analgesic effect observed after EAP in animals with extirpation of the orbitofrontal cortex and with elevation of the thresholds of the nociceptive response at levels 3, 4, and 5 after destruction of OFC.

By contrast, as our previous investigations showed [6], extirpation of the second somatosensory area of the cortex led to lowering of the thresholds of the nociceptive response at all levels of the conventional scale, and also prevented the development of reflex analgesia [4, 5], on account of reduced activity of the antinociceptive system of the brain.

Comparison of our previous results, pointing to an activating effect of the somatosensory cortex and, in particular, of its second somatosensory area, on the antinociceptive system of the brain, with the results of the present investigation thus suggests that the development of the analgesic effect in the case of reflex stimulation will depend on functional interaction between the somatosensory and orbitofrontal areas of the cortex, with their opposite influences on activity of the antinociceptive system of the brain.

LITERATURE CITED

- 1. A. V. Val'dman and Yu. D. Ignatov, Central Mechanisms of Pain [in Russian], Leningrad (1976)
- 2. R. A. Durinyan, M. L. Kukushkin, and V. K. Reshetnyak, Patol. Fiziol., No. 1, 63 (1984).
- 3. L. V. Kalyuzhnyi, Physiological Mechanisms of Regulation of Nociceptive Sensitivity [in Russian], Moscow (1984).
- M. L. Kukushkin, V. K. Reshetnyak, and R. A. Durinyan, Byull. Éksp. Biol. Med., No. 6, 650 (1986).
- 5. V. K. Reshetnyak, Progress in Science and Technology. Series: Human and Animal Physiology [in Russian], Vol. 29, Moscow (1985), pp. 39-103.
- 6. V. K. Reshetnyak and M. L. Kukushkin, Byull. Éksp. Biol. Med., No. 12, 645 (1986).
- 7. V. N. Chernigovskii, S. S. Musyashchikova, M. S. Sinyaya, and A. A. Mokrushin, Habituation in Visceral Systems [in Russian], Leningrad (1980).
- 8. W. P. Chapman, A. S. Rose, and H. C. Solomon, Am. J. Phychiat., 107, No. 3, 221 (1950).
- 9. L. Chavez-Noriega, P. Patino, and M. Garcia-Munoz, Brain Res., 379, No. 2, 300 (1986).
- 10. S. Itoh and G. Katsuura, Peptides, 6, 237 (1985).
- 11. W. D. Willis, Phil. Trans. R. Soc. London, B-308, No. 1136, 253 (1985).

EFFECT OF LATERALIZED ELECTRICAL STIMULATION OF THE BRAIN ON AUDIOGENIC CONVULSIONS IN RATS

V. F. Konovalov and N. A. Otmakhova

UDC 612.825.2

KEY WORDS: audiogenic convulsions; lateralized electrical stimulation

The phenomenon of audiogenic convulsions in rats is frequently used to analyze the physiological and biochemical mechanisms of epilepsy and in the search for methods of preventing and treating this disease. We now know that audiogenic convulsive sensitivity is reduced by systematic application of sound [4], by a raised level of biogenic amines [3, 5, 8] and opiates [10] in the brain, and also by an increase in the ratio of the level of inhibitory amino acids to the level of the activating kind [9].

It is important to study the possibility of using physical procedures as ways of protection against audiogenic epilepsy. We know, for example, that stimulation of the brain by an alternating electric current, as in the case of "electrosleep," has a beneficial effect on the state of the human nervous system [6]. It is logical to analyze the effect of electrical

Institute of Biophysics, Academy of Sciences of the USSR, Pushchino. (Presented by Academician of the Academy of Medical Sciences of the USSR, O. S. Andrianov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 108, No. 7, pp. 17-18, July, 1989. Original article submitted May 18, 1988.

TABLE 1. Distribution of Animals with Different Responses of Audiogenic Fit to Preliminary Electrical Stimulation or Its Simulation (control) Among Groups

Response	Group of animals			
	i	2	3	four (control)
All phases of fit preserved	2	1	1	1
Some phases dis- appeared Fit disappeared	5 3	2 3	4 4	5 4
Absent phases of fit appeared	0	6	I	0

stimulation on audiogenic epileptogenesis in rats. Data in the literature on asymmetry in the course of epilepsy in man [2] and also on the asymmetrical character of the consequences of lateralized electric shock treatment of mental diseases [1] must be taken into consideration. Lateralized procedures directed toward the rat brain, which also is characterized by certain forms of asymmetry, could serve as a convenient model for the experimental analysis of this phenomenon.

The aim of this investigation was to study the effect of electrical stimulation of the brain on sensitivity of rats to audiogenic convulsions.

EXPERIMENTAL METHOD

Experiments were carried out on 40 female Wistar rats weighing 200-250 g, chosen beforehand from a general population on the basis of the presence of audiogenic convulsions. All the rats were subjected to the action of an electrogenic factor (the ring of an electric bellwith an intensity of 100 dB), 1 month after selection, for 1 min, and the beginning and duration of all stages of the fit were recorded. Under pentobarbital anesthesia, 5-7 days after exposure of this factor, an operation was performed on the rats to fit surface electrodes for electrical stimulation to the skull. Four L-shaped electrodes were secured parallel to the transverse sutures of the skull in both hemispheres, in positions 1 mm anteriorly to the bregma and posteriorly to the lambda, and 1 mm laterally to these points. Between 3 and 5 days after the operation, the animals were subjected for 1 h to electrical stimulation by means of the "Élektroson-4T" apparatus with a frequency of 16 stimuli/sec. The strength of the current was 0.1-0.3 mA, and it was chosen individually for each animal: It was increased gradually from 0 until the appearance of the first signs of behavioral reactions (quivering of the whiskers, orienting movements), and then reduced until they just disappeared. Between 5 and 10 min after the end of electrical stimulation the rats were again subjected to the ringing of the bell and the time when the rats passed through all phases of the fit were recorded and later compared with the preoperative parameters.

Depending on the method of electrical stimulation the experimental animals were divided into four groups: 1) stimulation of the right hemisphere, 2) of the left, 3) bilateral stimulation, 4) control (the animals were kept for 1 h in the experimental box and connected through the electrodes to the apparatus, which was not switched on.

The significance of the results was determined by the signs and chi-square tests.

EXPERIMENTAL RESULTS

The audiogenic convulsion before the operation as a rule had the following course. From 5 to 15 sec after the beginning of ringing of the bell a short (1-2 sec) burst of stereotyped running was observed. The rat then stopped still, after which a second and longer phase of stereotyped running began at the 30th-45th second, and in 62% of cases this changed after 40-55 sec into the stage of tonicoclonic convulsions. In 88% of cases this was followed by the appearance of catatonia. In four rats catatonia was observed in the absence of tonicoclonic convulsions, but in nine animals only the stage of stereotyped running was observed.

In 14 of the 40 animals, after electrical stimulation or its simulation, the audiogenic fit disappeared (Table 1), in 70% of cases the second stage of stereotyped running was omitted

(p < 0.05), and in 92% of cases the tonicoclonic stage was missing (p < 0.01). However, this decrease in excitability cannot be distributed to the action of electrical stimulation, for it was observed in all groups, including the control. It was evidently due to the consequences of the operation performed under anesthesia for application of the electrodes.

By analysis of the data in Table 1 by the chi-square test, the parameters of the animals of group 2, in which the left hemisphere was stimulated, stand out from the rest. In this group there were significantly fewer rats in which the convulsion or its individual phases disappeared after electrical stimulation (p < 0.05). At the same time, cases of intensification of the fit were observed virtually in this group alone, i.e., cases when its previously absent phases appeared. With respect to this indicator, group 2 differed from the control at the p < 0.005 level and from group 3 at p < 0.02; one case of the appearance of previously absent catatonia also was observed in group 3.

Thus these experiments revealed the asymmetrical influence of lateralized electrical stimulation on the development of audiogenic convulsions in rats: the effect was potentiated if the left hemisphere was stimulated. This asymmetry is interesting because of its similarity with the asymmetries observed in man. Unilateral electrical shock in patients with a left-sided arrangement of the electrodes evokes both more severe disturbances of the brain on the EEG and more generalized convulsions at the periphery [1]. Dobrokhotova and Bragina [2], in their clinical observations, noted a closer connection of the left (compared with the right) cerebral hemisphere in man with the activating systems of the brain stem. On the basis of our own data it can be tentatively suggested that the asymmetry of a part of the hemispheres in the mechanisms of formation of the complete epileptic fit, observed in man, has certain prototypes in animals.

As regards the question of whether electrical stimulation can be used as a means of protection against audiogenic convulsions, this remains unanswered. The possibility of choosing frequency-specific parameters of stimulation for these purposes cannot be ruled out, as has been shown for epileptic fits, arising from "kindling" of the amygdala [7].

LITERATURE CITED

- 1. L. Ya. Balonov and V. L. Deglin, Hearing and Speech of the Dominant and Nondominant Hemispheres [in Russian], Leningrad (1976).
- 2. T. A. Dobrokhotova and N. N. Bragina, Functional Asymmetry and the Psychopathology of Focal Brain Lesions [in Russian], Moscow (1977).
- 3. Yu. A. Katkov, Fiziol. Zh. SSSR, No. 4, 501 (1984).
- 4. E. A. Ryabinskaya and S. Yu. Korotun, Byull. Éksp. Biol. Med., No. 12, 10 (1983).
- 5. N. G. Sergienko and L. D. Popova, Dokl. Akad. Nauk Ukr. SSR, Ser. B, No. 7, 73 (1982).
- 6. V. M. Banshchikov and S. R. Roitenburg (ed.), Theoretical and Clinical Aspects of Electrosleep and Electroanesthesia [in Russian], Moscow (1976).
- 7. J. Gaito, Bull. Psychonom. Soc., <u>21</u>, No. 6, 488 (1983).
- 8. P. C. Jobe, D. R. Brown, and J. W. Dailey, Life Sci., 28, 2031 (1981).
- 9. J. Laschet, J. Bontemps, G. Dandrifosse, and T. Grisar, Arch. Int. Physiol. Biochim., 92, No. 1, B41 (1984).
- K. Ornstein and M. Segal, Neurosci. Lett., 19, Suppl. 5, 300 (1980).