REORGANIZATION OF THE CORTICOSPINAL TRACT AFTER UNILATERAL INJURY TO THE NEOCORTEX

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As a result of injury to the central motor systems, functional, biochemical, and morphological changes take place in the CNS, aimed at restoring the disturbed motor function [1, 5, 6]. In recent years investigators have paid the closest attention to the period of early activation of compensatory mechanisms. It has been shown, for instance, that as early as 7 days afer unilateral injury to one hemisphere in adult rats, growth of axon collaterals of intact neurons of the contralateral thalamus toward denervated target cells of the ipsilateral thalamus is found [8]. It has also been shown that during the first 2 weeks after unilateral injury to the neocortex, marked functional reorganizations take place in the spinal cord, due to the appearance of oligopeptide factors, selectively activating spinal centers on the denervated side, in the CNS [2].

In connection with the facts described above, a fundamental problem arose, namely whether morphological changes in the corticospinal system in response to unilateral injury take place at times of neurohumoral activation of the denervated spinal centers (7-14 days). The aim of this investigation was to study morphological connections of the neocortex of the left and right hemispheres with the spinal cord by the retrograde horseradish peroxidase (HRP) transport method in normal animals and 7-14 days after left-sided injury to the sensomotor cortex.

EXPERIMENTAL METHOD

The investigation was conducted on 25 noninbred male albino rats weighing 180-230 g. The control group consisted of 13 intact rats, the experimental group of 12 rats with left-sided extirpation of the sensomotor cortex, into whose spinal cord HRP was injected 7 days (nine rats) and 14 days (three rats) after trauma to the CNS. To study the sources of the cortico-spinal tract, 0.1-0.2 μl of a 30-40% solution of HRP ("Sigma, " VI) was injected unilaterally into the animals in the right half of the spinal cord. The animals were killed 48 h later by perfusion, initially with physiological saline, but later with fixing solution consisting of 0.4% paraformaldehyde and 1.25% glutaraldehyde in 0.1M phosphate buffer, pH 7.4. The brain was removed and kept overnight in the same fixing solution at 4°C, after which it was transferred into 30% sucrose solution in 0.1M phosphate buffer, and allowed to stand for 24-48 h at the same temperature. Next, serial sections 40 μ thick were cut on a freezing microtome and stained by Mesulam's method [7]. The distribution of labeled neurons in the ipsilateral and contralateral hemispheres relative to the side of injection of HRP was estimated by a coefficient of asymmetry (CA). CA of the distribution of HRP-containing neurons was calculated by the equation:

$$CA = \frac{C_c - C_i}{C_c + C_i},$$

where C_c stands for the number of labeled neurons in the cortex of the contralateral hemisphere and C_i the corresponding number in the cortex of the ipsilateral hemisphere. Positive

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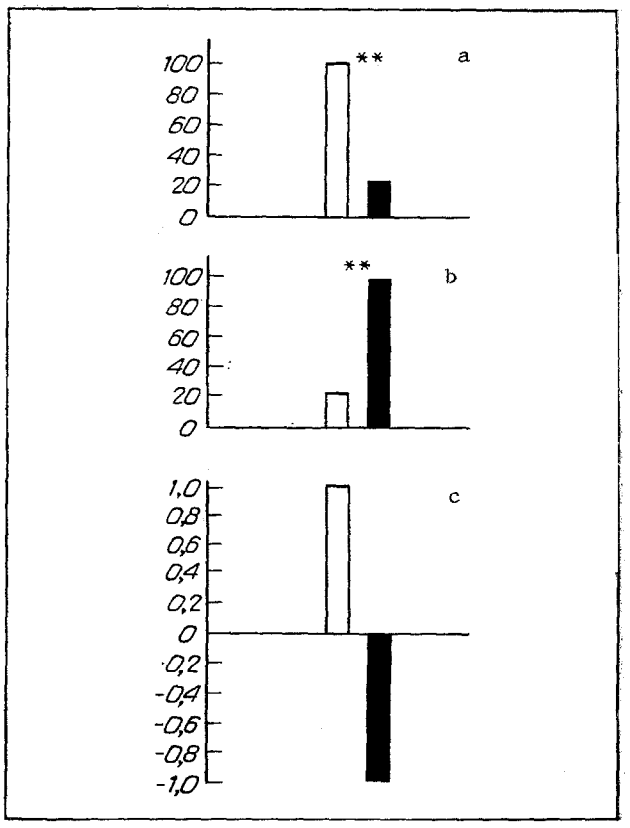

Fig. 1

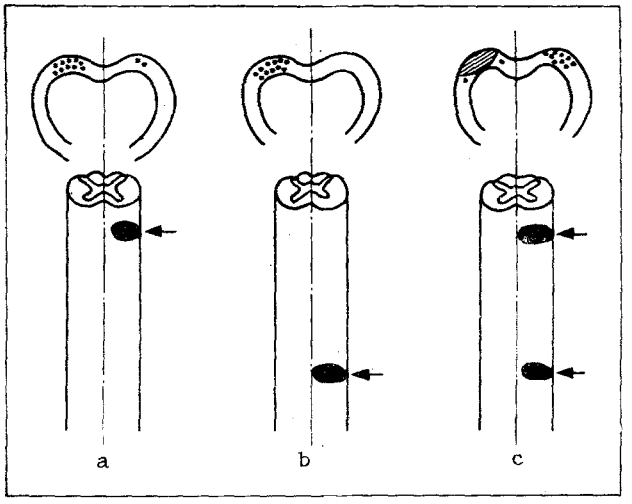

Fig. 2

Fig. 1. Redistribution of labeled neurons in left and right hemispheres after left-sided injury to sensomotor cortex. Ordinate, number of animals (in %) with HRP-containing neurons in left contralateral (unshaded columns) and right ipsilateral (black columns) hemispheres relative to injection of HRP, before (a) and after (b) left-sided injury to neocortex. Asterisks indicate significant differences ($p \leq 0.01$). c) Coefficient of asymmetry of distribution of labeled neurons before (unshaded column) and after (black column) trauma to left sensomotor cortex.

Fig. 2. Diagram of distribution of HRP-containing neurons before and after left-sided injury to neocortex. a) HRP injected into cervical, b) into lumbar segments of spinal cord of intact rats; c) the same after trauma to left neocortex. Dots indicate labeled neurons, arrows indicate site of injection of HRP.

values of CA corresponded to predominance of HRP-containing neurons in the contralateral hemisphere, negative values to predominance in the ipsilateral. The numerical data were subjected to statistical analysis by Fisher's method [4].

EXPERIMENTAL RESULTS

After unilateral injection of HRP into the spinal cord of intact animals at the level of the cervical (three rats) and lumbar (10 rats) enlargement, labeled pyramidal neurons of different sizes were found in the fifth layer of the sensomotor cortex of the contralateral hemisphere (Fig. 1a). Cells with well stained apical dendrites were as a rule arranged in groups of three or four neurons. Only in those three animals (23%) into which HRP had been injected at the level of the cervical segments were labeled neurons discovered not only in the contralateral, but also in the ipsilateral hemisphere (Figs. 1a and 2a). In none of the cases investigated when HRP was injected into the lumbar segments of the spinal cord were labeled neurons found in the ipsilateral hemisphere (Fig. 2b). CA of the distribution of labeled neurons for the control group was +0.99 (Fig. 1c).

In animals with left-sided injury to the sensomotor conrtex the distribution of HRP-containing neurons differed in principle from normal. For instance, in 100% of animals of

the experimental group, irrespective of the level at which HRP was injected, labeled neurons were found in the sensomotor cortex of the hemisphere ipsilateral relative to the site of injection of the enzyme (Figs. 1b and 2c). In 25% of cases (three rats) single HRP-containing-cells were found in the neocortex of the contralateral hemisphere, and were located next to the zone of destruction (Figs. 1b and 2c). CA of the experimental group was −0.98 (Fig. 1c).

Analysis of the morphologic material showed that mainly crossed corticospinal projections are revealed normally by the use of the retrograde HRP transport method. The corticolumbar projections, incidentally, were always crossed, whereas corticocervical projections were also bilateral. However, the number of fibers forming the direct pyramidal tract was very small. The results are in agreement with data in the literature on the existence of direct corticospinal connections which, in adult rats, reach the level of the cervical segments, but do not reach the lumbar segments of the spinal cord.

The atypical retrograde HRP transport discovered in the ipsilateral hemisphere after unilateral injury to the neocortex can be attributed, in our view, to the lateral sprouting of pyramidal tract axons of the intact hemisphere. The possibility cannot be ruled out that the discovery of HRP-containing neurons in the right, intact hemisphere is the result of growth of collaterals of crossed axons, terminating normally on neurons on the left side of the spinal cord. It can be tentatively suggested that after trauma, axons of pyramidal neurons of the "intact" hemisphere give off collaterals which cross the midline and reach centrally denervated target cells in the right half of the spinal cord.

Since neurohumoral peptide factors are, on the one hand, inducers of postdenervation hypersensitivity and, on the other hand, activators of early compensatory modifications in the CNS [3], it can be concluded that their appearance in the present case also provokes sprouting of intact corticospinal fibers

LITERATURE CITED

1. S. N. Ivanova, Mechanisms of Compensation of Motor Functions after Lateral Hemisection of the Spinal Cord [in Russian], Moscow (1980).
2. E. I. Varlinskaya, M. G. Rogachii, B. I. Klement'ev, and G. A. Vartanyan, Byull. Éksp. Biol. Med., No. 9, 281 (1984).
3. G. A. Vartanyan and B. I. Klement'ev, Ontogenez, No. 5, 529 (1985).
4. L. Z. Rushinskii, Mathematical Analysis of Experimental Results [in Russian], Moscow (1971).
5. A. J. Castro, Exp. Neurol., No. 1, 1 (1975).
6. G. Kartje-Tillotson, E. J. Neafsey, and A. J. Castro, Brain Res., 332, 103 (1985).
7. M. M. Mesulam, J. Histochem. Cytochem., No. 12, 1273 (1976).
8. M. Pritzel and J. P. Huston, Behav. Brain Res., 3, 43 (1981).