# EFFECT OF A UNILATERAL CORTICAL LESION ON THE MONOAMINE

### CONTENT IN THE CAT BRAIN

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The serotonin and noradrenalin content in the cerebral cortex, hypothalamus, and mesencephalon was investigated spectrofluorometrically in 12 cats on the 5th-6th day after the production of a pathological focus in the region of the occipital cortex. Diffuse changes of brain activity were recorded on the EEG at this period: spike-like waves and slow waves of increased amplitude. A considerable increase in the serotonin concentration was observed in the cortex, with the effect predominant in the region immediately adjacent to the pathological focus. A tendency for the serotonin level to fall was observed in the hypothalamus and mesencephalon. The noradrenalin concentration in these brain structures showed no significant change. The role of serotoninergic structures of the brain in the mechanisms responsible for restoring the functional state of the brain after experimental injury is discussed.

KEY WORDS: injury to the cerebral cortex; biogenic amines.

Investigations so far undertaken in an attempt to explain some aspects and pathways of compensation of the functions of the injured brain [1-7] shed insufficient light on the role of neuro-humoral mechanisms in repair processes. Yet research along these lines is important both theoretically and practically, for it would point the way to therapeutic action on compensatory processes of the brain with the aid of pharmacological preparations.

The investigation described below marks one step in the study of this problem.

### EXPERIMENTAL METHOD

Experiments were carried out on 12 cats, 6 experimental and 6 control. A pathological focus was produced in the posterior part of the lateral gyrus of the right hemisphere by coagulation of this region or by the introduction of a special rod, 8 mm in diameter, into the brain to a depth of 4-5 cm. The spontaneous EEG and the cortical response to regular flashes with a frequency of 1-15 Hz were recorded in the animals before and after the creation of the pathological focus. Electrodes for recording the EEG were inserted into the cranial bones in symmetrical regions of the two hemispheres above the suprasylvian gyri and the anterior and middle portions of the lateral gyri. The animals were decapitated 5-6 days after creation of the pathological focus. The concentration of monoamines (serotonin and noradrenalin) was determined spectrofluorometrically by the method of Welch and Welch [12] in the cerebral cortex, hypothalamus, and mesencephalon. Monoamines in the cortex were determined in

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TABLE 1. Changes in Serotonin and Noradrenalin Concentrations in Different Regions of the Cat Brain after Injury to the Right Occipital Cortex (mean values in ng/g tissue)

| Group of<br>animals     | Brain region and monoamine content |                   |                      |                    |                     |                   |
|-------------------------|------------------------------------|-------------------|----------------------|--------------------|---------------------|-------------------|
|                         | cortex                             |                   | hypothalamus         |                    | mesencephalon       |                   |
|                         | serotonin                          | nor-<br>adrenalin | serotonin            | nor-<br>adrenalin  | serotonin           | nor-<br>adrenalin |
| Control<br>Experimental | 253±96<br>364±150                  | 160±36<br>180±60  | 1184=708<br>1173=750 | 661±198<br>744±230 | 1234±270<br>930±290 |                   |

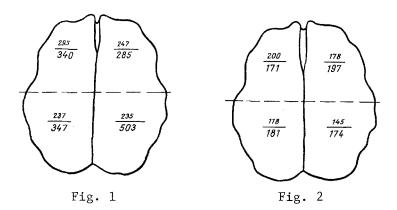


Fig. 1. Serotonin concentration (in ng/g tissue) in various parts of cat cerebral cortex before and after formation of pathological focus in right occipital region. Numbers above the line show serotonin concentration in control animals; numbers below the line show serotonin concentration in experimental animals.

Fig. 2. Noradrenalin concentration (in ng/g tissue) in various parts of cat cerebral cortex before and after formation of pathological focus in right occipital region. Numbers above the line show noradrenalin concentration in control animals; numbers below the line show noradrenalin concentration in experimental animals.

the region directly adjacent to the pathological focus, in the symmetrically opposite region of the left hemisphere, and also in the anterior zones of both hemispheres. The results of the biochemical tests were subjected to statistical analysis with the aid of Student's criterion.

## EXPERIMENTAL RESULTS

Injury was found to cause changes in the EEG of the animals, consisting chiefly of a more frequent appearance of spike-like waves and of high-amplitude slow waves than normally. Sometimes asymmetry was observed between the electrical activity of the right and left hemispheres, but this was inconstant in character. In the rhythm-binding response to flashes some decrease was found in the range of frequencies giving rise to well-marked and constant binding.

Against the background of these changes in cortical electrical activity, changes

were observed in the monoamine content, more especially with respect to serotonin. Changes especially in serotonin concentration were found in the cortex (Table 1). On the 5th-6th day after brain injury the serotonin concentration in all regions of the cortex studied was increased (Fig. 1). However, whereas this increase was ill-defined for the anterior zones and the left occipital region, in the right occipital region the serotonin level was more than doubled (P < 0.01).

A decrease in the serotonin concentration, most marked in the mesencephalon, was found in the subcortical structures (Table 1). In this brain region the serotonin concentration in the control animals in 5 of 6 cases was considerably above  $1000 \, \mathrm{ng/g}$ . In animals with brain injury the serotonin level was above  $1000 \, \mathrm{ng/g}$  in only 3 cases, and in 3 cases it was lower. The serotonin concentration in the hypothalamus in 4 of 6 cases varied between  $1500 \, \mathrm{and} \, 1800 \, \mathrm{ng/g}$ , but in the experimental animals in most cases its concentration did not exceed  $1134 \, \mathrm{ng/g}$ , and only in one case was it raised to  $2600 \, \mathrm{ng/g}$ .

Changes in the concentration of the other monoamine, noradrenalin, after the creation of the pathological focus were not significant. In the cortex its concentration increased by only 12.5%, and no particularly predominant change in its level was found in any region of the cortex studied (Fig. 2). A very slight tendency toward an increase in the concentration of this amine was observed in the hypothalamus, but in the brain stem it was virtually unchanged (Table 1).

Hence on the 5th-6th day after the formation of the pathological focus in the cerebral cortex the serotonin concentration was increased in the cortical structures, more especially in the zone next to the lesion, whereas the serotonin concentration in the mesencephalon and in the hypothalamus and cortex, are known to exist in the brain stem [9-11]. When these observations are compared with the results of the present investigation, it can be postulated that as a result of the creation of the pathological focus in the cortex changes took place in the activity of the whole serotonin-ergic system of the brain aimed at increasing the serotonin concentration in the injured brain zone. It is now known that serotonin helps to restore normal relations between excitation and inhibition, thereby forming a goal-directed response of the CNS [8]. The increase in the serotonin concentration in the cortex found in these experiments can therefore be regarded as one of the mechanisms concerned with restoration of the functional state of the CNS after its experimental injury.

#### LITERATURE CITED

- 1. P. K. Anokhin, Problems of the Center and Periphery [in Russian], Gor'kii (1935).
- 2. P. K. Anokhin, Internal Inhibition as a Problem in Physiology [in Russian], Moscow (1958).
- 3. N. A. Arkhipova and V. V. Gnezditskii, "Quantitative evaluation of the dynamics of rhythm binding on a model of a local lesion of the rabbit brain," in: Proceedings of the 6th All-Union Conference on Electrophysiology of the Central Nervous System [in Russian], Leningrad (1971), pp. 17-18.
- 4. N. A. Arkhipova, "Relationship between the global EEG and neurogenic activity of the cortex during the development of an experimental tumor of the cerebral hemispheres," Byull. Éksperim. Biol. i Med., No. 7, 17 (1973).
- 5. É. A. Asratyan, Physiology of the Central Nervous System [in Russian], Moscow (1953).
- 6. É. A. Asratyan, The Problem of Compensatory Adaptation [in Russian], Moscow (1960).
- 7. N. Yu. Belenkov, "New aspects of the structural and functional organization of the brain," Proceedings of the 23rd Conference on Problems in Higher Nervous Activity [in Russian], Gor'kii (1972), pp. 5-7.
- 8. S. N. Kozhechkin, "Microionophoretic study of the effect of biogenic amines on unit activity in the rabbit visual cortex," in: Physiological Mechanisms of Memory, Pushchino-on-Oka (1973), pp. 89-97.

- 9. N. E. Anden, A. Dahlström, K. Fuxe, et al., "Ascending monoamine neurons to the telencephalon and diencephalon," Acta Physiol. Scand., 67, 313 (1966).
- N. E. Anden, K. Fuxe, and U. Ungerstedt, "Monoamine pathways to the cerebellum and cerebral cortex," Experientia,  $\underline{23}$ , 838 (1967). K. Fuxe, "Distribution of monoamine nerve terminals in the central nervous sys-
- 11. tem," Acta Physiol. Scand., 64, Suppl. 247 (1965).
- A. S. Welch and B. L. Welch, "Solvent extraction method for simultaneous determination of norepinephrine, dopamine, serotonin, and 5-hydroxyindoleacetic acid in a single mouse brain," Anal. Biochem., 30, 161 (1969).