PHOTOGENIC EPILEPSY WITH EXCITATION GENERATOR LOCATED IN THE LATERAL GENICULATE BODY (THE SO-CALLED DETERMINANT DISPATCH STATION PHENOMENON)

G. N. Kryzhanovskii,* M. B. Rekhtman, B. A. Konnikov, and V. Kh. Petlyuk

UDC 616.853-092.9-02:616,831.46-001.15

In experiments on rats and cats a photogenic seizure syndrome was produced by injecting purified tetanus toxin into the lateral geniculate body. Seizures appeared both in response to a photic stimulus and spontaneously. In the period between seizures, flashes evoked photomotor spasms. It is concluded that as a result of disturbance of the mechanisms of inhibition by tetanus toxin a generator of pathologically enhanced excitation arises in the lateral geniculate body and forms the basis of a hyperactive so-called determinant dispatch station, that causes the appearance of the photogenic epilepsy described.

KEY WORDS: photogenic epilepsy; photomotor spasms; lateral geniculate body; excitation generator; determinant dispatch station; tetanus toxin.

One of the problems in the analysis of the principle of the so-called determinant dispatch station (DDS) [1, 3, 5] with respect to CNS pathology is the study of the conditions of formation, the mechanisms of development, and the character of the course of a certain category of pathological states based on the generation of pathologically enhanced excitation. The formation of a generator of pathologically enhanced excitation (GPEE) lies at the basis of the DDS as a hyperactive functional structure responsible for the formation of a neuropathological syndrome. An essential condition for GPEE formation is disturbance of inhibition in a neuron population [4, 10, 13]. The corresponding syndromes have been shown to be formed [3, 4, 6-9] after local injection of tetanus toxin (TT), which disturbs the mechanisms of inhibition [2, 12, 14].

A photogenic seizure syndrome arising in animals through the formation of a GPEE in the lateral geniculate body (LGB) by injection of ST into this nucleus, is described in this paper.

EXPERIMENTAL METHOD

Experiments were carried out on male nonibred albino rats weighing 250-300 g and cats of both sexes weighing 3-4 kg. TT was injected stereotaxically [18] by means of a glass cannula (external diameter not more than 100 μ), coupled with a glazed Nichrome electrode, used to record electrical activity and to coagulate the structures. Liquid purified concentrated TT was injected into LGB in volumes of $1 \cdot 10^{-4}$-$2.5 \cdot 10^{-4}$ ml (doses corresponding to 1-5 MLD for animals of that weight).

Brain electrical activity was recorded by bipolar silver ball electrodes fixed above the dura in the region of the visual and sensomotor areas of the cortex bilaterally. Monopolar recordings of activity of LGB were obtained by means of the glazed Nichrome electrode after injection of TT. The encephalograms were

* Corresponding Member 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. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 81, No. 1, pp. 22-25, January, 1976. Original article submitted June 14, 1975.

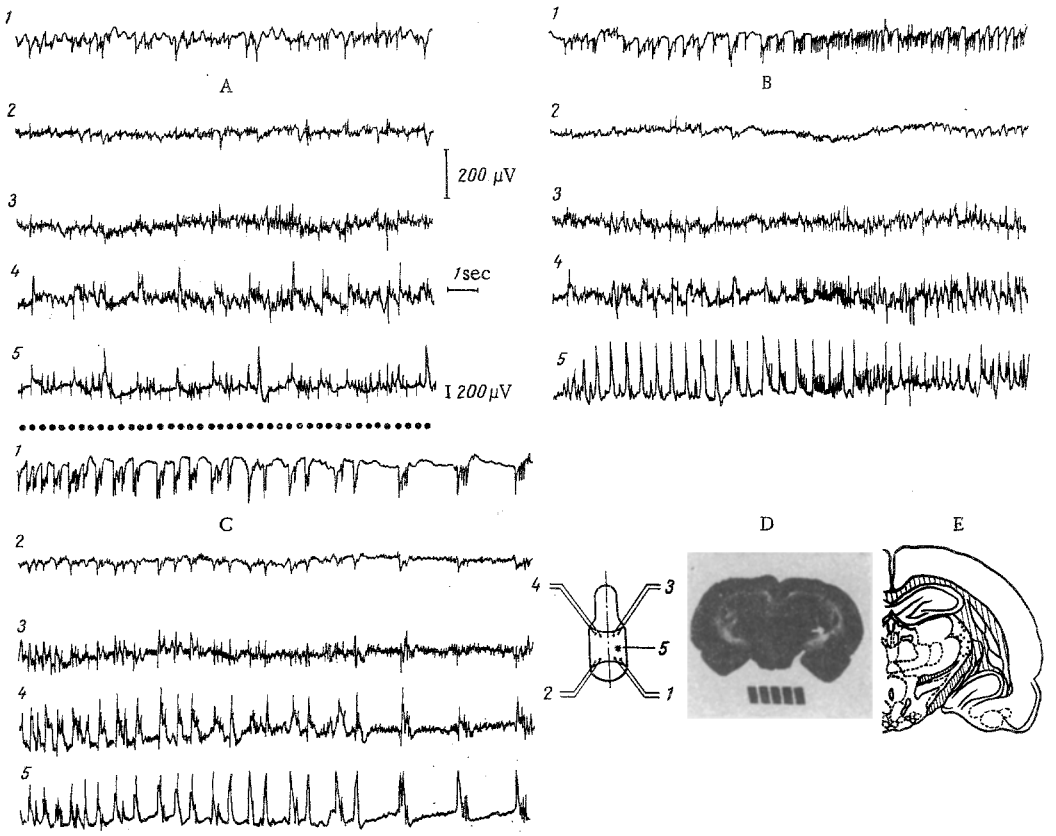

Fig. 1. Electrical activity of visual and sensomotor cortical areas and LGB of a rat during formation of seizure evoked by repetitive photic stimulation 21 h after injection of TT into LGB. A) Recorded during photic stimulation with a frequency of 3 Hz. Flashes marked by dots beneath record. B) Formation of clonic phase of seizure (A, B, C – successive fragments of record). D) Photographs of unstained section through rat brain with millimeter scale below; arrow indicates location of electrode tip and cannula for TT injection. E) Effective location of points of injection of TT into LGB of 15 rats (marked by dots), summarized on a scheme from a stereotaxic atlas of the rat brain [18]. 1) Right, 2) left visual cortex; 3) right, 4) left sensomotor cortex; 5) right LGB, point of injection of TT.

recorded on waking animals fixed in special jackets, without restriction of limb, head, or tail movements. Brain electrical activity was recorded on an eight-channel RM-85 polygraph. Photic stimuli were generated by a Sanei PS-101 photostimulator. The location of the electrode tip and cannula was verified morphologically by coagulating the region studied postvitally with an anodal current of 4 mA for 15 sec. After fixation for a week in 10% formalin, unstained brain sections 30-60 μ thick were photographed with a magnification of 4-6 times.

EXPERIMENTAL RESULTS AND DISCUSSION

The period of time from injection of TT to the appearance of spontaneous or photogenic motor responses under the experimental conditions used was 10-15 h. The attacks of motor excitation in the rats appeared spontaneously after the lapse of the latent period or they could be provoked by photic stimulation: by single flashes, by repetitive photic stimulation, or as on and off responses to continuous illumination. The attack began with stereotyped running and with high jumps, followed by a phase of spasms with clonic and in some cases tonic components. The clonic spasms were accompanied as a rule by noisy breathing and they gave way to uncontrolled locomotor movements, running, and jumping. An example of an encephalographic record of a seizure is given in Fig. 1: After a period of repetitive photic stimulation with a frequency of 3 Hz (A) a seizure began to form after the end of photic stimulation (B); in records A and B the gradual grouping of the initially randomized spikes is clearly visible. The short tonic phase of the seizure (the end of B to the beginning of C) was followed by the clonic phase (the end of C). After the clonic phase of the

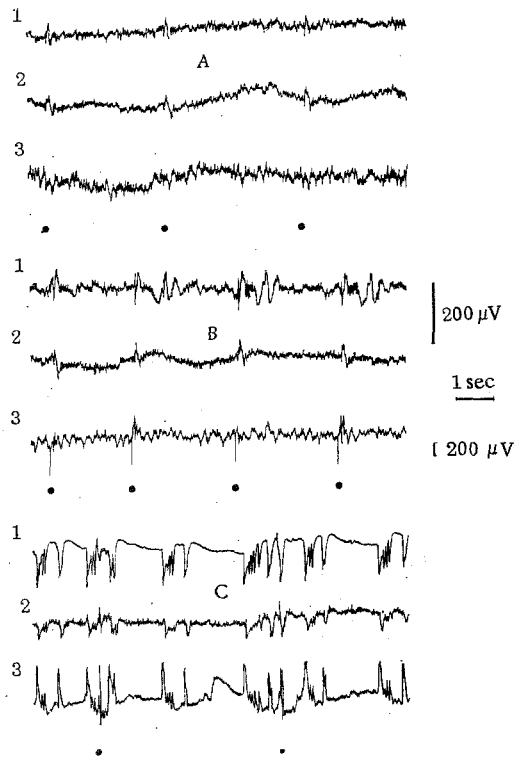

Fig. 2. Evoked potentials to photic stimulation in visual cortex and LGB of a rat: A) 3 h, B) 9 h, and C) 21 h after TT injection; 1) right, 2) left visual cortex; 3) LGB into which TT was injected. Flashes marked by dots above record.

seizure, in the period of chaotic locomotor movements, reactivity of the animals to light was restored and the rat was able to jump in response to each flash. Evoked potentials to flashes at this period are illustrated in Fig. 2C. Clearly, in its shape, the evoked response recalls spontaneous pointed waves, but the amplitude of the evoked potential depended on the phase of spontaneous electrical activity: The first flash presented during the course of spontaneous pointed waves was accompanied by a low-amplitude reactive potential. A second flash in the interval between spontaneous discharges led to the appearance of a pointed wave of higher amplitude than the spontaneous components of the activity. The record in Fig. 2A gives some idea of evoked responses to photic stimuli at the beginning of the latent period of GPEE formation of LGB: This record for the visual cortex was virtually indistinguishable from the before TT injection.

The change in reactivity of the ipsilateral visual cortex toward the end of the latent period of GPEE formation is interesting. The record obtained 9 h after TT injection (Fig. 2B) shows that ordinary components of the evoked potential were followed by replacement of the late response by several low-amplitude high-frequency spikes, and these again were followed by an after-discharge consisting of two slow high-amplitude waves. No such changes were recorded in the contralateral visual cortex.

Photic stimulation after a seizure evoked specific jerky movements in the rats. As a rule these were leaps backward and to the side ipsilateral to the side of injection of TT. Similar leaps occurred in response to a single flash, or as on and off responses to continuous illumination (the latter was usually the most stable), and rhythm binding could take place in response to presentation of flashes at a frequency of up to 3 Hz. This curious "rhythmic dance" could last for tens of seconds, but stopped immediately when the photic stimulation ceased. Single leaping movements could occur in the period between seizures or spontaneously in the rats, but meanwhile the normal locomotion of the animals was undisturbed. Usually the animals died in status epilepticus.

The effect of a hyperactive DDS in LGB of cats was manifested at the end of the first day after TT injection. The hyperactive DDS in LGB led to seizures which were spontaneous or evoked by photic stimulation (single or repetitive flashes). In most cases the onset of generalized seizures was preceded by an aura; at first the animal made tracking movements of the eyes to the side opposite to that of TT injection, after which the head and the whole trunk took part in the movements, the cat fell on its side (toward the side of the injected LGB), and the seizure then developed. At the beginning of the seizure the spasms spread to muscles of the lower limb and the contralateral half of the trunk, then to muscles of the ipsilateral side. During the seizure the animal's pupils were widely dilated and salivation was profuse. The seizure could last for several minutes. Usually alternation of its phases was observed: clonus–tonus–clonus. The attack ended with a harsh cry of the animal as a result of spasm of the chest muscles. After the end of the seizure the animal went into an atonic state, but after a short time it was able to get up and walk about. In the terminal stage of the process, the separate seizures could turn into status epilepticus, resulting in death.

The target of action of TT is the apparatus of liberation of inhibitory mediators: glycine and GABA [1, 12, 14, 17]. Since a well-developed system of recurrent postsynaptic inhibition exists in LGB [15], and since GABA is considered to participate in it as an inhibitory mediator [16], it can be postulated that the de-inhibitory action of TT in LGB evidently also causes a GPEE to be formed in it.

Toward the period of formation of the hyperactive DDS, marked changes in the reactivity of the visual cortex develop in the animals and the ipsilateral visual cortex responds to flashes by a complex series of

potentials (Fig. 2B), indicating the formation in LGB of a functional structure generating an increased volley of excitation. Under these conditions the afferent signal becomes a trigger stimulus activating the generator which forms pathologically enhanced excitation from LGB into the visual cortex. After the seizure spontaneous activity is inhibited in that same region of the visual cortex, with a cyclic change of reactivity associated with spontaneous epileptiform potentials (Fig. 2C). Optomotor pathways leaving LGB are also evidently reactivated [19, 20], as is shown by the stable leaping movements arising in rats in response to the presentation of different series of flashes. This phenomenon could be connected with the spread of the GPEE region in the rats to the relatively extensive zone of the optic relay nucleus, including its dorsal and ventral parts. In the cat, a more limited zone of the nucleus only can be included in the region of GPEE. The pattern of the precursors of the seizure in the cat largely coincides with the early manifestations of the seizure syndrome in monkeys when immunized with homologous antigens from LGB [11]; this evidently illustrates the specific character of the seizure pattern when the focus is located in LGB.

The investigations thus showed that a "dispatch station" of pathologically increased excitation, essentially determining activity of various parts of the animal's brain, can be formed in the thalamic relay nucleus of the visual system. The local excitation generator leads to changes in reactivity of the visual cortex, and in the late stages also of the sensomotor cortex and reticular activating system, and in response to a specific afferent signal or nonspecific stimulation of the animal, characteristic impulsive responses (leaps) and generalized seizures arise. Besides its neurological importance on its own account as a photogenic seizure syndrome of genicular origin, the syndrome described above is a useful model with which to study the mechanisms of epilepsy.

LITERATURE CITED

1. G. N. Kryzhanovskii, Tetanus [in Russian], Moscow (1966).
2. G. N. Kryzhanovskii (G. N. Kryzhanovsky), in: Principles of Tetanus, Bern (1967), p. 207.
3. G. N. Kryzhanovskii, in: General Neurophysiology and Experimental Pathology of the Nervous System [in Russian], Moscow (1970), p. 43.
4. G. N. Kryzhanovskii, in: Simulation of Diseases [in Russian], Moscow (1973), p. 120.
5. G. N. Kryzhanovskii, Pat. Fiziol., No. 4, 3 (1973).
6. G. N. Kryzhanovskii, in: Convergence and Synapses [in Russian], Moscow (1973), p. 109.
7. G. N. Kryzhanovskii, V. N. Grafova, E. I. Danilova, et al., Byull. Éksperim. Biol. Med., No. 7, 15 (1974).
8. G. N. Kryzhanovskii, S. I. Igon'kina, V. N. Grafova, et al., Byull. Éksperim. Biol. Med., No. 11, 16 (1974).
9. G. N. Kryzhanovskii and V. K. Lutsenko, Neirofiziologiya, No. 3, 234 (1975).
10. G. N. Kryzhanovskii, F. D. Sheikhon, and M. B. Rekhtman, Neirofiziologiya, No. 6, 616 (1975).
11. L. Mikhailovich and D. Chupich, in: The Simulation of Diseases [in Russian], Moscow (1973), p. 82.
12. Yu. S. Sverdlov, Neirofiziologiya, No. 1, 25 (1969).
13. F. D. Sheikhon and M. B. Rekhtman, in: Covergence and Synapses [in Russian], Moscow (1973), p. 109.
14. V. B. Brooks, D. R. Curtis, and J. C. Eccles, J. Physiol. (London), 135, 655 (1957).
15. W. Burke and A. J. Sefton, J. Physiol. (London), 187, 201 (1966).
16. D. R. Curtis and A. K. Tebecis, Exp. Brain Res., 16, 210 (1972).
17. D. R. Curtis, D. Felix, and C. G. A. Game, Brain Res., 51, 358 (1973).
18. E. Fifková and J. Maršala, in: J. Bureš et al., Electrophysiological Methods in Biological Research, Prague (1967), pp. 653 and 712.
19. S. Polyak, The Vertebrate Visual System, Chicago (1957), p. 288.
20. P. D. Wall, A. G. Remond, and R. I. Dobson, Electroenceph. Clin. Neurophysiol., 5, 385 (1953).