electrode in these animals was located either in area CA1 of the dorsal hippocampus or in the amygdala (area anterior).

In four rabbits which did not develop the syndrome of increased predisposition to seizures, the stimulating electrode likewise was located in area CA1 of the dorsal hippocampus. The strength of the stimulating current applied to these animals was small (80 μA) and the duration of ES was only 0.5 sec. Despite the fact that stimulation of this kind was sufficient to induce a short after-discharge, it did not induce progressive predisposition to seizures. The parameters of ES must evidently have an important role in the development of this syndrome. As the investigation showed, ES applied to the limbic structures (amygdala or hippocampus) by a current of moderate strength (about 267 μA), repeated regularly for 2 sec every 5 min, induce the development of a stable and severe epileptic syndrome in the course of 2-4 h in conscious rabbits, an important feature of which is the long-term suppression of postictal inhibition.

LITERATURE CITED

1. G. N. Kryzhanovskii, A. A. Shandra, R. F. Makul'kin, and L. S. Godlevskii, Byull. Eksp. Biol. Med., No. 5, 527 (1985).
2. G. V. Goddard, D. C. McIntyre, and G. K. Leech, Exp,. Neurol., 25, 295 (1969).
3. G. V. Goddard, The Kindling Model of Limbic Epilepsy, Sydney (1980), pp. 107-116.
4. J. G. Fitz and J. O. McNamara, Electroenceph. Clin. Neurophysiol., 47, 592 (1979).
5. Mitsumoto Sato and Takashi Moriwake, Epilepsia, 25, 545 (1984).
6. S. Puckprink and A. Stuart, Epilepsia, 25, 471 (1972).
7. T. Ulrich, A. Paananen, and J. Tuomisto, Eur. J. Pharmacol., 85 (1974).
8. G. Stock, L. Klimpel, V. Sturm, and K. H. Schlor, Exp. Neurol., 69, 239 (1980).

STRUCTURAL SPECIFICITY OF FACTORS INVOLVED IN CHEMICAL REGULATION OF MUSCLE TONE AT THE SPINAL LEVEL

G. A. Vartanyan, E. I. Varlinskaya,
S. V. Shatik, A. V. Tokarev,
S. G. Chernyaev, and B. I. Klement'ev

UDC 612.817.3.084

KEY WORDS: muscle tone; spinal cord; postural asymmetry factors.

Oligopeptide factors found in the CNS, known as postural asymmetry factors (PAF), have a selective activating action on flexor motor centers in the lumbar enlargement of spinalized recipients, located to the right or left of the median sagittal plane [2-4, 7, 10]. The presence of focal lesions of the CNS, the specific features of the action of PAF on either side are determined by anatomical connections of the damaged structure with the segmental apparatus. For instance, trauma to structures with direct (uncrossed) connections with the spinal cord is accompanied by activation of PAF, inducing increased muscle tone in the ipsilateral limb relative to the focus of injury [3, 10]. Conversely, destruction of the higher motor centers, whose spinal projections are crossed, leads to activation of PAF inducing an increase in flexor tone on the contralateral side [2, 7]. This is evidence of differences in the chemical regulation of the symmetrically opposite lumbar centers for the right and left limbs in unilateral brain injury. At the same time, it is well known that in certain local lesions of the human brain, motor disturbances are formed and are accompanied by increased muscle tone only in one of the four limbs [11], reflecting the somatotrophic organization of higher motor centers.

These clinical data and also the experimental results described above suggested the existence of specific chemical regulation of muscle tone of each of the four limbs. The dis-

I. P. Pavlov Physiological Department, Research Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad.

(Presented by Academician of the Academy of Medical Sciences of the USSR N. P. Bekhtereva.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 107, No. 3, pp. 268-271, March, 1989. Original article submitted June 23, 1988.

0007-4888/89/0003-0288 $12.50

TABLE 1. Induction of Postural Asymmetry of Fore- and Hindlimbs on Rat Brain Stem Preparation

Test material	Dose, mg	Total number of recipients	PA of forelimbs		PA of hindlimbs	
			right side	left side	right side	left side
Extract of left half of intact spinal cord	10^{-2}	10	8*	2	2	8*
Extract of right half of intact spinal cord	10^{-2}	11	0	9*	8*	0
Arg^8-vasopressin	10^{-11}	11	0	9*	10*	0
	10^{-12}	10	0	8*	8*	1
	10^{-13}	12	0	10*	9*	2
	10^{-14}	12	0	11*	11*	0
Extract of spinal cord of animal with injury to neocortex	10^{-3}	8	3	0	8*	0
	10^{-4}	10	0	3	9*	0
	10^{-6}	10	2	3	10*	0
Freeze-dried CSF of patient with left-sided hemiparesis	10^{-4}	12	0	9*	1	10*

Legend. Asterisk indicates significance of difference between fraction of animals with right-sided PA and fraction with left-sided PA, at $p \leq 0.05$.

covery of PAF in the intact CNS [1, 8, 9] enabled this hypothesis to be extended also to the chemical mechanisms of regulation of muscle tone under normal conditions.

The present investigation was conducted on material obtained from the intact and injured CNS, in order to determine structural specificity of factors involved in the chemical regulation of muscle tone. A brain-stem preparation, by means of which the action of factors could be studied simultaneously on the spinal centers regulating muscle tone of the hindlimbs and forelimbs simultaneously, was chosen as the test object.

EXPERIMENTAL METHOD

Experiments were carried out on mature noninbred male rats weighing 180-200 g. Under hexobarbital anesthesia the test material was injected into the cisterna magna in a volume of 10 µl. After 10 min the cranial cavity was opened, the cerebellum removed, and an incision made in the frontal plane through the superior angle of the rhomboid fossa, after which the cerebral hemispheres were removed. The cranial cavity was then packed. After 3 h the appearance of postural asymmetry (PA) of the limbs was discovered in the recipient animals: the hindlimbs in response to simultaneous stretching of the flexors of the knee, and the forelimbs, to simultaneous stretching of the flexors of the elbow. PA was considered significant if the length of projection of the segment of a straight line connecting symmetrical points of the limbs on the long axis of the animal's body exceeded 5 mm. As the test material we used extracts of the left and right halves of the spinal cord of intact rats, an extract of the spinal cord of an animal after removal of the cortical representation of the right hindlimb, arg^8-vasopressin, and the CSF of a patient with left-sided hemiparesis, obtained at diagnostic lumbar puncture. Extraction was carried out by the standard method [2]. Fisher's exact method was used for statistical analysis of the data.

EXPERIMENTAL RESULTS

The results of testing of the extracts and CSF, which induced the development of PA of the hindlimbs in recipients cordotomized at the level of the upper thoracic segments, on the brain-stem preparation are given in Table 1. The test material was found to preserve ability to induce flexion of the same hindlimb as in spinalized animals. The response of the forelimbs depended on the source of the material.

Thus after injection of extracts of intact spinal cord into the animals, combined flexion of one hindlimb and the opposite forelimb always took place. PAF from the intact nervous system activated simultaneously the spinal centers either of the right hind- and left forelimbs (extract of right half of the spinal cord) or of the left hind- and right forelimbs

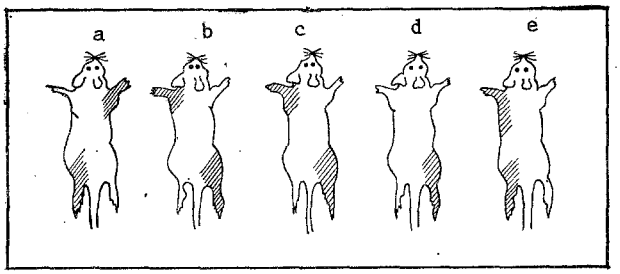

Fig. 1. Induction of flexor responses of fore- and hindlimbs on rat brain-stem preparation. Shaded areas indicate limbs whose flexor response appeared to injection of: extract of the left (a) and right (b) halves of the intact spinal cord; of arg^8-vasopressin (c), of extract of the spinal cord of an animal after removal of the cortical representation of the right hindlimb (d), and CSF of a patient with left-sided hemiparesis (e).

(extract of the left half of the spinal cord – see Fig. 1a, b). Thus, PAF acting simultaneously and crosswise on centers of the lumbar and cervical enlargements were found in the right and left halves of the spinal cord of an intact animal. It was not yet clear whether this crossed regulation is realized by one or by several factors, some of which activate selectively the hemicenters of the lumbar enlargement, others – those of the cervical enlargement.

To solve this problem we studied the action on a brain-stem preparation of arg^8-vasopressin, an inducer of flexion of the right hindlimb in spinalized animals [6]. It will be clear from Table 1 that this peptide, which is known to be present in the spinal cord of intact animals [12], also had a crossed action over a wide range of doses: it induced flexion of the right hindlimb and of the left forelimb (Fig. 1c). The possibility therefore cannot be ruled out that under normal conditions chemical regulation of muscle tone is realized through factors, each of which can synchronously activate the motor hemicenters of the lumbar and cervical enlargements, thus forming a spinal system of coordination of the fore- and hindlimbs.

When brain tissue from intact animals was used as the source of PAF, changes of the monosyndrome type, i.e., a selective increase of muscle tone in one limb only, could not be reproduced in the biological test. An extract of spinal cord of an animal with local destruction of the cortical representation of the right hindlimb was therefore used. In recipients it induced a flexor response of only the right hindlimb, but did not act on the forelimbs (Fig. 1d), i.e., it possessed a strictly specific action and point of application.

Since hemisyndromes were most frequently observed in brain lesions, i.e., involvement of the fore- and hindlimb on the same side, we attempted to induce a syndrome of hemitype by using CSF from the patient with left-sided spastic hemiparesis. This CSF induced flexion of the hind- and forelimbs in recipients on the left side (Fig. 1e).

Thus structural specificity was found in the chemical regulation of the spinal centers for the fore- and hindlimbs in the intact and damaged CNS. Under normal conditions this structural specificity is manifested as selective activation of crossed motor hemicenters. It can be tentatively suggested that the factors we found are specific relative to the spinal system for coordination of the fore- and hindlimbs.

Brain injuries modify the character of chemical regulation on muscle tone: in the CSF and total extract of spinal cord, factors with affinity for brain zones deprived of their normal corticospinal connections begin to dominate. As a result the leading role in chemical regulation of muscle tone begins to be played by PAF whose properties depend on the location of the brain damage.

LITERATURE CITED

1. G. Ya. Bakalkin, K. N. Yarygin, A. G. Kobylyanskii, et al., Dokl. Akad. Nauk SSSR, 260, 1271 (1981).
2. E. I. Varlinskaya, M. G. Rogachii, B. I. Klement'ev, and G. A. Vartanyan, Byull. Eksp. Biol. Med., 98, 281 (1984).
3. G. A. Vartanyan and Yu. V. Balabanov, Byull. Eksp. Biol. Med., 86, 147 (L978).
4. G. A. Vartanyan and B. I. Klement'ev, Fiziol. Cheloveka, 9, 122 (1983).
5. E. V. Gubler, Computational Methods of Analysis and Diagnosis of Pathological Processes [in Russian], Leningrad (1978).

6. B. I. Klement'ev, A. S. Molokoedov, V. N. Bushuev, et al., Dokl. Akad. Nauk SSSR, 291, 737 (1986).
7. G. N. Kryzhanovskii, V. K. Lutsenko, M. Yu. Karganov, and V. I. Torshin, Byull. Eksp. Biol. Med., 92, 404 (1981).
8. G. N. Kryzhanovskii, V. K. Lutsenko, and M. Yu. Karganov, Byull. Eksp. Biol. Med., 93, 14 (1982).
9. G. N. Kryzhanovskii, V. K. Lutsenko, and M. Yu. Karganov, Byull. Eksp. Biol. Med., 102, 528 (1988).
10. I. P. Shul'gina, B. I. Klement'ev, and G. N. Vartanyan, Byull. Eksp. Biol. Med., 98, 394 (1984).
11. A. Brodal, Neurological Anatomy in Relation to Clinical Medicine, Oxford (1969).
12. R. E. Lang, J. Heil, D. Gauten, et al., Brain Res., 260, 166 (1983).

EFFECT OF BRAIN EXTRACTS FROM RATS SUBJECTED TO METRAZOL KINDLING ON GENERALIZED EPILEPTIC ACTIVITY

G. N. Kryzhanovskii,* M. Yu. Karganov,
A. A. Shandra, L. S. Godlevskii,
V. K. Lutsenko, R. F. Makul'kin, and
A. M. Mazarati

UDC 616.853-092.9-07

KEY WORDS: kindling; brain extract; metrazol; epileptic system.

It can be postulated that not only neuronal connections between formations of the CNS, but also certain substances, products of neuronal activity, can participate in the formation of the pathological systems (PS) lying at the basis of corresponding neuropathological syndromes [2]. Appearing together with PS as a result of its activity, they contribute to the further formation of the PS, to intensification of its activity, and to the formation of new, similar PS. One type of PS is the epileptic system [1, 2]. It has been shown that during chronic daily injection of metrazol in subconvulsive doses (metrazol kindling) animals develop increased predisposition to convulsions, expressed by the fact that to each subsequent injection of metrazol, seizures of increasing intensity arise [4]. This form of epileptogenesis is based on the formation of an epileptic system, the primary pathological determinant of which is a hyperactivated hippocampus [3]. The aim of the present investigation was to discover substances in the brain of animals subjected to metrazol kindling capable of giving rise to proepileptogenic effects, i.e., facilitating the formation and/or activity of the epileptic system.

EXPERIMENTAL METHOD

Donor Animals. To obtain brain extracts for the investigations, 40 male Wistar rats weighing 180-250 g were used. A convulsive kindling syndrome was induced in 20 rats by the method described previously [4]. Repeated daily injections of metrazol in a subconvulsive dose (30 mg/kg) led to a gradual increase in predisposition to convulsions, so that the same doses of metrazol induced seizure responses of increasing severity — from single twitches to generalized clonicotonic fits, with the animals falling on their side, with autonomic disorders, and with postictal depression. Before brain tissue was taken, the average severity of the seizure manifestations in animals of the experimental group was 3.5 ± 0.2 points. In the control group of animals (20 rats), which received the same volume of physiological saline every day, no seizure responses occurred. The rats were decapitated 24 h after the last injection, i.e,. 24 h after a seizure, and the brain together with the cerebellum and brain stem

*Academician of the Academy of Medical Sciences of the USSR.

Laboratory of General Pathology of the Nervous System, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Department of Pathophysiology, N. I. Pirogov Odessa Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 107, No. 3, pp. 271-274, March, 1989. Original article submitted June 30, 1988.

0007-4888/89/0003-0291$12.50