CHANGES IN ACTIVITY OF POSTURAL ASYMMETRY FACTORS AND RECOVERY OF MOTOR FUNCTION AFTER CORTICAL LESIONS OF THE LEFT AND RIGHT HEMISPHERES

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Some fundamentally new data on the participation of neurohumoral factors of peptide nature in the pathogenesis of central motor disturbances have been obtained in recent years. For instance, oligopeptide factors (postural asymmetry factors — PAF), selectively increasing muscle tone of one limb, have been found in the brain of animals with unilateral lesions of the central motor system and in the cerebrospinal fluid (CSF) of patients with central hemipareses [2-4, 6]. It has been shown that the time course of PAF activity determines the sequence of functional reorganizations taking place at the spinal cord level in neocortical trauma [1]. In all previous investigations, we examined only processes taking place at the segmental level of ventilation in a model situation when the spinal cord was separated from all supraspinal influences of the higher motor senses. Meanwhile the problem of whether a connection exists between the dynamics of PAF activity and recovery of voluntary motor responses remained unsolved.

In the investigation described below the time course of recovery of motor function and PAF activity was investigated after unilateral neocortical lesions in the right and left hemispheres.

EXPERIMENTAL METHOD

The experiments were carried out on 257 noninbred male rats weighing 180-200 g. The motor cortex on the left (67 animals) and right side (70) was removed by means of a vacuum pump under hexobarbital anesthesia. The experimental animals were divided into two groups. The animals of group 1 were donors of CSF, which was taken from the cisterna magna at various times after unilateral destruction of the neocortex. At each time of the investigation 10 rats with extirpation of the motor cortex on the left and right sides were used as donors. PAF in the CSF was identified by bioassay. Under ether anesthesia, 50 μl of CSF from the donors was injected intracisternally into intact recipient animals. Cordotomy was performed at the C_7—T_1 level 5 min after the injection. The development of postural asymmetry (PA) in response to simultaneous complete plantar flexion of the foot and extension of the hip and knee joints of both limbs was determined in the recipients 1 h after cordotomy. PA was considered to be significant if the length of projection of the segment of the straight line connecting the great toes of the hind limbs on the longitudinal axis of the animal's body exceeded 5 mm.

To assess PAF activity, the coefficient of activity (CA) was calculated by the equation:

$$CA = \frac{N_c - N_i}{N},$$

where N_c is the number of recipients with flexion of the hind limb on the side contralateral to the neocortical lesion, N_i the number of recipients with flexion of the ipsilateral limb, and N the total number of recipients (not less than 10 in each case). CA of the brain varied from +1.0 to −1.0, and reached extreme values in cases when the donors' CSF induced flexion

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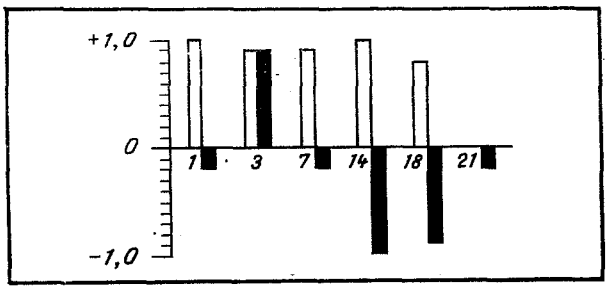

Fig. 1. Trend of PAF activity after injury to neocortex of right and left hemispheres. Abscissa, time of taking CSF from donor (days after destruction of motor cortex); ordinate, values of CA for PAF in CSF of donor animals with damage to neocortex of left (unshaded columns) and right (black columns) hemispheres.

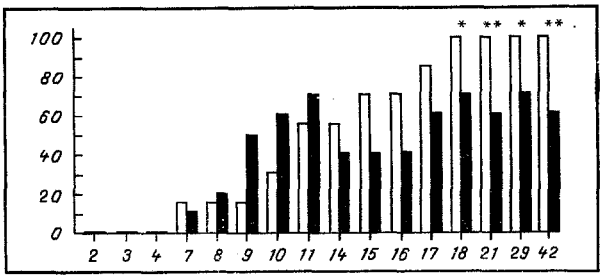

Fig. 2. Recovery of motor function of hind limb in animals with neocortical lesion of left and right hemispheres. Abscissa, time (days after unilateral destruction of neocortex); ordinate, percentage of animals with recovery of the holding reflex. Unshaded columns — destruction of motor cortex of left (seven animals), black columns — of right hemispheres (10 animals). Significance of differences between groups with lesion on the left and right side: $*p \leq 0.05$, $**p \leq 0.01$.

of the same limb in all recipients. Positive values of CA corresponded to the presence in the CSF of PAF, causing an increase in muscle tone of the limb contralateral to the lesion, whereas negative values corresponded to increased tone of the ipsilateral limb.

Recovery of voluntary movements was estimated in the animals of group 2 by the test of holding on to a metal rod 10 mm in diameter by the hind limbs [7]. In the early stages after injury to the neocortex, no holding reflex was present in the limb contralateral to the lesion in any of the animals. Later animals demonstrated attempts to give this reaction. Successful holding with a latent period of not more than 3 sec was taken as the criterion of recovery of motor function. The data were subjected to statistical analysis by Fisher's accurate method [5].

EXPERIMENTAL RESULTS

Injury to the neocortex of the left hemisphere was followed by the appearance of PAF in the CSF 24 h after trauma; the PAF induced flexion of the right hind limb, i.e., it selectively increased muscle tone in the limb contralateral to the lesion. This factor was found in the CSF for 18 days, after which it could no longer be detected by bioassay (Fig. 1). The percentage of animals in which the response of holding with the right limb recovered increased steadily and reached 100 by the end of the 3rd week (Fig. 2).

After injury to the motor cortex of the right hemisphere a PAF increasing muscle tone of the contralateral limb (in this case the left) also appeared in the CSF, not on the 1st day, however, but not until the 3rd day after trauma. However, after only 1 week the activity of this factor disappeared, after which a factor with the opposite action was revealed by bioassay, for it induced flexion of the ipsilateral limb (Fig. 1). Restoration of motor function in animals with a cortical lesion of the right hemisphere followed a different course from that associated with a neocortical lesion of the left hemisphere. The rapid rates of

recovery during the 1st week were followed by a decrease in the percentage of animals which compensated their motor defect (14-16 days). This worsening coincided in time with disappearance of the factor increasing muscle tone of the contralateral limb from the CSF and the appearance of a PAF with the opposite action. By the end of the period of observations recovery of motor function was observed in only 60-70% of the animals (Fig. 2).

It can be concluded from these observations that recovery of voluntary motor responses after unilateral neocortical lesions is linked with the time course of PAF activity in the CSF. For instance, it was found that compensatory adaptations leading to recovery of the disturbed motor function take place more effectively against the background of a constant level of activity of a factor selectively increasing muscle tone of the contralateral limb (injury to the left hemisphere) in the CSF. If for some reason or other the activity of this factor is unstable (trauma to the right hemisphere), compensation of motor function is impaired.

These results are evidence of the important role of PAF in the activation of early intracentral adaptation leading to recovery of the lost motor function. The discovery of differences in the time course of recovery of voluntary movements in animals with neocortical lesions of the left and right hemispheres and the discovery of neurohumoral correlates of these differences suggest that interhemispheric asymmetry in brain pathology is based on a special neurochemical mechanism regulating the activity of oligopeptide PAF.

The discovery of PAF with analogous biological activity in the CSF of patients with central hemipareses of traumatic and vascular etiology does not rule out the possibility that known differences in the clinical picture of right- and left-sided motor disturbances in man may be attributed to the same mechanism.

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