

# PATHOLOGICAL PHYSIOLOGY AND GENERAL PHYSIOLOGY

## THE EXPERIMENTAL PRODUCTION OF A NEUROSIS IN MONKEYS BY CHANGING THE DIURNAL RHYTHM

G. M. Cherkovich

From the Laboratory of Physiology and Pathology of Higher Nervous Activity (Head—Candidate Med. Sci. the late D. I. Miminoshvili) of the Institute of Experimental Pathology and Therapy (Director—Candidate Biol. Sci. I. A. Utkin) of the AMN SSSR, Sukhumi

(Received September 23, 1958. Presented by Academician the late K. M. Bykov)

The higher nervous activity of monkeys is distinguished by its great complexity and it has many special features which enable it to withstand traumatic influences. For this reason, attempts to induce neurosis in monkeys by means of the ordinary methods used with success in dogs have been inconclusive. A neurosis was developed only in monkeys with a weak type of nervous system and with inert nervous processes, in response to very complicated and difficult tasks [1, 3, 6, 8].

Greater success attended D. I. Miminoshvili's [7] attempt to induce a neurosis in monkeys by the use of conflict, on the basis of natural stimuli addressed to different cortical and subcortical centers mutually inducing each other.

In the present research an attempt was made to produce a neurotic state by changes in the diurnal rhythm, or stereotype.

The diurnal rhythm, which has been developed on the basis of a whole series of daily repeated stimuli, is a dynamic stereotype in which the leading role is played by conditioned reflexes to the time of action of these stimuli. By changing the place and time of action of the components of the diurnal stereotype, i.e., by transferring the lighting up and feeding to the hours of night or by repeating them twice in the 24 hours, it is possible to obtain a new reflex to time, in the form of a distorted or biphasic diurnal rhythm [1, 9, 11, 12]. If the diurnal stereotype is changed to one directly opposite without waiting for the reorganization of the physiological functions in accordance with the new regime to be completed, then this break may cause disturbances in the working of the cerebral cortex.

### EXPERIMENTAL METHOD AND RESULTS

The experiment was originally carried out on 3 monkeys of the species Papio hamadryas: Bronenosets, Nosorog and Dog. In all three monkeys, motor alimentary conditioned reflexes were induced to a simple stereotype, a light and a bell as positive conditioned signals, and a tone as a differential signal.

By the use of special tests it was ascertained that all 3 monkeys were of the strong type, but that Bronenosets was weaker than the others. In Nosorog the excitation process was predominant. As regards the mobility of their nervous processes Dog and Bronenosets were inert and Nosorog mobile.

After this had been done, the monkeys were transferred to a special artificial diurnal regime in which the stimuli were arranged in the opposite order before the monkeys were able to reorganize themselves to the new regime assigned to them. Alternation of the artificial diurnal regimes took place in the following order: a natural diurnal regime was replaced by a distorted regime (rest and darkness by day and illumination and

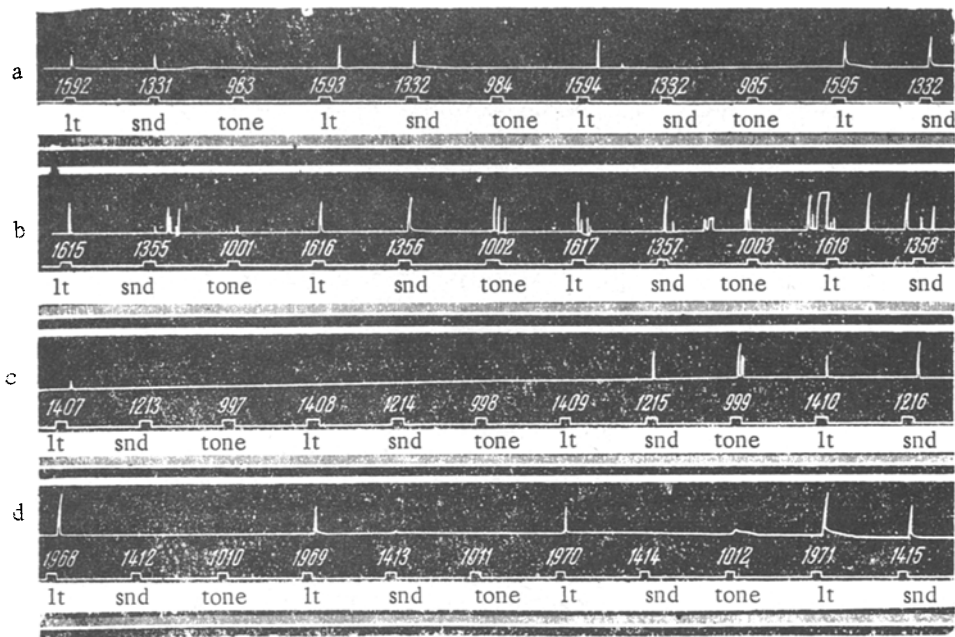


Fig. 1. Changes in the conditioned reflex activity of monkeys under normal conditions and during the development of a neurosis. a) Under normal conditions; b) derangement of the nervous activity leading to excitation; c) derangement of nervous activity leading to inhibition; d) paradoxical phase. Legend from above down: pressure on the lever; stimulus marker; time marker in seconds.

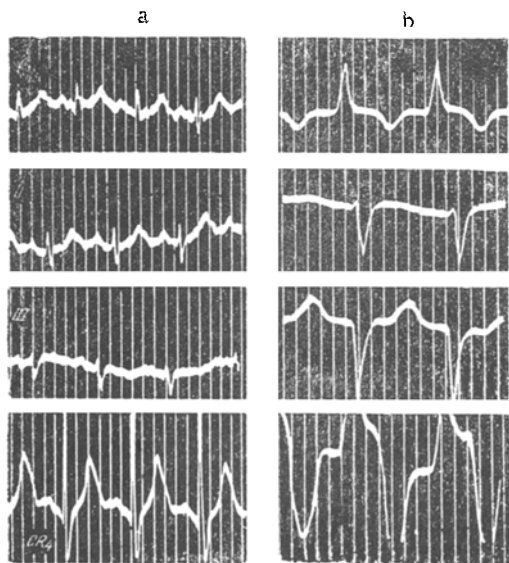


Fig. 2. Changes in the electrocardiogram in Nosorog. a) Before the illness; b) during illness; I, II, III) standard leads.

feeding by night). As soon as the monkeys had begun to adapt themselves to the new conditions, the regime was changed to one of biphasic days (2 "days" and 2 "nights", each of 6 hours' duration, in the course of 24 hours), followed by biphasic days again, but with the opposite sign, i.e., where there had been a "night", a "day" was substituted, and vice versa. Illumination for 24 hours continuously was then replaced by darkness for 24 hours continuously, and so on.

As a result of this traumatization, all three monkeys developed a neurosis after 2 months of the experiment. Their conditioned reflex activity was severely deranged. The monkey Nosorog was very excited, and pressed several times on both the positive and the differential signal lever (Fig. 1, b). Dog sat in a corner all the time, not reacting to signals, and only at the end of the experiment did he press on the lever from time to time, although he did not come near the bait (Fig. 1, c). Bronenosets showed a well marked paradoxical phase, for the light was followed by a stronger pressure on the lever than the bell (Fig. 1, d). This neurosis continued

for a few months after the monkeys had been transferred back to their normal regime.

The initial kymograms of conditioned reflex activity were identical in all the monkeys (Fig. 1, a).

Nosorog took part in the experiment without showing any signs of derangement of cardiac activity (Fig. 2, a). Two months after the end of the experiment the monkey became relatively immobile and sluggish and had frequent bouts of trembling. A few days later she began to eat, and lay motionless on the floor of the cage all the time.

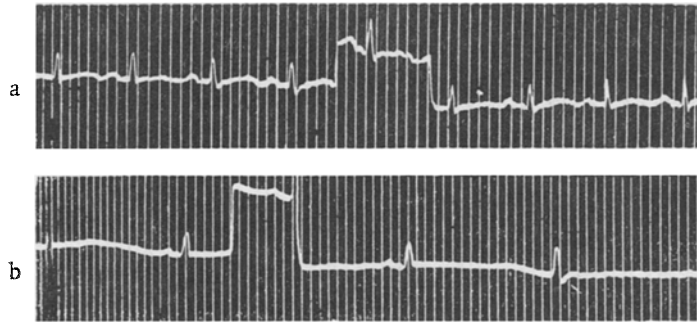


Fig. 3. Changes in the electrocardiogram in Khisar (lead II).  
a) Initial heart rate 171 per minute; b) bradycardia as a result of neurosis; heart rate 70-77 per minute.

The electrocardiogram at this time showed a negative T-wave and the presence of a QS peak; the QRS complex was drawn out, in the CR<sub>4</sub> chest lead a deep negative T-wave was observed, and the S-T interval was elevated 6 mm above the isoelectric line (Fig. 2,b). Four days later the monkey died with signs of acute coronary insufficiency. At autopsy circulatory disturbances were found and micronecroses were present in the heart. No visible abnormalities were found in the other organs.

Subsequently, when a neurosis was induced in another group of monkeys by disturbance of the diurnal stereotype, in addition to coronary insufficiency other forms of disturbance of cardiac activity were observed—the so-called "vagus neurosis". Under these circumstances the bradycardia reached 75-80 beats per minute, with an initial normal heart rate of 170-180 per minute (Fig. 3).

Such a strong influence of changes in the diurnal rhythm on the cardiovascular system of the monkeys is probably accounted for by the fact that these changes constituted the elements of a conflict. When the nerve cells, by virtue of the conditions created, had fallen into a state of inhibition, stimuli were put into action leading them into a state of excitation, and vice versa.

These changes in the diurnal rhythm were continued for long periods of time, each day, and not briefly during the experiment in the chamber.

Any interference with the stereotype and the intrinsic rhythm of work is tolerated badly, both by animals and by man. Experiments have shown [4, 5] that heterorhythmic stimuli are tolerated badly by the nervous system, and lead to neurosis in dogs and rabbits. According to the findings of M. B. Tsukker and L. M. Khvan [10] and of Pierach [13], work on different shifts often leads, in man, to neurosis and to consequent somatic disease.

It may be postulated that the neuroses and attendant diseases which we induced by interference with the diurnal stereotype are close in their nature to certain clinical disturbances encountered in man.

#### SUMMARY

Neurosis was experimentally induced in *Papio hamadryas* through systematic interference with their diurnal routine (for the period of 2 months) by varying the periods of illumination and feeding.

This neurosis took the form of disturbances of the conditioned reflex activity and of the appearance of somatic pathology: coronary insufficiency, micronecroses in the heart (in one monkey) and cardiac "vagus neurosis" with pronounced bradycardia.

Neurosis thus produced is of special interest, since by its etiology and complications, it is very similar to disorders occurring in man.

#### LITERATURE CITED

- [1] K. M. Bykov, *The Cerebral Cortex and the Internal Organs*. Moscow-Leningrad, 1947. [In Russian].
- [2] S. D. Kaminski, *Dynamic Disturbances of the Activity of the Cerebral Cortex*, Moscow, 1948 [In Russian].

- [3] V. Ya. Kryazhev, *The Higher Nervous Activity of Animals in Groups*, Moscow, 1955. [In Russian].
- [4] N. S. Kupalov, *Transactions of a Conference on Neuroses*, pp. 5-10, Petrozavodsk, 1956. [In Russian].
- [5] M. N. Livanov and T. A. Korol'kova, *Gagrskie Besedy*, 1, 301-311 (1949).
- [6] D. I. Miminoshvili, *Sixteenth Conference on Problems of Higher Nervous Activity*, pp. 144-145, 1953 [In Russian].
- [7] D. I. Miminoshvili, *Theoretical and Practical Problems of Medicine and Biology in Experiments on Monkeys*, pp. 46-57, 1956. [In Russian].
- [8] L. N. Norkina, *Zhur. Vysshei Nerv. Deyatel.*, 1, 56-63 (1958).
- [9] A. D. Slonin and O. P. Shcherbakova, *Experimental Study of Periodic Changes in the Physiological Functions of the Body*, pp. 156-167, 1949. [In Russian].
- [10] M. B. Tsukker and L. M. Khvan, cited by D. K. Lunev, *Vestnik Akad. Med. Nauk SSSR*, No. 4, 80-83 (1956).
- [11] G. M. Cherkovich, *Experimental Study of the Regulation of Physiological Functions of Animals in Natural Conditions of Existence*, vol. II, pp. 187-199, 1953. [In Russian].
- [12] O. P. Shcherbakova, *Experimental Study of Periodic Changes in the Physiological Functions of the Body*, pp. 42-64, 1949. [In Russian].
- [13] A. Pierach, *Acta med. Scand.*, 152 suppl. N. 303, p. 159-166 (1955).