



Fig. 3. Dynamics (in percent, ordinate) of reduction in number of slips by hind limb after removal of left (continuous line) and right neocortex (broken line).

is reversed, and later its value in animals of series II remains on average 15% higher than in animals with left-sided brain damage.

On the whole this investigation suggests that transfusion of CSF from compensated donors may be a method of accelerating the restoration of motor function after unilateral brain trauma, but provided that the side of the lesion and, as far as possible its location, in the brain are identical in donors and recipients.

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#### UNILATERAL PERIPHERAL INFLUENCES ON THE MOTOR SYSTEM AS ACTIVATORS OF POSTURAL ASYMMETRY FACTORS IN ANIMALS WITH AN INTACT NERVOUS SYSTEM

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UDC 616.822.6+612.821.6+612.8.015

KEY WORDS: motor system, postural asymmetry, nervous system

In the initial stages of the study of induction of postural asymmetry (PA), as a result of the appearance of substances in the nervous system modifying the working of the motor centers of the spinal cord asymmetrically, it has been considered that these phenomena are the result of asymmetrical processes in the nervous system, caused solely by unilateral influences on the motor structures of the brain [1-3]. Later it was shown that PA can be induced by a change in the peripheral afferentation to the spinal cord [4]. The aim of this investigation was to test the hypothesis of the possible induction of asymmetrical processes in the intact nervous system, leading to PA, as a result of a systemic response of the recipient.

#### EXPERIMENTAL METHOD

Noninbred male albino rats weighing 180-200 g were used. The animals were anesthetized with ether, the skin divided in the right or left thigh, and the thigh muscles divided with a sharp razor at the middle level, down to the femur, after which the skin was sutured and

Department of Physiology, Research Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. P. Bekhtereva.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 110, No. 11, pp. 466-468, November, 1990. Original article submitted March 20, 1990.

TABLE 1. Testing CSF of Donor Animals after Unilateral Division of the Thigh Muscles

Time after operation	Number of recipients			PAF activity
	with right-sided PA	with left-sided PA	without PA	
Right limb				
1 day	2	4	2	—
2 days	1	9	1	L +
Left limb				
2 h	2	3	3	—
4 h	7	0	0	R +
1 day	12	0	0	R +
3 days	14	1	0	R +
10 days	13	2	0	R +
1.5 months	9	0	1	R +
3 months	7	1	0	R +
6 months	9	0	1	R +
Injection of physiological saline	1	1	11	—

Note. Here and in Table 2: P+) significant right-sided PAF activity,  $p < 0.05$ ; L+) significant activity of left-sided PAF,  $p < 0.05$ .

TABLE 2. Testing CSF of Animals with Unilateral Immobilization of the Hind Limb

Time after operation	Number of recipients			PAF activity
	with right-sided PA	with left-sided PA	without PA	
	Right limb			
1 day	3	2	2	—
2 days	1	9	1	L+
	Left limb			
4 h	3	3	1	—
1 day	16	1	0	R +
Injection of physiological saline	1	1	11	—

the wound treated in the usual way. Unilateral immobilization of the hind limbs was carried out on another group of animals, by surrounding the ankle and knee joints with a rubber tube 20 mm long and with an internal diameter of 6 mm, which made it impossible to use that limb during walking. A metal tube was applied above the rubber tube, to prevent the animal from removing it. At various times after these manipulations, 40-60  $\mu$ l of CSF was taken from the cisterna magna by puncture, and injected into the cisterna magna of intact recipients. The recipients were spinalized at the C5-C6 level 5 min after the injection. PA of the limbs of the spinal animals was tested by the method described in [1] 1 h after spinalization.

The chemical nature of the postural asymmetry factors (PAS) was determined by treating the freeze-dried CSF with trypsin. For this purpose, 0.1 mg of the freeze-dried CSF was dissolved in 0.2 ml of 0.05M Tris-HCl buffer, pH 7.4, and introduced into a column filled with sepharose-4B with immobilized trypsin (volume of column 3 ml, quantity of immobilized trypsin 15 mg). The incubation time at 37°C was chosen in accordance with the time of complete hydrolysis of the azoalbumin solution. The digest was eluted and PAF activity determined by biological testing. The molecular mass of the PAF was determined by the method described in [5], using gel-filtration on Sephadex G-25 in 1M acetic acid. The resulting fractions were freeze-dried and kept at -20°C. The presence of activity in the fractions was determined by biological testing [1].

All groups of spinal animals were compared with respect to the presence of PA with groups of spinal animals into whose cisterna magna 50  $\mu$ l of physiological saline was injected. The results were subjected to statistical analysis by Fisher's test [6].

## EXPERIMENTAL RESULTS

Testing the CSF of donor animals undergoing the operation of division of the left limb muscles revealed significant PAF activity, causing right-sided PA in intact spinal recipients (hereafter described as PAFR). The study of the dynamics of PAFR activity in the cerebrospinal fluid of the donors showed that PAFR activity was apparent 4 h after the operation, and it persisted at least until 6 months after the operation (Table 1). The CSF of donors after right-sided division of the muscles caused significant left-sided PA, but not until two days after the operation (Table 1).

The results demonstrate conclusively that exposure to stress and pain are not decisive in the induction of PAF activity or manifestation of the lateralization of its action. It can be tentatively suggested that one such factor is a change in muscle tone in the afferent flows, arising because of a change in the body schema in space, due to the experimental situation and an increase in the load on the sound limb. This hypothesis was tested by an additional investigation in which asymmetry of muscle tone of the hind limbs was induced by immobilization of one hind limb. Unilateral immobilization was found to lead to the appearance

of PAF activity in the CSF, causing PA of the oppsite limb in biological testing (Table 2), which confirms the hypothesis mentioned above. It is a noteworthy fact that left-sided procedures lead to significantly shorter time intervals of the appearance of PAF activity than right-sided. This is probably a reflection of the chemical asymmetry of the nervous system and of the body as a whole.

Gel-filtration of the digest of the donors' CSF 10 days after left-sided of the thigh muscles showed that the molecular mass of the PAFR is 0.5-1.5 kDa. Treatment of the CSF containing PAFR with trypsin led to its complete inactivation.

Thus the PAF induced in the intact nervous system by a change in the animal's body schema, caused by peripheral action on the motor system, is a substance of oligopeptide nature, just like the PAF appearing in the CNS in animals with unilateral organic lesions of the CNS.

Generalizing the results of the investigations cited above it can be postulated that asymmetrical modification of activity of the spinal centers is common to all of them. In experiments with supraspinal disturbances [1-3] the increase in their activity is achieved as a result of denervation [7]. Injection of procaine or division of a nerve [4] also causes an increase in reflex excitability of spinal  $\alpha$ -motoneurons [8] on the corresponding side. In All these cases, lateralization of the action of the PAF which appears is determined by lateralization of activated spinal center. In the case of our own experiments, activation of the spinal centers takes place directly through the involvement of the intact limb in compensatory processes, linked with the regulation of posture and the position of the center of gravity, when disturbed by experimental procedures on the limb. These processes lead to activation of the corresponding motor centers and to the production of PAF, the lateralization of whose activity corresponds to the side of the limb not subjected to experimental procedures.

The investigation thus demonstrated that PAF activity can be induced by a long-term change in the motor coordination of the body, which is systemic and asymmetrical in character.

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