A NEW EXPERIMENTAL MODEL OF NEUROGENIC CARDIAC ISCHEMIA IN MONKEYS

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Neurosis was induced in monkeys by immobilization, acting as a stressor, preceded by physical exertion. As a result the natural hyperfunction of the heart was converted into a conditional stimulus for defensive dominant focus and caused the development of chronic and progressive ischemic changes in the heart reflected in the ECG.

Individual investigators have attempted to obtain coronary insufficiency and myocardial infarction in monkeys by induction of neurosis through conflict between foodgetting, sexual, herd, and defensive reflexes [3-7]. In addition, in an investigation on monkeys kept at the Sukhumi Nursery and subjected to no special procedures coronary insufficiency was found [1-3, 5], evidently as a result of the conditions of keeping in captivity.

Some progress toward a solution of the problem of selective envolvement of functional systems in neuroses was provided by Startsev's [8-11] simulation of systemic diseases by neurosis induced by immobilization.

In the investigation described below the method of conversion of physiological hyperfunction of the heart during natural physical exertion into the conditional stimulus of defensive excitation, by the use of immobilization as a psychoemotive stressor, was investigated.

EXPERIMENTAL METHOD

The investigation was carried out on four clinically healthy male baboons (Papio hamadryas) aged 2 years (Nos. 9337, 9361, 9382, and 9383). In successive series of experiments the ECG of the fasting animals was recorded in 12 leads and the arterial pressure (AP) measured by Korotkov's method. Each of the first four series consisted of five repetitions (once a day) of the test. In the first series of experiments the ECG and AP were recorded at rest; in series II after running in the cage for 5 min (the monkeys ran away from the assistant who pretended to catch them); and in series III 1 h after the beginning of immobilization, consisting of fixation of the limbs and trunk of the animal to a plank in recumbency in the supine position; and in group IV 1 h after the beginning of period of immobilization which was preceded by running for 5 min. The experiments of series V consisted of a study of the dynamics of the ECG and AP at various times after the end of the procedures producing neurosis in the animals.

EXPERIMENTAL RESULTS

The initial ECG's in the experiments of series I showed inconstant changes in the T_{III},aVF wave, in the form of flattening or slight inversion in three monkeys. The ECG picture was normal in animal No. 9337.

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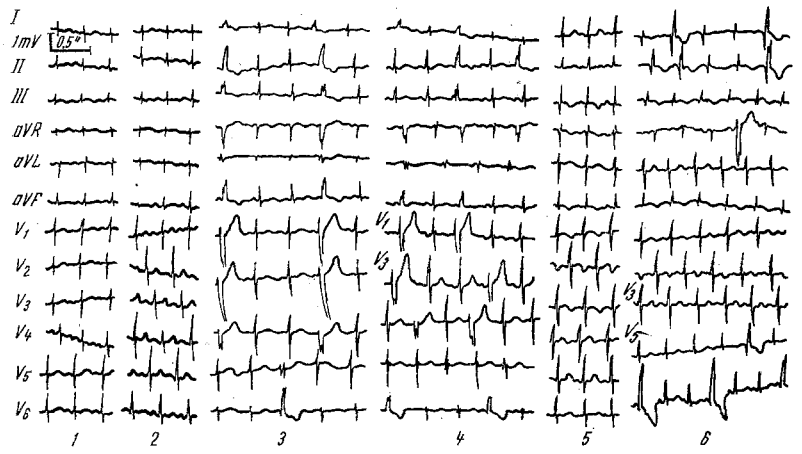

Fig. 1. ECG of monkey No. 9361 in leads (from top to bottom) I, II, III, aVR, aVL, aVF, and V_{1-6}. 1) At rest; 2) after physical exertion; 3) 1 h after beginning of immobilization; 4) 1 h after beginning of immobilization preceded by physical exertion; 5) 1 month and 6) 80 days after end of immobilization session.

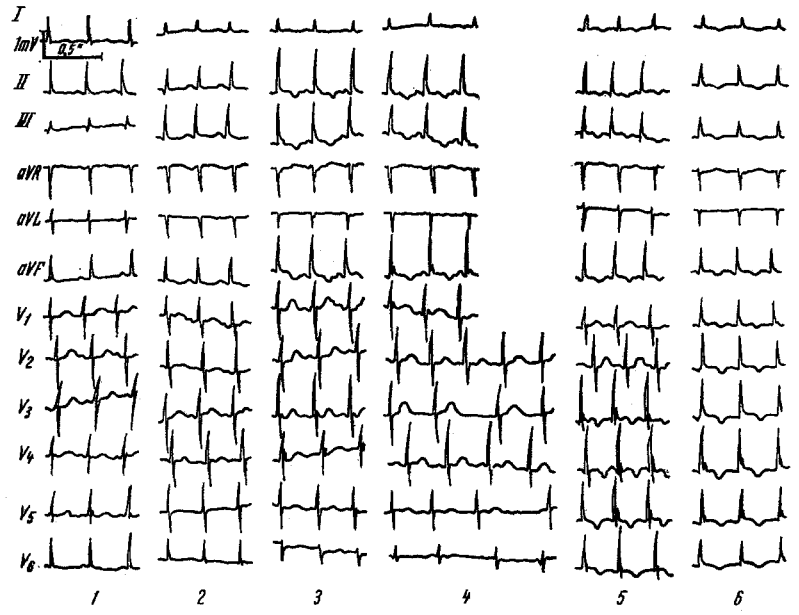

Fig. 2. ECG of monkey No. 9383. Legend as in Fig. 1.

In the experiments of series II (after running) inconstant inversion of T_{III}, aVF was found in monkey No. 9383, while a normal ECG was recorded in the other animals.

In the next experiments with immobilization either alone or preceded by running, a normal ECG pattern was recorded only in monkey No. 9337. The ECG of the other animals was characterized by a gradual increase in severity of pathological changes of ischemic type.

In monkey No. 9361 (Fig. 1) pathological ventricular complexes with irregular periodicity, arising after 2-4 or more normal cycles, were recorded during the first session of immobilization. These changes, constituting the picture of alternate block of the left branch of the bundle of His, were maintained steadily throughout the sessions of immobilization. One week after the end of immobilization, the signs of block were accompanied by a pathological Q_{III} wave and inversion of the T_{III}, aVF waves, and 1 month after the end of immobilization also by inversion of the $T_{V_{1-3}}$ wave with upward displacement of the ST segment.

After 80 days, inversion of the T_{II} wave and pathological Q_{I-II} waves were added to this picture.

In monkey No. 9382 immobilization was accompanied by the appearance of negative T_{III},aVF waves with elevation of the ST segments above the isoelectric line, and when running was combined with immobilization, by inversion of the T_{II} waves. One week, 1 month, and 80 days after the end of the mobilization experiments, inversion of the T_{II-III} waves and upward displacement of the ST segment, together with a flattened, biphasic, or completely negative T wave, were observed in the right chest leads.

Changes in the ECG of monkey No. 9383 (Fig. 2) during the immobilization experiments consisted of an isoelectric T_I,aVL wave, a negative $T_{II,III}$,aVR,aVF wave, upward displacement of the ST segment, and lengthening of the R–R intervals in individual cycles by 40-60%. One week after the end of the immobilization sessions these changes were supplemented by inversion of the $T_{V_{3-6}}$ waves and elevation of the ST segment above the isoelectric line, and after 80 days by a negative T wave combined with displacement of the ST segment in all leads except aVL.

In monkey No. 9337 in all stages of the experiment the ECG picture was normal.

As a result of a combination of physiological hyperfunction of the heart with immobilization to induce neurosis, three of the four experimental monkeys thus developed pathological changes in their ECG of ischemic type, progressing for 3 months after the end of the immobilization sessions.

The dynamics of the systemic AP was similar in all monkeys. It showed a decrease in pulse pressure, on account of an increase in diastolic pressure during the period of immobilization and stabilization of the diastolic pressure, at about 100 mm Hg or higher in the after-period. The systolic pressure did not differ significantly from its initial level.

Previous investigations showed that certain pathological changes in the ECG can be induced entirely by immobilization, but if the immobilization is not accompanied by hyperfunction of the heart due to natural motor activity the ECG changes are not so clearly defined and are not consolidated in the after-period.

The results of the present investigation confirm the concept put forward previously [9] that chronic pathological phenomena in a particular functional system can be evoked by the natural stimuli of that system if they are converted into conditional stimuli for a pathological defensive dominant focus. In the writers' opinion, the resulting model of ischemic heart disease reproduces the fundamental mechanisms of the corresponding human pathology most adequately.

LITERATURE CITED

1. G. Ya. Kokaya, Byull. Éksperim. Biol. i Med., No. 12, 23 (1954).
2. G. Ya. Kokaya, The Electrocardiogram of Healthy Monkeys of Different Species and Ages. Candidate's Dissertation, Sukhumi (1958).
3. G. O. Magakyan, D. I. Miminoshvili, and G. Ya. Kokaya, Klin. Med., No. 7, 30 (1956).
4. G. O. Magakyan, Investigations into the Pathogenesis of Hypertension, Coronary Insufficiency, and Myocardial Infarction in Experiments on Monkeys. Doctoral Dissertation, Sukhumi (1965).
5. G. O. Magakyan, in: Medical Primatology [in Russian], Tbilisi (1967), p. 190.
6. D. I. Miminoshvili, G. O. Magakyan, and G. Ya. Kokaya, in: Theoretical and Practical Problems in Medicine and Biology in Experiments on Monkeys [in Russian], Moscow (1956), p. 87.
7. D. I. Miminoshvili, Abstracts of Proceedings on an Extended Session of the Bureau of the Department of Medico-biological Sciences, Academy of Medical Sciences of the USSR [in Russian], Sukhumi (1957), p. 36.
8. V. G. Startsev, Abstracts of Proceedings of the Tenth Congress of the I. P. Pavlov All-Union Physiological Society [in Russian], Vol. 2, No. 2, Moscow–Leningrad (1964), p. 292.
9. V. G. Startsev, in: Medical Primatology [in Russian], Tbilisi (1967), p. 148.
10. V. G. Startsev, in: Problems in Physiology and Experimental Pathology [in Russian], Sukhumi (1968), p. 219.
11. V. G. Startsev and S. K. Shestopalova, in: Problems in Physiology and Experimental Pathology [in Russian], Sukhumi (1968), p. 205.