Structural Changes in Visual Cortex Area 17 in Children with Aftereffects of Perinatal Injury to the Central Nervous System

V. N. Sal'kov and R. M. Khudoerkov

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Structural characteristics of the visual cortex area 17 were studied by computer morphometry on autopsied specimens of the brain from children with perinatal injury to the central nervous system and in a group of control children without symptoms of brain injury. In children with perinatal pathology, the thickness of the cortex and its individual layers (IV, V, VI+VII) increased unevenly during the 1st year of life, the density of neurons decreased, while the content of neuroglia increased. These disorders reflect nonspecific structural and functional changes in the visual cortex associated with perinatal cerebral pathology.

Key Words: *brain; visual cortex; neurons; gliocytes; perinatal disease*

Traumas, infections, and intoxications, as well as hypoxia and endocrine disorders play an important role in the etiology of perinatal injuries to CNS (PICNS) [3,9]. Neurological disorders (motor disorders, convulsive, hydrocephalic syndromes, *etc.*) detected in children from the first days of life are referred to PICNS consequences, the most unfavorable outcome of which is cerebral palsy (CP). The incidence of CP is 2.5 to 9.0 cases per 1000 children [4].

The leading symptoms in CP are central (spastic) pareses [4,6]. Vision disorders augmenting clinical picture and social adaptation of patients are detected in 25% patients with CP [1,2]. Specific interactions between the visual and motor analyzers during vertical posture maintenance were noted in children with CP. The main morphological changes in the motor cortex and brain stem in PICNS and CP were studied [5,7,8]. However, we found no reports about morphological changes in the visual cortex.

Laboratory of Functional Morphochemistry, Institute of Brain Research, Russian Academy of Medical Sciences, Moscow. ***Address for correspondence:*** neurolab@yandex.ru. V. N. Sal'kov

We studied quantitative neuromorphological parameters of the visual cortex area 17 in children with a history of PICNS.

MATERIALS AND METHODS

Morphological studies were carried out on autopsy material from the brain of children with PICNS consequences (6 cases) dead from intercurrent diseases. Life-time diagnosis of CP was made in 3 patients. Brain specimens (autopsy material) from children suffering from somatic diseases (3 cases) served as the control. The pathological and life-time diagnoses were in sufficiently good agreement.

The thickness of the visual cortex and its individual layers (IV, V, VI+VII) in area 17 and the density of neurons and gliocytes in layers V and VI+VII were studied in paraffin sections of the brain (15 μ) stained with cresyl violet. The density of neurons and gliocytes was evaluated in the visual field of the microscope through the computer monitor. Thirty visual fields were examined in each section. The measurements were carried out at the levels of 3 planes of the section depth. The results

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were summed up. The volume of visual field of the preparation was calculated as the product of the microscope visual field area by the section thickness. The result was 25,000 μ^3.

Morphometry of histological preparations was carried out on a Leica-DMLB microscope connected to a videocamera and Leica QWin image analysis sytem.

The results were statistically processed using Student's *t* test.

RESULTS

In infants aged under 12 months with a history of PICNS, the differentiation of the cortical area 17 into layers was not completed. There was no interface between layers II and III and between layers III and IV; clarification in sublayer IVB was clearly seen, while cell density in sublayer IVC remained high. Clear-cut separation of layers was detected in bottom layers of the cortex (V and VI+VII). Radial striation was detected only in layers VI+VII. In hypertrophied layer I, hyperplasia of glial nuclei and accumulation of Cajal—Retzius cells at the surface were seen. Layer II was presented by small round undifferentiated cells. Poorly differentiated pyramidal neurons predominated in layer III with high density of cells. Solitary Meynert nerve cells scattered in layer V reached the highest morphological maturation.

Ischemic changes in neurons were seen in all layers of the cortex, irrespective of infant's age.

Morphometric studies showed that the thickness of the cortex (area 17) during 8 months of life increased by 351 μ (31%) in the control group and by 390.9 μ (34%) in infants with prenatal pathology. A direct linear relationship between the increase in cortical thickness and infant's age was detected in the control group (Fig. 1), but no clear-cut correlation between these parameters was detected in infants with PICNS (Fig. 2).

The most significant changes in the morphometric parameters were observed in cortical layers IV, V, VI+VII. The thickness of cortical layer IV increased by 160.6 μ (60%) during 8 months in controls and by 92.4 μ (28%) in infants with perinatal pathology. The thickness of cortical layer IV increased linearly in controls (Fig. 1) and nonlinearly in patients with perinatal pathology (Fig. 2). In both groups, the thickness of layer V less significantly changed with age (Figs. 1, 2). The thickness of layers VI+VII in the course of cortical plate growth changed unevenly (Fig. 1, 2).

In infants with PICNS, neuronal density and count differed significantly from the corresponding parameters in controls (Tables 1, 2). For instance,

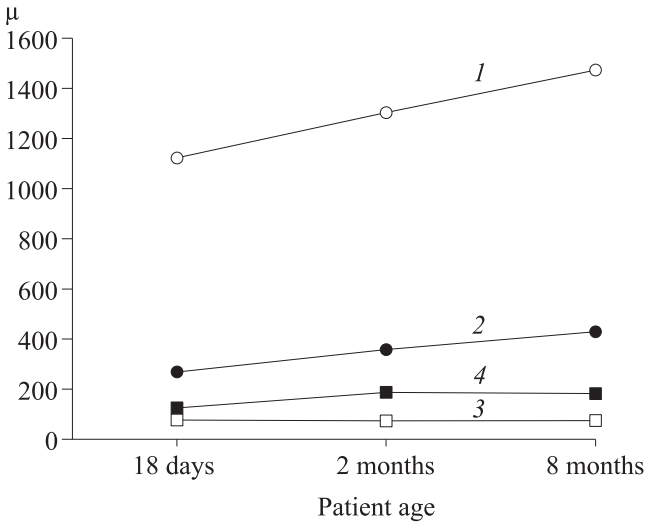

Fig. 1. Age-related changes in the thickness of visual cortex area 17 (*1*), layers IV (*2*), V (*3*), VI+VII (*4*) in infants with somatic diseases. Here and in Fig. 2: ordinate: cortical thickness.

in an infant with severe PICNS, who died at the age of 17 days, the densities of neurons in layer V and in layers VI+VII were 23.2 and 39.9 per 25,000 μ^3, while in a infant of the same age without symptoms of CNS injury these values were 46.9 and 88.3, respectively (Tables 1, 2).

During the early postnatal ontogeny, the density of gliocytes in control infants tended to decrease, while in infants with PICNS this parameter remained practically unchanged. In the control group, the density of gliocytes in layer V in infants aged 18 days and 2 months was 28.6 and 11.9, while in infants of the same age with PICNS the corresponding values were 12.7 and 14.3, respectively (Table 1).

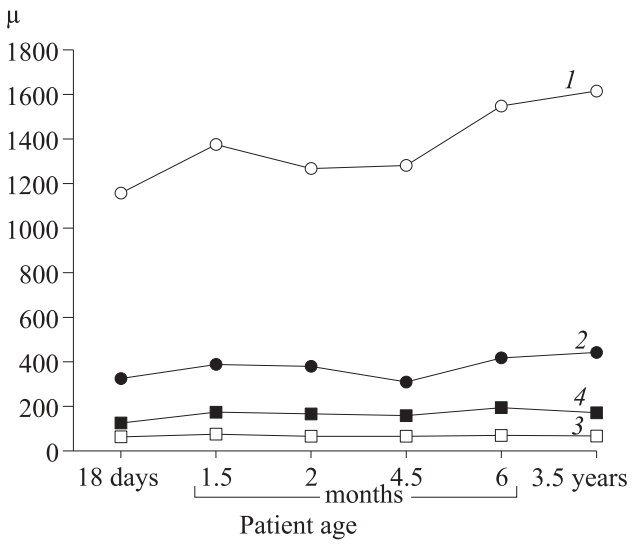

Fig. 2. Age-related changes in the thickness of visual cortex area 17 (*1*), layers IV (*2*), V (*3*), VI+VII (*4*) in infants with brain involvement consequences of PICNS and CP.

TABLE 1. Density of Neurons and Gliocytes in Cross-Section of Cortical Area 17 Layer V in Healthy Infants and Infants with PICNS Aged under 1 Year in Health and with PICNS (cells per 25,000 μ³; *M*±*m*)

Group	Age	Neurons	Gliocytes	Astrocytes	Oligodendrocytes
Normal level	18 days	46.90±1.39	28.60±1.17	21.00±0.78	7.60±0.49
PICNS	17 days	23.20±1.21*	12.70±0.78*	9.60±0.57	3.10±0.27
Normal level	2 months	29.9±0.5	11.90±0.31	7.80±0.23	4.10±0.19
PICNS aftereffects	1.5 months	20.30±0.45	10.30±0.44	7.20±0.33	3.10±0.21
	2 months	21.90±0.53	14.3±0.5	9.0±0.3	5.30±0.29
Normal level	8 months	20.50±0.84	9.20±0.38	6.60±0.34	2.60±0.17
CP	4.5 months	17.90±0.27	15.70±0.55*	6.80±0.35	8.90±0.36
	6.5 months	19.0±0.6	12.20±0.54	7.90±0.44	4.3±0.4

Note. Here and in Table 2: *$p<0.05$ for values in infants with PICNS compared to normal. Normal: infants without neurological abnormalities dead from somatic diseases.

TABLE 2. Density of Neurons and Gliocytes in Cross-Section of Cortical Area 17 Layers VI+VII in Healthy Infants and Infants with PICNS Aged under 1 Year in Health and with PICNS (cells per 25,000 μ³; *M*±*m*)

Group	Age	Neurons	Gliocytes	Astrocytes	Oligodendrocytes
Normal level	18 days	88.30±2.13	35.40±0.99	26.40±0.83	9.00±0.37
PICNS	17 days	39.9±2.3*	16.40±1.13*	12.10±0.79	4.30±0.43
Normal level	2 months	53.6±0.9	15.00±0.84	10.10±0.24	4.90±0.27
PICNS aftereffects	1.5 months	40.50±0.83	12.30±0.43	9.1±0.3	3.20±0.21
	2 months	43.5±0.9	17.90±0.47	11.20±0.35	6.70±0.24
Normal level	8 months	31.50±0.88	10.50±0.43	7.90±0.73	2.60±0.19
CP	4.5 months	32.90±0.67	18.60±0.59*	8.40±0.47	10.20±0.36
	6.5 months	29.30±0.71	13.00±0.51	8.10±0.39	4.90±0.52

By the second half-year of life, the density of gliocytes in layer V in patients with PICNS was higher than in controls (Table 1). Similar changes in the density of neurons and gliocytes were noted in cortical layers VI+VII (Table 2).

The thickness of visual cortex area 17 increased unevenly in patients with PICNS in comparison with patients with somatic diseases, the most significant changes were observed in layers IV, V, and VI+VII. The thickness of these layers increased less significantly than in infants suffering from somatic diseases and changed unevenly with age: no relationship between the increment in the thickness of these layers and of the cortical transverse section could be detected. The density of neurons in the visual cortex of infants of the 1st year of life with perinatal pathology was lower than in infants without neurological symptoms, while the density of gliocytes virtually did not change. However, the density of gliocytes in the visual cortex in infants without neurological symptoms decreased during the first year of life.

The detected changes in the neuroglial parameters of the visual cortex correlate with published data on cerebral formations in the motor system of children with PICNS consequencies [4,7]. Changed thickness of the motor cortex [4], thinning of layer V in area 4 [7], and reduced density of large pyramidal neurons in this cortical layer were noted [4], as well as decreased density of neurons near the nuclei of craniocerebral nerves. On the other hand, the count of gliocytes in this area and in the initial segments of the spinal cord increased [4].

These results together with published data suggest that in children with a history of perinatal cerebral injury the number of neurons per unit volume of visual cortex decreases with age, while the content of glial elements increases. This can be caused by the death of nerve cells and development of substitutive gliosis. Presumably, these changes result from nonspecific reaction of the nerve tissue of the developing fetus (or newborn) to hypoxia, infection, intoxication, and other factors. Neuronal death caused by these factors, no doubt, prevents normal formation of the brain and seems to promote the development of combined clinical symptoms in the CNS [6].

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