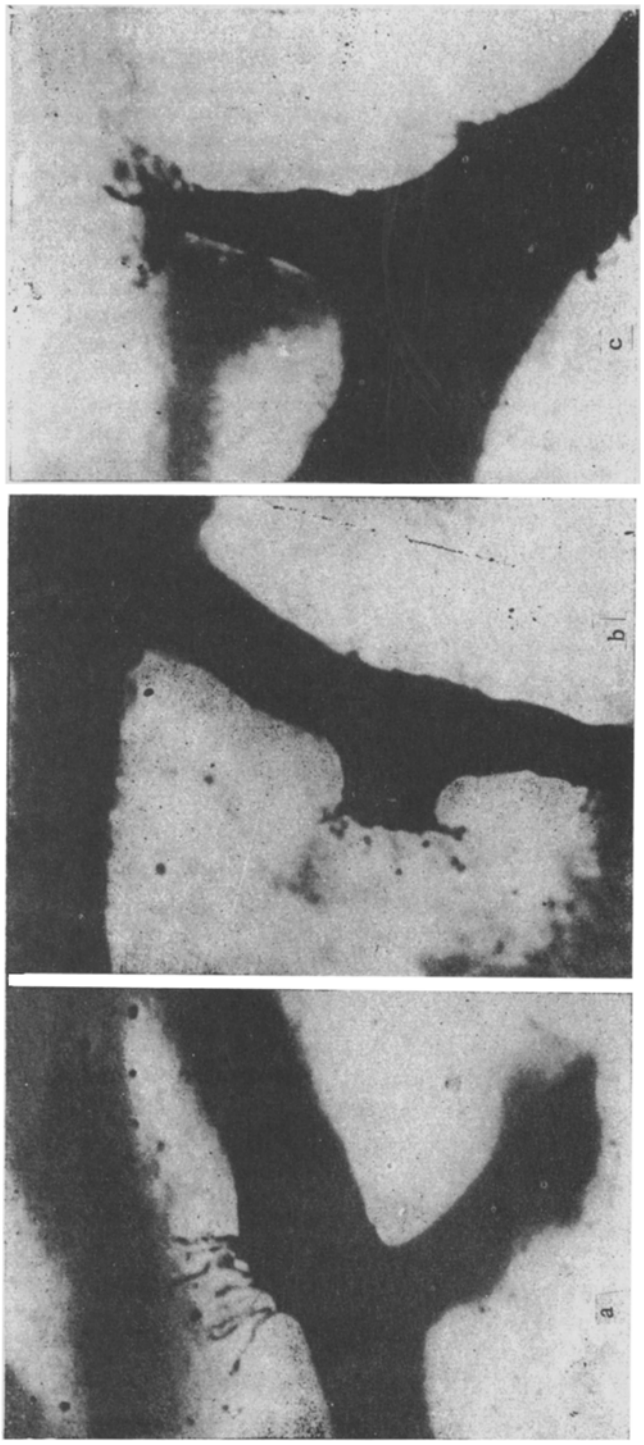
Stage	Newborn rat	30-day cat
"Buds"	76	7
"Polyps"	40	11
"Hydroids"	96	44
Various	5	1

As age increases, besides an increase in the total number of newly-formed capillaries, there is a very noticeable reduction in the number of "bud" stages,as a result of which the "hydroid" form comes to preponderate. Usually, a large number of "bud" stages is characteristic of the period of most intense multiplication ("explosive" growth of capillaries).

In animals which are newborn or a few days old, capillary growth in the brain shows several characteristic features. Protoplasmic outgrowths of the growing capillaries of newly-born animals are short, and usually few in number. The growing capillaries themselves have a thickened foot, which is apparently associated with a general expansion of the vascular-capillary net in the brain caused by the influence of the birth process itself. In different animals, the number of growing capillaries in the brain immediately after birth varies over a wide range. Even one day after birth, the newly-formed capillaries usually are longer and have a larger number of protoplasmic outgrowths.

In rats, and to a smaller extent in cats, in the first few days after birth it can be seen that capillaries grow out not only from branches of capillaries having a diameter of 4-7 μ, but also from the larger vessels whose diameter is 15-20 μ. Sometimes two or three neighboring buds join and give rise to a branch whose foot is 2-3 times greater in diameter than are the surrounding capillaries (see figure). Evidently such a branch will represent the origin of a vessel larger than a capillary.

In rats aged 13-18 days and more, and in cats after the 20th day, capillary vessels can be seen growing near nerve cells or near their outgrowth. This effect was usually noticed on preparations where the vascular capillary plexus and isolated nerve cells with all their outgrowths were impregnated together. As a rule, there are only a small number of growing capillaries in the white matter. The increase in the density of the vascular capillary



Examples of the growth of capillaries by branches from large vessels. Brain of rat aged 7 days. Impregnation by Klosovskii's method. Magnification 600 ×.

plexus of the brain in the postnatal period should be associated not only with an increase in brain size, but also with the active function of the nerve cells themselves. The latter occurs chiefly after birth, and is shown by E. N. Kosmarskaya's experiments [11]. She found that an indication of increased function in various receptors, for example the vestibular receptor, in the first few days or weeks after birth leads to hypertrophy of the bodies of the nerve cells and to an increase in the density of the vascular plexus of the corresponding nuclei in the brain stem.

Besides these general features of the growth of the vascular capillary plexus which takes place by branches, other processes also take place in the cat and rat brain, and they run their course usually during the first few days after birth. In the rat the multiplication of the capillaries is much more rapid at this time in all parts of the brain. Also, in the rat the growth of capillaries from the large vessels is also better shown, and in the first few days of life the growth of vessels by branches penetrating into the pia mater, particularly in the region of the cerebellum, can be observed. Possibly these differences are due to the fact that rats attain full maturity sooner (they are sexually mature by the second month, whereas cats are not mature until the sixth month). Probably the very rapid development of the vascular capillary plexus in the rat brain is associated with this rapid structural and functional development.

Thus, studies of the vascular capillary cerebral plexus in animals of different ages has shown that in different parts of the brain and also in different parts of the cerebral cortex, the maximal rate of capillary development occurs at different times, and the effect is to be attributed to the different periods of morphological and functional maturation of the various parts. The different rates of multiplication of the cerebral capillaries, even in parts of the brain which are not far removed from each other, indicates that apparently there are local factors of some kind which facilitate their multiplication in a particular area. Further specially directed studies will be required to determine the nature of these factors, how they are associated with the development of nerve cells, with the myelinization of the nerve fibers, and particularly with the development of oxidative enxyme systems.

SUMMARY

The brain was impregnated with silver by B. N. Klosovskii's method, and the newly-formed

capillaries were counted in serial sections. In rats and in cats it was found that both in different parts of the brain as well as in different cortical areas, the majority of new capillaries are formed by way of offshoots which develop at various times postnatally. Their formation is associated with the functional and morphological maturation of the corresponding nerve centers. Capillary branching ceases first in the brain stem and in the subcortical areas; after birth the process continues longest in the cerebral and cerebellar cortices.

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