BRAIN CHEMICAL FACTORS IN THE FORMATION OF STABLE READJUSTMENTS IN THE CENTRAL NERVOUS SYSTEM

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Stable structural and functional readjustments in the CNS, including those of a pathological kind [3], are considered to be based on molecular-chemical processes [1, 4-7, 10]. However, the concrete nature of these processes remains unexplained. The writers showed recently, on a model of spinal postural asymmetry [8], that direct injection of brain extract from a donor with unilateral destruction of the anterior lobe of the cerebellum into the subdural space of the spinal cord of an intact spinalized recipient below the level of transection induces postural asymmetry in the recipient, analogous to the asymmetry present in the donor [3].

Considering the fundamental importance of these data it was decided to study whether this "humoral" transfer of stable readjustment of centers can take place only after destructive lesions of the cerebellum or whether it can be obtained also after other central lesions. It was also hoped to shed light on the role of the CSF in the mechanism of this transfer.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male rats weighing 250-300 g. A circumscribed area of the motor cortex, stimulation of which by means of needle electrodes led to contraction of the contralateral hind limb, was destroyed in the animals. As a result of the operation the animals developed flexion of the contralateral hind limb. Division of the spinal cord at level T7 was performed on animals of different groups (eight rats in a group) 3, 11, 19, and 25 h after destruction of the cortex in order to determine the time required for fixation of the resulting postural asymmetry.

To study the role of the CSF in the mechanism of transfer of postural asymmetry two models were used: the cerebellar model described previously [3] and a cortical model. On the cerebellar model, on 15 animals, immediately after development of postural asymmetry the spinal cord was ligatured at the level of the middle thoracic segment and the ligature was tied to create a mechanical obstacle to the movement of CSF. The spinal cord was divided 60-80 min later to test fixation of spinal asymmetry. CSF was withdrawn from the cisterna magna in a volume of 0.05-0.1 ml and tested on the same animals by injection into the subdural space of the spinal cord below the level of transection. In addition, CSF from

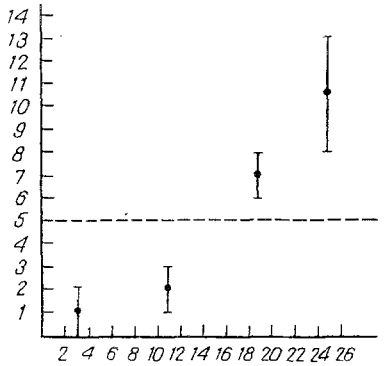

Fig. 1. Determination of fixation time of postural asymmetry in rats with unilateral destruction of motor cortex at the spinal level. Abscissa, time (in h); ordinate, asymmetry (in mm) between ends of animal's hind limbs. Asymmetry exceeding 5 mm was regarded as significant.

KEY WORDS: central nervous system; stable structural-functional readjustments.

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TABLE 1. Species-Specific Transfer of Postural Asymmetry after Unilateral Destruction of Anterior Lobe of Donor's Cerebellum

Donor	Recipient	Substance injected	Number of symmetrical recipients	Total number of recipients	PAF activity
Rat	Rat	Extract	37	40	+
"	"	CSF	22	23	+
"	Guinea pig	Extract	9	9	+
Rabbit	Rat	CSF	6	6	+
Cat	"	"	18	22	+

donors undergoing the operation was tested on 23 intact spinalized recipients by subdural injection in the same doses below the level of transection. Similar tests of CSF on 18 rats were carried out after cortical injury to the donors.

The species-specificity of postural asymmetry factor (PAF) was tested by performing the operation on the cerebellum in rats, rabbits, and cats, and testing their CSF on intact rats and guinea pigs by subdural injection into the peripheral zone of the spinal cord, divided at the thoracic level, in a volume of 0.05-0.1 ml. In another series of experiments activity of the low-molecular-weight fraction 1 [2] of brain extract of animals of different species undergoing the operation on the cerebellum was tested.

EXPERIMENTAL RESULTS

To examine the first of these problems, not the anterior lobe of the cerebellum but a circumscribed area of the motor cortex, responsible for movement of the contralateral hind limb, was destroyed in the experimental rats. Fixation of spinal asymmetry of cortical origin was found to take a longer time: Maximal postural asymmetry developed 25 h after destruction of the motor cortex (Fig. 1).

The most likely ways of spread of PAF within the CNS are the axonal current and CSF. The CSF pathway of spread of PAF was tested on a model of cerebellar asymmetry. Immediately after the onset of postular asymmetry the spinal cord was ligatured and the ligature tied. Under these circumstances asymmetry of the hind limbs was preserved. If transfer of PAF were effected through the flow of CSF, constriction of the spinal cord ought not to allow PAF to spread to the lumbar segments and, consequently, division of the spinal cord after 45 min would lead to loss of asymmetry. In all 15 animals used in the experiments division of the spinal cord 60-80 min after application of the ligature was accompanied by loss of asymmetry. CSF was then withdrawn from the cisterna magna of these animals and injected into them below the level of division, into the subdural space of the spinal cord. All 15 animals developed postural asymmetry. In addition, in 22 of the 23 intact spinalized recipients, asymmetry could be induced by injection of 0.1 ml of CSF of donors undergoing the operation into their subdural space.

Having obtained these data, it was possible to test whether asymmetry of cortical origin can be transferred by injection of CSF of donors with a destructive lesion of the motor cortex into the cisterna magna of intact recipients. This transfer was carried out on 18 animals. In all 18 cases the recipients developed the same asymmetry as the donors.

It was thus shown that the cerebellar model of transfer is not unique, that similar transfer takes place after cortical lesions, and that PAS accumulates in sufficient quantities for transfer in the CSF, which is evidently one pathway of spread on these factors in the CNS.

The oligopeptide nature of the PAF, general concepts of evolution, and data in the literature [9] on the development of postural asymmetry in different animals in the presence of unilateral damage to the cerebellum suggested that peptide factors for transfer of central readjustments may be species-nonspecific. The experimental data in Table 1 fully confirmed this suggestion. Table 1 shows that spinal postural asymmetry arose in all cases of transfer between different species and between different orders, indicating that after injury to a particular brain structure in mammals of different species a substance of the same or very similar structure is evidently produced.

There is reason to suppose that the CSF is not the only pathway of spread of peptide factors for readjustment of central interconnections. Differences in the fixation time of

spinal asymmetry in the cerebellar (45 min) and cortical (24 h) models are noteworthy. Considering that in the first case short-axon intracerebellar and cerebellolumbar pyramidal projections are involved, it can be tentatively suggested that the signal heralding the onset of injury to nerve cells in a particular "center" is effective in the first relay of the damaged neurons, and, judging from its realization time, on account of the rapid axonal current. However, this suggestion requires direct experimental proof.

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EXPERIMENTAL PROTECTION OF THE MYOCARDIUM AGAINST ANOXIC INJURIES WITH A WEAK SOLUTION OF FORMALIN

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In modern cardiovascular surgery the advantages of operations on the arrested heart are well known — the heart is bloodless, relaxed, can easily be retracted, and so on [2, 6]. Existing methods of cardioplegia, despite their great diversity (anoxic, hypothermic, pharmacological, combined methods) are not without disadvantages. That is why the search for new methods of prolonged ischemic cardiac arrest is still an urgent problem in cardiac surgery and transplantology.

It was shown previously [5] that the use of formaldehyde solutions in low concentrations to preserve bone, cartilage, skin, blood vessels, and cardiac valves prevents proteolysis, inhibits energy metabolism, and reversibly inhibits enzymes, thus contributing to preserve the viability of the tissues. These properties of formaldehyde are due to its ability to take part in chemical dissociating reactions with organic substances of all classes possessing a mobile H^+ ion, through the formation of unstable methylol bonds RNH=CH OH. On hydrolysis of methylol compounds $RN\begin{matrix}H\\H\end{matrix} + HO{=}CH_2{=}OH$ the functional properties of proteins, lipids, and carbohydrates participating in metabolic processes are restored [3, 4, 8, 9].

It was shown previously [7] that intravenous injection of 1% formalin solution into animals causes cardiac arrest and disappearance of contractility in response to direct electrical

KEY WORDS: cardiac ischemia; cardioplegia; formaldehyde; protection of the myocardium.

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