DYNAMICS OF ACTIVITY OF POSTURAL ASYMMETRY FACTOR AFTER UNILATERAL INJURY TO THE MOTOR CORTEX

E. I. Varlinskaya, M. G. Rogachii, B. I. Klement'ev, and G. A. Vartanyan

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It was shown previously that after unilateral injury to the cortex of the anterior lobe of the cerebellum a postural asymmetry factor (PAF), inducing a state of postural asymmetry (PA), manifested as predominant flexion of the hind limb on the same side as in the donor [2], in intact recipient animals, is found in the brain tissue and cerebrospinal fluid (CSF) [2]. Later investigations demonstrated the species-specificity of PAF, established its peptide nature, determined its approximate molecular weight (which is between 1 and 2 kilodaltons [1]), and demonstrated the presence of PAF in the CSF of patients with traumatic hemiplegia [4]. The further study of the role of PAF in functional adaptations of the CNS requires a study of the dynamics of PAF activity at different stages of post-traumatic changes in the system regulating motor function, and the investigation described below was carried out for this purpose.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male albino rats weighing 140-160 g. Under pentobarbital anesthesia the cortical representation of the right hind limb was extirpated from the animals by the method described previously [3].

In the early stages after the operation the animals were spinalized at the level of the upper thoracic segments, and 1 h after spinalization, PA was recorded both visually [7] and by calculating the coefficient of asymmetry (CA) of bioelectrical activity of homonymous (biceps and quadriceps) thigh muscles of the two hind limbs. CA is the ratio of the difference between potentials of the electromyogram (EMG) of muscles of the right and left limb, integrated for frequency and amplitude, and their sum. After recording of PA, CSF was collected from the cisterna magna, after which the animals were decapitated and the brain removed. The tissue was minced in liquid nitrogen and homogenized in a fivefold excess (by volume) of 0.2 M HCl, after which it was centrifuged at 100,000g for 90 min. The supernatant was neutralized with 0.2 M KOH to pH 6.7, centrifuged, and the supernatant was freeze-dried. The protein concentration in the extract was determined with Coomassie Brilliant Blue G-250 [6]. PAF in the CSF and in the extract was determined by biological testing: From 20 to 100 μl of CSF or of the freeze-dried extract, dissolved in 50 μl of physiological saline, was injected intracisternally into intact recipients. The animals were spinalized 15 min after the injection and their PA was recorded. Activity of PAF was estimated by determining minimal active doses, i.e., minimal quantities of CSF or extract inducing PA in the recipients. Each dose was tested on no fewer than 10 recipients. The results of the tests were subjected to statistical analysis by the criterion of signs [5].

EXPERIMENTAL RESULTS

During the first 10 days after destruction of the left motor cortex, PA of the hind limbs, detectable after spinalization, remained in virtually all the animals (Fig. 1). The magnitude of PA, exhibited as flexion of the right limb, contralateral to the side of injury (right-sided PA), averaged 7.0 ± 1.0 mm. According to the EMG data, right-sided PA at these times was accompanied by an increase in electrical activity in the flexor muscle of the right thigh and the extensor muscle of the left thigh (Fig. 2). Toward the end of the 2nd week after injury

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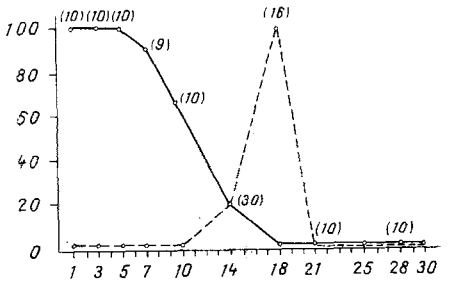

Fig. 1. Percentage of animals with visually recorded right-sided (continuous line) and left-sided (broken line) PA. Abscissa, time after injury to left motor cortex (in days); ordinate, percentage of animals with PA, from the total number of animals indicated between parentheses.

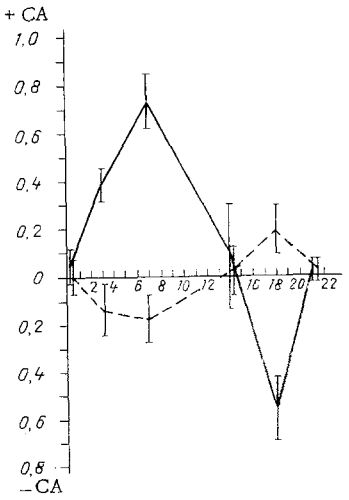

Fig. 2. Changes in CA of flexors (continuous line) and extensors (broken line) of the thigh following injury to the left motor cortex. Abscissa, time after injury (in days); ordinate, values of CA: +CA) predominance of bioelectrical activity in muscles of right limb, −CA) predominance of electrical activity in muscles of left limb.

the number of animals with PA fell to 40%; right-sided PA was preserved in only 20% of animals, whereas in the remaining 20% of animals with PA, it appeared on the left side and was detected subsequently (on the 18th day after trauma) in all rats undergoing the operation. From the 21st through the 30th day after injury no PA could be found. In the course of structural changes in the segmental apparatus induced by unilateral destruction of the motor cortex, three stages can be distinguished: 1) the onset of functional asymmetry of the segmental apparatus and maintenance of that state; 2) inversion of the initial PA; 3) the return of the segmental centers to a symmetrical level of function.

To elucidate the role of PAF in the structural changes discovered, the dynamics of activity of the factor in the CSF and in brain tissue was studied. As Fig. 3 shows, maximal activity of PAF in the CSF was preserved during the first 7 days after injury. In this period the minimal active dose of PAF, inducing PA in intact recipients, was contained in 20 μl of the test CSF. Activity of PAF in the CSF began to fall 10 days after injury to the motor cortex, and at the end of the 3rd week it could not be detected by bioassay. Incidentally, the donor's CSF contained PAF which induced only right-sided PA (right-sided PAF). The appearance of left-sided PAF could not be observed at the stage of inversion of the original asymmetry.

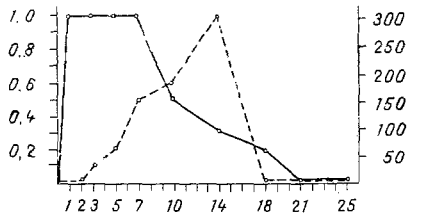

Fig. 3. Dynamics of PAF activity in CSF (continuous line) and in brain tissue (broken line). Abscissa, time after injury to left motor cortex (in days); ordinate, activity of PAF determined by serial dilution of test material pooled from 10 donors; PAF activity in CSF (on left), at maximal level of activity, taken as 1.0 unit. PAF activity in brain extract (on right) is expressed as number of minimal active doses calculated per microgram protein.

PAF activity in the brain was found 2 days after injury and reached maximal values toward the end of the 2nd week, and then fell to zero on the 18th day after trauma (Fig. 3). Like CSF, in brain extracts tested only right-sided PAF could be found. It is an interesting fact that activity of brain PAF was discovered by bioassay within a dose range, the values of which (ratio of maximal active dose to minimal active dose) fell from 1000 (3rd day after trauma) to 10 (14th day after trauma). Reduction of the dose range took place chiefly through a fall in the values of the maximal active dose, which may be associated with accumulation of another factor (or factors), competing with PAF or inactivating it, in the brain tissue in the late stages after trauma.

The dynamics of PAF activity in the CNS thus undergoes regular changes depending on the stage of functional modifications to the segmental apparatus: The onset of PA is accompanied by activation of PAF, and return of the spinal centers to a symmetrical level of function takes place against the background of inactivation of PAF. The results confirm data obtained previously on the inducing role of PAF in the mechanisms of early post-traumatic structural changes [1, 4]. Meanwhile the question of the endogenous mechanisms of inactivation of PAF, leading to compensation of postural asymmetry, which arises after unilateral destruction of the motor cortex, remains unexplained. Further investigations will be devoted to a study of this problem.

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