# MORPHOLOGICAL CHANGES IN THE CEREBRAL CORTEX DURING COMPENSATION OF DISTURBED FUNCTIONS

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The problem of the compensation of disturbed functions of the central nervous system, a matter of considerable theoretical and practical importance, has been investigated by several Soviet neurophysiologists [2-4]. Animal experiments have shown that the compensation of disturbed functions associated with substantial injuries to the central nervous system takes place on account of preserved structures, "spare" pathways, and scattered cells. It has also been shown that the development of compensatory phenomena in higher animals possesses obvious features of education, and that the cerebral cortex plays an organizing role in the process of restoration of disturbed functions. However, the morphological basis of these physiological observations has not been adequately studied.

The object of the present investigation was to study the morphological changes in the cerebral cortex during the compensation of disturbed functions.

## EXPERIMENTAL METHOD

The investigation was carried out on 24 adult animals (cats and dogs), on which a lateral hemisection of the spinal cord was carried out in aseptic conditions under Nembutal anesthesia: on 11 cats at the level of the 7th-8th thoracic segment, and on 2 cats and 11 dogs at the level of the 2nd-3rd cervical segment. The animals were sacrificed after various periods (from 10 days to 5 months after the operation): the cats by intrapertoneal injection of Nembutal in a dose of 50 mg/kg, the dogs by injection of a 10% solution of formalin into the heart.

The brain and spinal cord were fixed in 10% formalin solution, pieces of the brain were embedded in celloidin, and serial sections were cut to a thickness of 10 and 20 $\mu$. These were stained with toluidine blue by Nissl's method and for medullated fibers by Spielmeyer's method. Individual areas of the spinal cord and brain were stained for neuroglia by the methods of Snesarev and Miyagawa—Aleksandrovskaya. The controls were healthy animals (4 cats and 4 dogs) of the same weight as the experimental animals. The brain of the control animals was treated by the histological methods mentioned above.

## EXPERIMENTAL RESULTS AND DISCUSSION

Investigation of the site of hemisection showed that in 16 animals (8 cats and 8 dogs) the division of the spinal cord was strictly confined to one half, while in the other animals, the posterior column on the opposite side in addition was partially or completely severed. Comparison with the physiological observations showed that functions were restored quicker and more fully in those animals in which only half the spinal cord was injured, as in the rest recovery took place much more slowly, and an appreciable defect still remained even a long time after the operation.

As a result of hemisection of the spinal cord, profound and irreversible changes took place at the site of operation and below it. These consisted of destruction of tissue, death of neurons, especially internuncial, the develo - ment of gliosis, and the formation of a dense connective-tissue scar. As the distance from the site of injury increased, these changes diminished, and beyond the second or third segment from the level of hemisection, only a reaction of gliosis or demyelination (in the late stages) was observed along the course of the divided tracts throughout their extent in ascending and descending directions. Marked changes in the neurons, followed by atrophy and death of some of them, were found in the cell formations giving origin to the divided tracts, retrograde changes (Fig. 1b), and also, in the structures where these tracts terminate, transneuronal changes were found. The retrograde changes were clearly expressed in the cells of Clarke's column, in the large neurons of the reticular formation of the brain stem and of Deiters' nucleus – on the side of the hemisection, and also in the red nucleus and the neurons of the motor cortex, mainly in the large pyramidal cells of the 5th layer – on the opposite side. The transneuronal changes were largely

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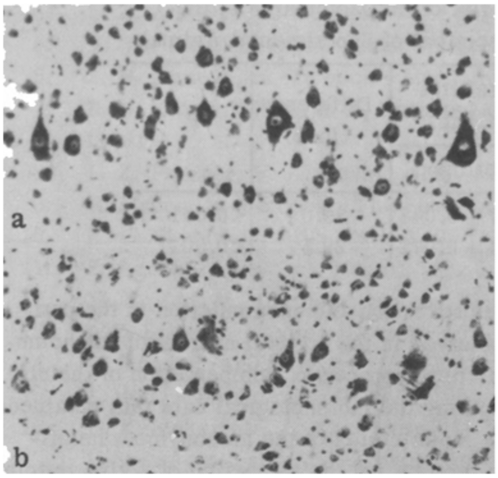

Fig. 1. Atrophy of large neurons of layer 5 of the motor cortex of the right hemisphere in a cat 2.5 months after left-sided hemisection of the spinal cord at the level of the 2nd-3rd cervical segment: a) control; b) experiment. Stained by Nissl's method. Objective 10, ocular 7.

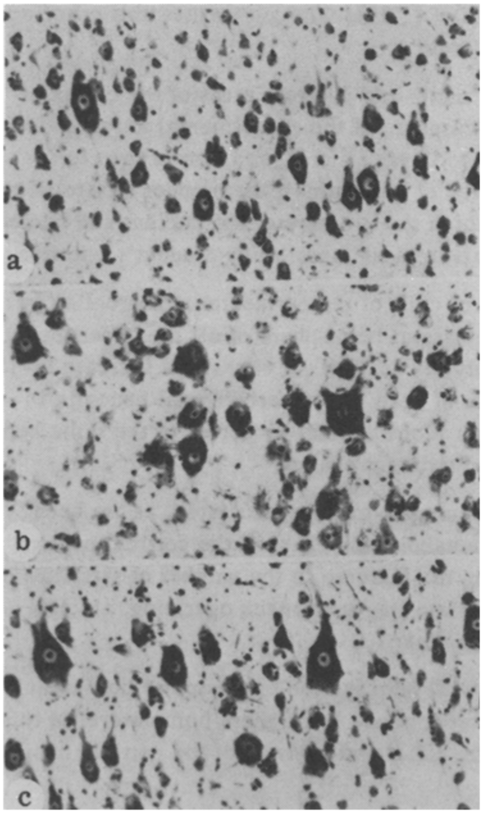

Fig. 2. Neurons of layer 5 of the motor cortex in a control cat (a) and experimental cats (homonymous hemisphere) 28 days (b) and 2.5 months (c) after hemisection of the spinal cord. Stained by Nissl's method. Objective 10, ocular 10.

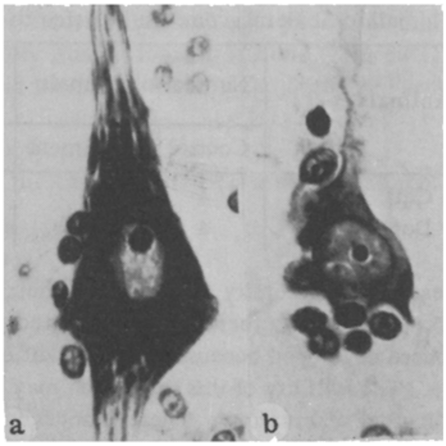

Fig. 3. Neurons of layer 5 of the motor cortex of a dog's hemisphere on the same side as the hemisection, with perineuronal neuroglia 45 days after hemisection of the spinal cord. Stained by Nissl's method. Objective 60, ocular 10, immersion.

observed in the cells of the nuclei of Goll and Burdach on the side of the hemisection, but to a lesser degree they were also present in the cells of the ventrolateral nucleus of the thalamus of the opposite side.

During the investigation of the uninjured symmetrical structures, changes were observed mainly in the motor cortex of the "intact" hemisphere, i.e., the hemisphere on the side of the hemisection.

By the 15th day after hemisection, the cortical neurons, especially the large pyramidal cells of the 5th layer, had increased in size, their bodies were rounded, and their nuclei and nucleoli were slightly swollen. The tigroid in these cells was not clearly defined, but some was scattered in the peripheral zone of the cytoplasm and some concentrated near the nuclear membrane, where it stained more brightly than in other parts of the cell body. The cells showing changes of this type were much larger than the analogous neurons of the control animals, and their tigroid was stained more intensively than normal, especially near the nucleus (Fig. 2b). At the end of one month these changes were most marked. Later (2 months or more after the operation) the structure of the tigroid returned to normal, its granules became more clearly defined, the body of the cells acquired its usual pyramidal shape, but the cells still remained larger than normal (Fig. 2c), and in some such neurons the nucleoli were distinctly enlarged.

The changes described above in the neurons of the motor cortex of the hemisphere on the same side as the hemisection may be interpreted as evidence of the increased functional activity of the cortical nerve cells during development of compensation of the disturbed motor functions. There are reports in the literature that an increase in the functional activity of neurons is accompanied by enlargement of their body, their nuclei [7, 10,11,13,15], by hypertrophy of their processes [11,12,17,18], Changes in the Number of Cells of the Perineuronal Neuroglia of the Motor Area of the Homolateral Hemisphere (in Relation to the Side of Hemisection) of Experimental Animals

| Animals | Number of animals | | Number of satellites per neuron (M ± m) | | Difference (in %) | P |
|---|---|---|---|---|---|---|
| | Control | Experiment | Control | Experiment | | |
| Cats | 4 | 9 | 1.7 ± 0.035 | 2.37 ± 0.048 | 39.0 | <0.001 |
| Dogs | 4 | 9 | 2.8 ± 0.076 | 3.64 ± 0.072 | 29.5 | <0.001 |

and by an increase in the intensity of staining of their tigroid, with its redistribution and accumulation in the perinuclear zone [5,8,14]. It may therefore be suggested that the changes observed in the cortical neurons of the homonymous hemisphere developed because of their additional functional load in the process of compensation of the disturbed functions. The validity of this suggestion may be judged by comparing the morphological data thus obtained with the physiological observations. These changes in the neurons of the motor cortex of the homonymous hemissphere were most clearly defined at the end of the first month after hemisection, i.e., in the period of active restoration of the motor functions, which corresponds according to physiological evidence to the phase of increased excitation of the undamaged structures, or the phase of "exaltation" [3,4]. It is also important to note that increase activity of the cortical neurons of this hemisphere has been recorded electrophysiologically [6].

Consequently, the increased functions of the neurons in the motor cortex of the homonymous hemisphere, caused by their involvement in the compensation of the disturbed functions, was accompanied by structural changes in these elements. However, neurons are connected with their surrounding neuroglial cells into a single functional system [9], so that it might be expected that the increase in the functional activity of the cortical neurons during compensation of functions would cause a reaction of the neuroglia. Morphologically, the reaction of the neuroglia to an increase in the functional activity of the neurons may be determined by an increase in the amount of perineuronal neuroglia, or by an increase in the so-called perineuronal satellites [1,16]. The author used this criterion to assess the state of the glio-neuronal relationships in the present experiment.

The perineuronal satellites (Fig. 3) were counted in layer 5 of the motor and auditory areas of the cortex of the homonymous (homolateral in relation to the side of hemisection) hemisphere of the experimental animals (9 cats and 9 dogs) at various periods after hemisection of the spinal cord (from 15 days or more), and also in the corresponding areas of the cortex off control animals. In each area of the cortex of one animal, the number of satellites was determined for 500-1000 neurons, reckoning only those neurons in which the structure of the nucleus and nucleolus was clearly visible. The results of the counting were analyzed by statistical methods, using Student's criterion.

It was found that a statistically significant increase in the number of cells of the perineuronal neuroglia (by comparison with the controls) took place in the motor cortex of the homolateral hemisphere of all the experimental animals, and in most animals the proportion of satellites rose considerably (by 20-50%), a very small increase (6-12%) being observed in only four cases. On the average (see table) the number of cells of the perineuronal neuoglia increased in the cats by 39% and in the dogs by 29.5%. Meanwhile, in layer 5 of the auditory cortex of the same hemisphere of the experimental animals the number of satellites showed no significant change.

The observed increase in the number of cells of the perineuronal neuroglia may be associated, as has been shown experimentally [1,9,16], with an increase in the intensity of the metabolic processes of the cortical neurons during an increase in their functional activity. The results demonstrating the increase in the number of satellites in the motor area of the homonymous hemisphere, in both the early and the late stages after the operation, are evidence of the existence of a constant, increased load on the neurons in this area.

Hence, the compensation of the disturbed motor functions after lateral hemisection of the spinal cord in animals is accompanied by morphological changes in the structure of the cortex of the hemisphere homolateral in relation to the side of hemisection, changes which indicate an increase in the functional activity of the cortical neurons taking part in the compensatory process.

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