# MECHANISM OF TRANSMISSION OF EXCITATION GENERATED IN THE ORBITOFRONTAL CORTEX

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Experiments on cats showed that interhemispheric generalization of strychnine seizure potentials from the orbitofrontal cortex takes place mainly by the callosal route. Unlike other projection and association areas of the cortex, not the whole of the corpus callosum but only its anterior part (genu and rostrum) participates in the transmission of strychnine spikes. The results agree with the general concept of the determinant dispatch station (DDS) in the integrative activity of the nervous system. They show that DDS formation induces secondary foci of excitation which exactly reproduce the pattern of activity of the DDS. Removal of these "mirror" foci, which behave as "destination stations," from the influence of DDS leads to abolition of the activity induced in them.

KEY WORDS: orbitofrontal cortex; corpus callosum; strychnine seizure activity; determinant dispatch station.

To investigate interhemispheric pathways of spread of seizure activity (SA) the method of creating a strychnine epileptiform focus in the neocortex is widely used. It is considered that the potentials thus produced are equivalent to SA of the cortex in certain forms of epilepsy [13]. The elucidation of the mechanisms of bilateralization of epileptiform discharges is important for the understanding of the pathogenesis of the generalized epileptic fit and of interhemispheric functional interaction. The study of this problem is interesting in connection with the elaboration of the principle of the determinant dispatch station (DDS) and its role in integrative activity of the nervous system [2-5], for the primary strychnine focus, inducing a focus of activity in the opposite hemisphere, is a hyperactive DDS.

As yet there is no general agreement regarding the role of callosal [1, 6, 8] and extracallosal pathways [7-9] in the interhemispheric transmission of excitation or the part played by various regions of the corpus callosum (CC) in this process.

To shed light on these problems the pathways of generalization of strychnine seizure potentials were studied during the creation of an epileptogenic focus in the orbitofrontal cortex (OFC), the commissural pathways of which, unlike those of other cortical zones, are not diffusely distributed in CC but occupy a narrow bundle in the rostrum and genu of CC [14], whereas subcortical connections with the brainstem reticular formation and diencephalic structures have well-developed projections [10-12].

## EXPERIMENTAL METHOD

Acute experiments were carried out on 30 cats. Under barbiturate anesthesia (25-35 mg/kg, intraperitoneally) and with a midline incision running from the nasal bones to the occiput, the skin and subcutaneous fascia were divided. The eyes were drained. Burr-holes in the vault of the skull and orbit gave wide access to OFC of both hemispheres. The dura was divided with a cruciate incision 1 mm laterally to the longitudinal

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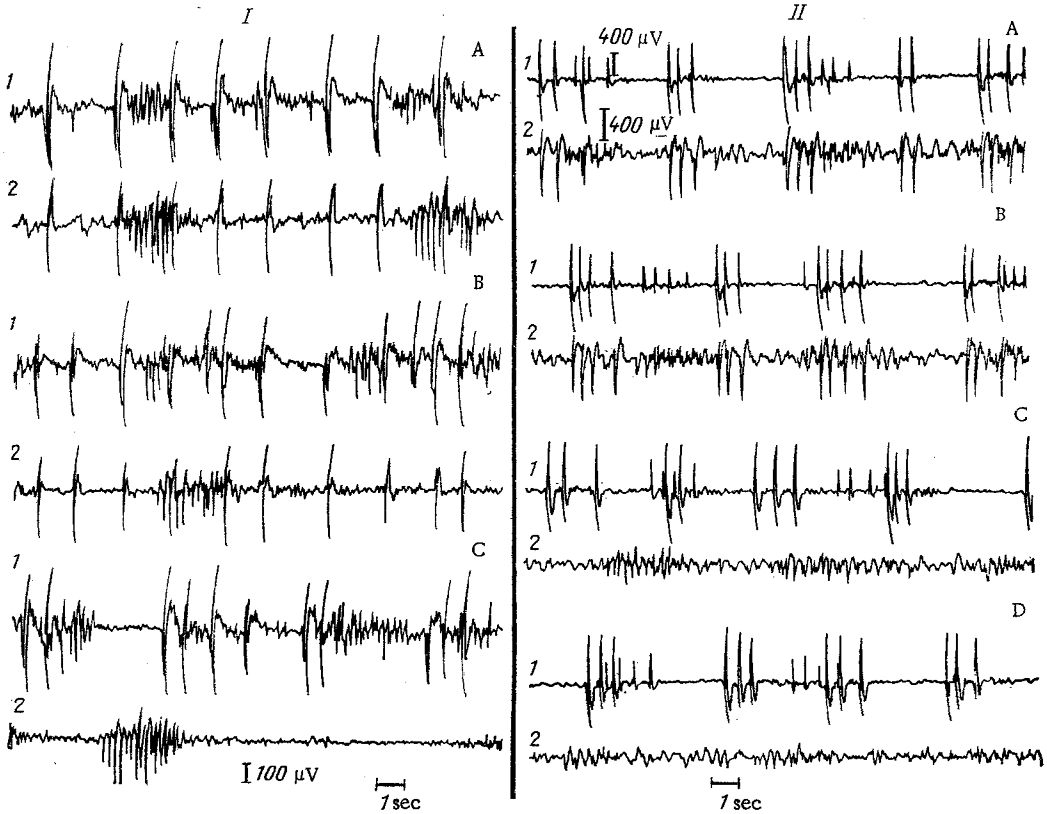


Fig. 1. Interhemispheric transmission of excitation from orbitofrontal cortex after division of anterior commissure and various parts of corpus callosum (CC). I: A) Interhemispheric transmission of strychnine discharges before division; B) after division of posterior two-thirds of CC; C) after division of rostral part of CC; 1) left proreal gyrus (focus of strychninization); 2) right proreal gyrus; II: A) interhemispheric transmission before division; B) after division of anterior commissure; C) after division of rostral part of CC; D) interhemispheric transmission of strychnine discharges is not restored after treatment of contralateral proreal gyrus with a subconvulsive dose of strychnine (0.05%).

sinus, and its edges were retracted sideways. Strychnine was applied to various parts of OFC (with a piece of filter paper 2 $mm^2$ in area, soaked in 1-3% strychnine nitrate solution). Potentials were derived by mono- and bipolar methods and recorded on a 4-ÉÉG-1 ink-writing electroencephalograph. The reference electrode was fixed in the nasal bones. To discover the pathways of interhemispheric transmission of strychnine excitation, total and partial divisions of CC and the anterior commissure were carried out. The rectal temperature was maintained at 38°C. Completeness of the sections was verified histologically.

## EXPERIMENTAL RESULTS

During strychninization of different parts of the orbital and proreal gyri strychnine spikes appeared at homotopical points of OFC of the opposite hemisphere, identical in their frequency and amplitude characteristics to spikes in the focus of strychninization (Fig. 1). Division of the anterior commissure did not interfere with conduction of the strychnine discharges to the "mirror" focus of the opposite hemisphere (Fig. 1: IIB). Division of the rostral part of CC completely blocked interhemispheric transmission of strychnine spikes (Fig. 1: IIC). In the primary DDS SA showed no substantial changes under these circumstances, which did not confirm the possible nonspecific inhibitory effect of brain trauma.

To enhance excitability in the "mirror" zone of the opposite OFC strychnine was applied to it in a convulsive dose (0.03-0.05%). Under these conditions of increased excitability, however, no activity likewise was induced from the strychnine focus (DDS), indicating complete division of the connections between these symmetrical points of OFC (Fig. 1: IID).

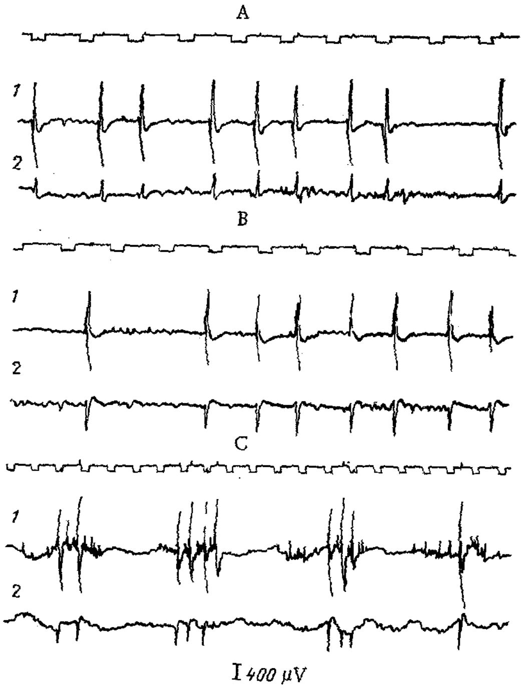


Fig. 2. Effect of division of genu and rostrum of CC on interhemispheric transmission of excitation induced in temporal (A), parietal (B), and occipital (C) cortex. A: 1, 2) sylvian gyrus of left (focus of strychninization) and right hemispheres respectively; B: 1, 2) suprasylvian gyrus of left (focus of strychninization) and right hemispheres respectively; C: 1, 2) posterior lateral gyrus of right (focus of strychninization) and left hemispheres respectively.

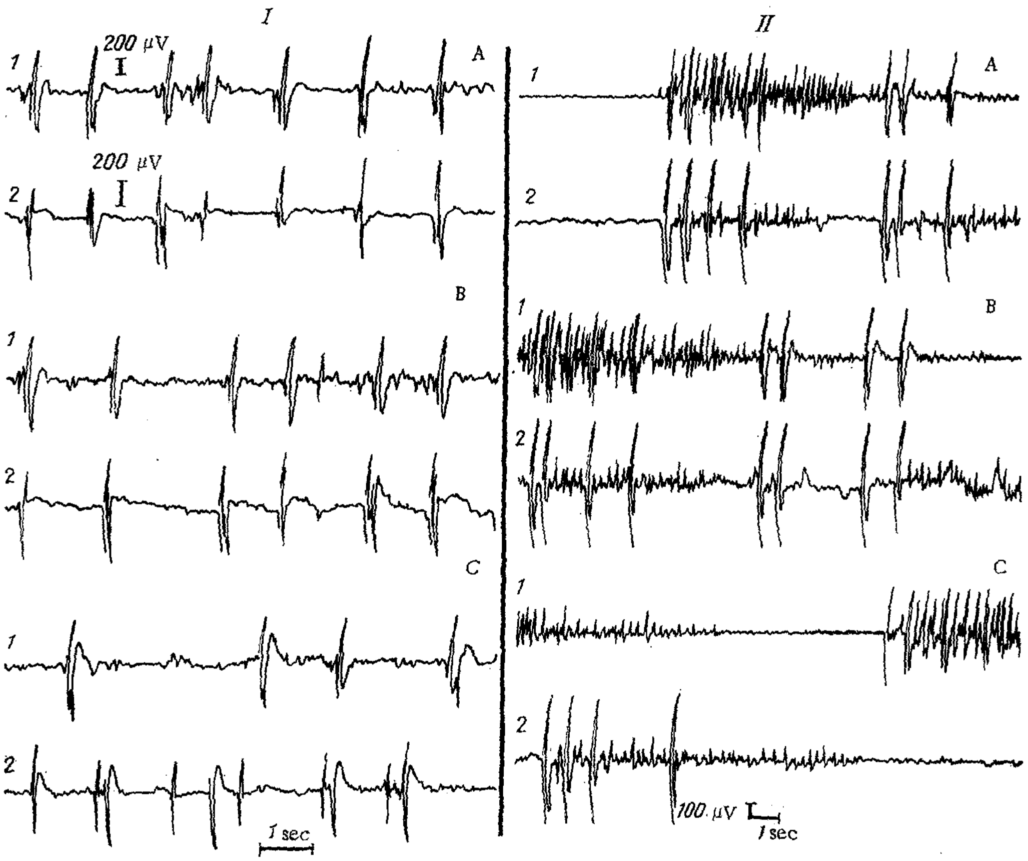


Fig. 3. Effect of division of genu and rostrum of CC and of anterior commissure on synchronization of strychnine discharges induced in orbitofrontal cortex. I: A) Period of synchronization of discharges in proreal gyri before division, B) after division of anterior commissure, C) after division of rostral part of CC; II) legend as for strychnine foci created in orbital gyri.

In another series of experiments the after-effects of isolated and combined injury to the brain stem and of the splenial part of CC with preservation of the rostrum and genu were studied. Under these conditions, the effect of trauma on the functional state of the cortex should have been stronger. Despite this, division of the specified zones of CC had no effect on interhemispheric transmission of SA (Fig. 1: IB).

The object of the next series of experiments was to study the effect of division of the genu and rostrum of CC on interhemispheric transmission of SA during the creation of a strychnine focus (DDS) in other cortical regions (temporal, parietal, occipital). These experiments showed that division of the above-mentioned parts of CC did not affect interhemispheric transmission of SA from these zones of the neocortex (Fig. 2).

In a separate series of experiments two foci of strychnine activity were formed at homotopical points of OFC of both hemispheres. These experiments simulated the creation of two DDS. In the first stages of DDS formation SA appeared asynchronously and the two DDS functioned independently. Complete synchronization of their activity was established later. Division of the anterior commissure did not affect the synchronization of activity of the two DDS. Division of the genu and rostrum of CC, however, led to a disturbance of synchronization and to the appearance of strychnine spikes in both foci; under these conditions the two DDS functioned independently with their own patterns of activity (Fig. 3).

The results of these investigations thus indicate that the transmission of excitation from OFC of one hemisphere to OFC of the other hemisphere takes place through the genu and rostrum of CC. This conclusion is in harmony with the results of morphological investigations [14] which showed that callosal fibers connecting the two OFC run through the genu and rostrum of CC. The main mass of callosal fibers are evidently responsible for interhemispheric transmission from the other cortical zones. These findings are also in agreement with existing morphological and electrophysiological data [1, 6].

The results of these investigations support the general concept of the DDS principle in the integrative activity of the nervous system [2-5]. They show that the appearance of a DDS induces secondary foci of excitation which reproduce exactly the pattern of activity of DDS. Removal of these "mirror" foci, which behave as "destination stations," from the influence of DDS leads to abolition of the activity induced in them. The possibility of synchronizing the activity of two functionally linked DDS and of their functioning in independent regimes after anatomical uncoupling is of great interest. These experiments can be used as a model of polytopical pathology of the CNS and for research into the problem of epilepsy.

## LITERATURE CITED


1. N. Yu. Belenkov and V. D. Chirkov, Zh. Vyssh. Nerv. Deyat., No. 3, 512 (1961).
2. G. N. Kryzhanovskii, in: General Neurophysiology and Experimental Pathology of the Nervous System [in Russian], Moscow (1970), pp. 42-46.
3. G. N. Kryzhanovskii, Pat. Fiziol., No. 4, 3 (1973).
4. G. N. Kryzhanovskii, in: The Simulation of Diseases [in Russian], Moscow (1973).
5. G. N. Kryzhanovskii (Kryzhanovsky), in: International Union of Physiological Sciences. Abstracts of Proceedings of the 26th International Congress, Vol. 11, No. 475, New Delhi (1974), p. 159.
6. V. M. Mosidze et al., The Split Brain [in Russian], Tbilisi (1972).
7. V. M. Okudzhava, in: Proceedings of the 10th Congress of the I. P. Pavlov All-Union Physiological Society [in Russian], Vol. 2, No. 2, Moscow—Leningrad (1964), p. 145.
8. V. M. Okudzhava and S. A. Chipashvili, Zh. Nevropat. Psikhiat., No. 11, 1679 (1973).
9. V. N. Shelikhov, Zh. Nevropat. Psikhiat., No. 2, 145 (1960).
10. P. Brodal, J. Comp. Neurol., 142, 127 (1971).
11. O. Millhouse, Brain Res., 15, 341 (1969).
12. W. J. H. Nauta, in: The Dynamic Localization of Brain Functions [Russian translation], Moscow (1968), p. 67.
13. W. Penfield and H. Jasper, Epilepsy and the Functional Anatomy of the Human Brain, Boston (1954).
14. T. Voneida and B. Trevarthen, Brain Res., 12, 384 (1969).