EFFECT OF SYSTEMATIC EXPOSURE TO SOUND ON PREDISPOSITION OF KM RATS TO SEIZURES

UDC 616.8-009-24-092.92.09.2-02:615.834+615.837.015.4:616.8-009.24-092.9

E. A. Ryabinskaya and S. Yu. Korotun

KEY WORDS: audiogenic epileptic fit; level of predisposition to seizures; intervention over incomplete and complete ranges of stimulus intensity.

Audiogenic epileptic fits in KM rats are used as a model of seizure activity [4]. To study the mechanism of formation of adequate behavior, a comparative physiological study is made of Wistar and KM rats, and methods of blocking seizures and inducing normalization of higher nervous activity in KM rats are sought [1, 2, 6, 7].

In the investigation described below the effect of systematic exposure of KM rats to sound on the level of seizure readiness (LSR) was studied.

EXPERIMENTAL METHOD

Experiments were carried out on KM rats of both sexes aged 3 months. The rats were exposed to sound under conditions described previously [2]. LSR was determined by means of a scale of assessment (in points) of four stages of the epileptic seizure [4]. In the experiments of series I the rats were exposed to sound (90 dB) for 60 sec once a day for 15 successive days. In the experiments of series II, on the first day the animals were exposed to sound (90 dB, 60 sec) 12 times at intervals of 30 min. Control testing was carried out 24 h later. In series III the effect of systematic exposure to sound of increasing intensity on LSR was studied. In the first version of the experiments a control exposure to sound was carried out (90 dB, 60 sec). The experiments began 9 days later (once a day). In the course of five experiments the rats were exposed to the action of sound of gradually increasing intensity. The minimal intensity of the sound was always the same, 75 dB. The action of sound of that intensity did not cause epileptic seizures in most animals. The maximal intensity and duration of action of the sound increased day by day: first experiment 75 dB, 25 min; second experiment from 75 to 78 dB, 30 min; third — from 75 to 84 dB, 35 min; fourth — from 75 to 92 dB, 40 min (Fig. 1b). This procedure we conventionally called intervention over the incomplete range of stimulus intensity (IIRSI). Next followed the procedure of intervention over the complete range of stimulus intensity (ICRSI). In three experiments, the rats were exposed to the action of sound the intensity of which increased from 75 to 110 dB in the course of 63 min (Fig. 1a). SCR was then tested in the rats 2 h (first test), 24 h (second test), 2 days (third test), 7 days (fourth test), and 11 days (fifth test) after the last experiment under ICRSI conditions. The intensity and duration of the testing stimulus were the same as in the control (90 dB, 60 sec). In the second version of the experiments of series III the intensity of the control and testing stimuli was greater than in the first version — 110 dB (60 sec). The procedure of IIRSI was as follows: For six experiments the rats were exposed to the action of sound in accordance with the same scheme: In all experiments exposure to sound lasted 30 min and its intensity was increased from 75 to 80 dB (Fig. 1c). Next followed only one experiment under ICRSI conditions. Otherwise the conditions of the first version of the experiments were maintained. The results were analyzed by Fisher's accurate method and by the signs test [3].

EXPERIMENTAL RESULTS

In the experiments of series I 13 rats in which epileptic fits developed in the first experiment, going on to the completion of stages III or IV, were used (Fig. 2a). In the next

Department of Physiology of Higher Nervous Activity, A. A. Zhdanov Leningrad University.
(Presented by Academician of the Academy of Medical Sciences of the USSR V. S. Rusinov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 96, No. 12, pp. 10-12, December, 1983. Original article submitted December 31, 1982.

0007-4888/83/9612-1655$07.50

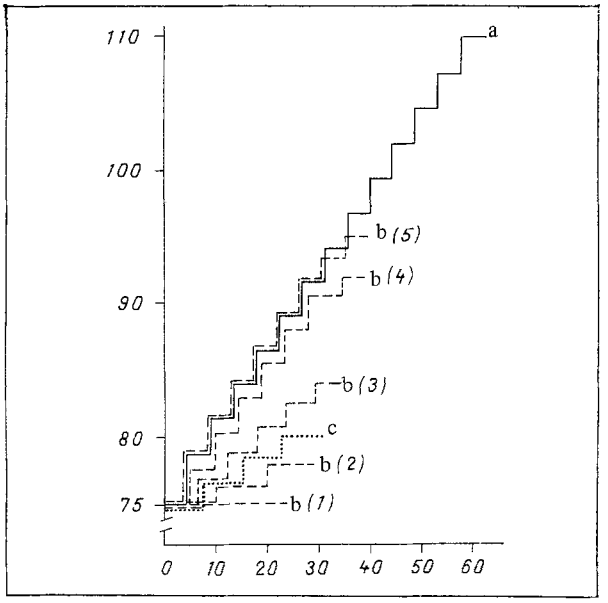

Fig. 1. Dynamics of changes in sound intensity. a) ICRSI; b, c) IIRSI in first and second versions of experiments of series III respectively. Numbers in parentheses indicate serial numbers of experiments. Abscissa, duration of exposure (in min); ordinate, intensity of sound (in dB).

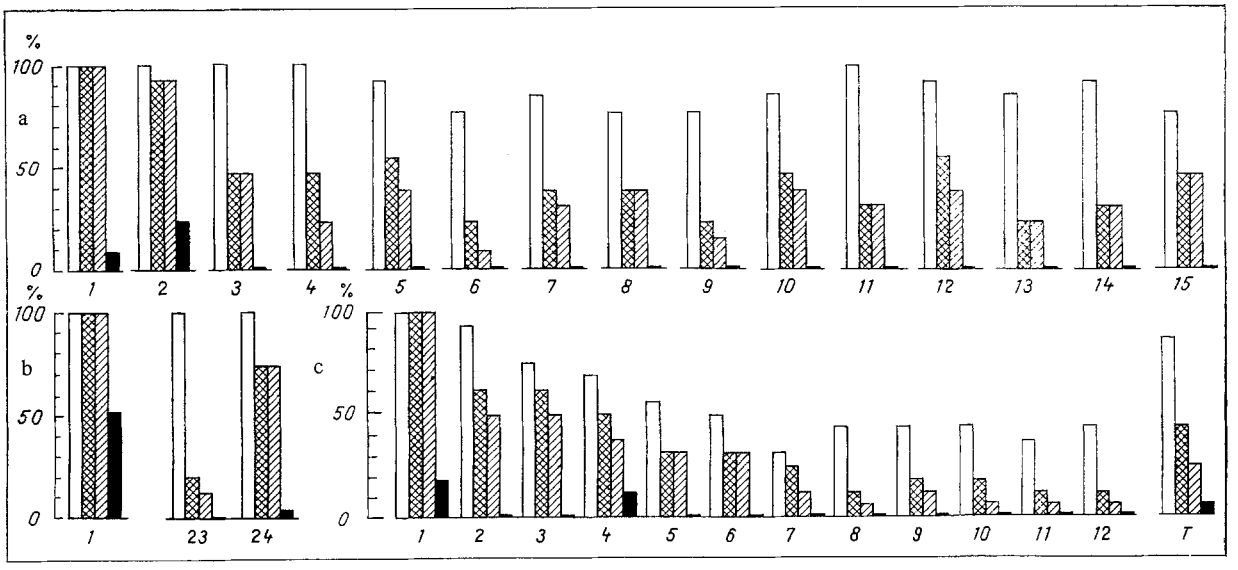

Fig. 2. Effect of systematic exposure to sound on LSR in rats. a and b) Experiments of series I, c) of series II. Abscissa: a) Nos. of experiments with exposure to sound; b) experiments with exposure to sound with a strength of 90 dB (1 and 23) and 110 dB (24), c) testing after 24 h (T); ordinate, percentage of animals in which sound evoked stage I (unshaded column), stage II (cross-hatched column), stage III (obliquely shaded column), and stage IV (black column) of epileptic fit.

3-15 experiments, the number of animals in which sound evoked seizure activity (stages II-IV of the fit) was less than in the first experiment ($P < 0.025$). Only the first preparoxysmal stage — the "motor aura" [8] — was relatively stable. In addition, in 15 rats with initially high LSR in this series of experiments, after 22 exposures to sound with a strength of 90 dB the responses to a stimulus of the same intensity and to stimuli of greater intensity (110 dB) were compared. In most ($P < 0.01$) animals ($n = 13$) in 23 experiments sound with a power

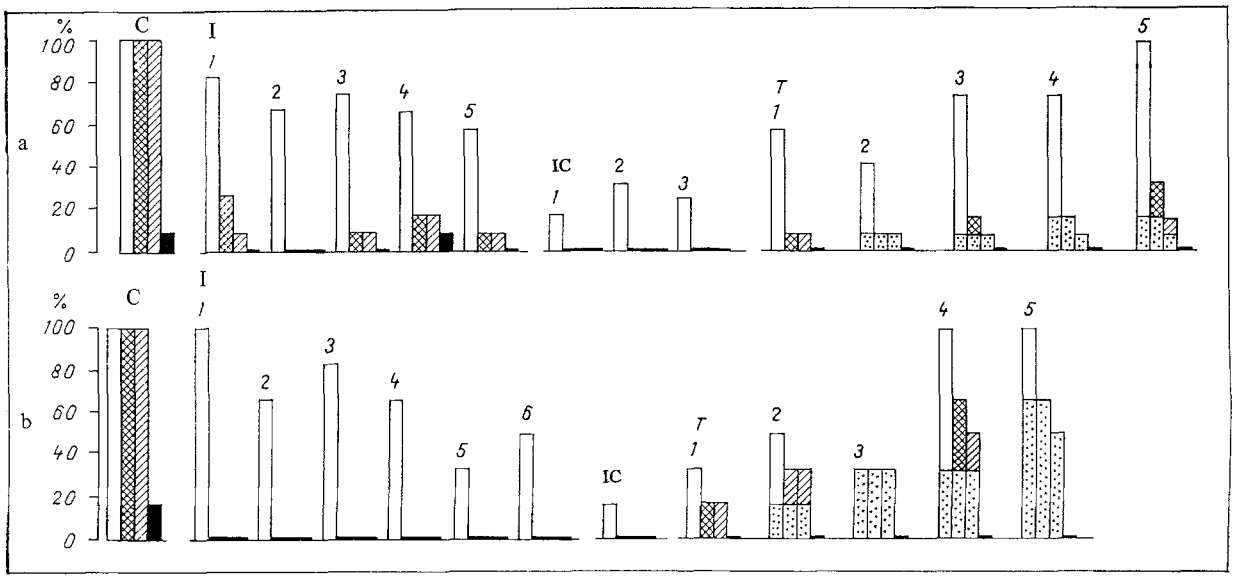

Fig. 3. Effect of sound of gradually increasing intensity on LSR in rats. a, b) First and second versions of experiments of series III respectively. C) Control experiment. I) IIRSI, IC) ICRSI, T) testing. Columns with dots — percentage of animals in which a seizure occurred during previous testing. Numbers denote serial numbers of experiments under the different conditions. Remainder of legend as to Fig. 2.

of 90 dB did not evoke seizure activity (Fig. 2b). An increase in the intensity of the sound (110 dB) led to a significant decrease in the number of resistant (i.e., without seizure reactions) rats (n = 4).

In the experiments of series II 15 rats in which seizure activity occurred in the first experiment (Fig. 2c) were used. In this case, during the 2nd to the 12th exposures to sound and in the test conducted 24 h later, fewer animals ($P < 0.025$) were observed with a seizure reaction.

The first version of the experiments of series III was conducted on 16 rats with high LSR in the control experiment. During periods of IIRSI and ICRSI, seizure activity occurred in only some of the animals (and not in all experiments). Significantly more rats ($P = 0.05$; $n = 12$) were resistant to the action of sound during the period of ICRSI. In these 12 rats, LSR was tested later (Fig. 3a). Until the fifth test, in most rats ($n = 9$) sound did not evoke a seizure reaction. During the testing period after the rats had developed a seizure (stage II or III) the experiments on it were stopped, for a series of fits affects LSR, and for that reason further investigation of the duration of the effect of ICRSI on LSR on that particular animal could not be justified. Accordingly, in Fig. 3 cumulation graphs are given, from which it is possible to determine the number of animals remaining resistant to sound to a given moment.

In the second version of the experiments nine rats sensitive to sound were used. In six of these animals during ICRSI no seizure activity was found, and their LSR was tested (Fig. 3b). In the first test five rats were resistant to sound (110 dB). In two rats which remained resistant in the fifth test also, LSR was tested 18 and 32 days later. In one rat on the 18th day sound evoked a fit which culminated in stage II, whereas in the other rat no seizure activity was observed on the 32nd day. In all rats in which the testing stimulus did not evoke a seizure reaction, an orienting reflex to sound with an intensity of 70 dB was present.

Systematic exposure to sound (90 dB, 60 sec), which in the first experiments induced a seizure reaction, thus lowers the LSR of KM rats. A similar phenomenon also is observed during exposure to sound given once a day or at intervals of 30 min. In the latter case the effect persists for at least 24 h. LSR is also lowered after systematic and prolonged exposure to sound which, as a rule, does not evoke seizure activity (gradually increasing intensity, starting with below the threshold). Under these conditions the effect continues for several days. The length of time during which the effect lasts may perhaps depend both on the intensity and duration of the stimulus in IIRSI and on the intensity of the control and

testing stimuli. During systematic exposure to sound of greater intensity (112 dB) seizure activity in KM rats does not disappear, incidentally, but myotonic convulsions do appear [4, 5]. Thus depending on the conditions of presentation and the intensity of the stimulus, different effects are observed. It can be postulated that the lowering of LSR which we observed is based on habituation or adaptation processes.

LITERATURE CITED

1. A. S. Batuev and E. A. Ryabinskaya, in: Searching Activity, Motivation, and Sleep [in Russian], Baku (1981), p. 12.
2. A. S. Batuev, E. A. Ryabinskaya, and N. V. Gudimova, Dokl. Akad. Nauk SSSR, 248, No. 6, 1496 (1979).
3. E. V. Gubler and A. A. Genkin, The Use of Nonparametric Statistical Criteria for Evaluating Differences between Two Groups of Observations in Medico-Biological Research [in Russian], Moscow (1969).
4. L. V. Krushinskii, The Formation of Animal Behavior under Normal and Pathological Conditions [in Russian], Moscow (1960).
5. L. N. Molodkina, Nauch. Dokl. Vyssh. Shkoly, Biol. Nauki, No. 4, 38 (1968).
6. E. A. Ryabinskaya and I. M. Gabibov, Zh. Vyssh. Nerv. Deyat., No. 1, 47 (1982).
7. E. A. Ryabinskaya, O. V. Kropotina, and V. Vrakha, Dokl. Akad. Nauk SSSR, 261, No. 6, 1499 (1981).
8. V. M. Salimov and D. A. Fless, Byull. Éksp. Biol. Med., No. 6, 649 (1977).

EFFECT OF LONG-TERM HYPOKINESIA ON BIOGENIC AMINE CONTENT IN RAT BRAIN SYNAPTOSOMES

N. N. Panusheva

UDC 612.822.2:577.175.82].06:612.766.2

KEY WORDS: hypokinesia; synaptosomes; noradrenalin; dopamine; serotonin.

Considerable attention has begun to be paid in recent years to metabolism of biogenic amines (BA) in connection with the study of the adaptive role of the sympathicoadrenal system in stress situations and various experimental procedures. Investigations [1, 5, 11, 14] have shown divergent changes in catecholamine (CA) and serotonin (5-HT) metabolism in the brain of animals during hypokinesia. However, data obtained by individual workers are rather contradictory, evidently because of the different experimental conditions used and the different approaches to the research.

The aim of this investigation was to study the dynamics of changes in the CA and 5-HT concentrations at the subcellular level in some parts of the motor system of the rat brain at different stages of long-term hypokinesia.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 140-170 g. A state of hypokinesia was induced by keeping the animals in individual restraining cages, limiting their movement severely. The test parameters were determined on the 30th, 60th, and 90th days of the experiment. Synaptosomes were isolated from the sensomotor cortex and caudate nucleus

Laboratory of Cytochemistry, Brain Institute, All-Union Mental Health Research Center, Academy of Medical Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR I. P. Ashmarin.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 96, No. 12, pp. 12-14, December, 1983. Original article submitted March 25, 1983.

0007-4888/83/9612-1658$07.50