INHIBITION OF THE PHYSIOLOGICAL ANTICLOTTING SYSTEM DURING PROLONGED EXPOSURE TO SOUND

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Experiments on 152 albino rats, exposed to the action of sound (94-96 dB, 2 Hz) showed that in the early periods of exposure (30 min) a tendency toward hypercoagulation develops, followed by activation of the fibrinolytic system whether exposure to sound is continued or not. A similar sequence of hypercoagulation followed by fibrinolysis was observed after exposure to sound for 2 days. It is claimed that the inhibition of the anticlotting system observed during prolonged experimental exposure to sound is a result of its exhaustion associated with periodic activation during exposure.

During prolonged exposure to sound (94-96 dB, 2 kHz, 5 h daily for 130 days) transient changes in blood coagulation were observed in rats. On the 130th day of the experiment the tolerance of the animals to thrombin was lowered, indicating inhibition of the anticlotting system [1].

Assuming that inhibition of the anticlotting system in this case is the result of its exhaustion due to periodic activation occurring in the course of exposure to sound, in the present investigation the order of appearance and the dynamics of development of changes in the level of pro- and anticoagulants were studied in the early periods of exposure to sound.

EXPERIMENTAL METHOD

Experiments were carried out on 152 albino rats kept on a standard diet as recommended by the Institute of Nutrition, Academy of Medical Sciences of the USSR. The sound (94-96 dB, 2 kHz) was generated by a type GZ-10 apparatus. Acoustic stimulation was given for 15 and 30 min, 1, 2, and 5 h, and 2, 5, and 10 days (5 h daily). Blood was taken from the jugular vein immediately after the end of acoustic stimulation and at various times thereafter. The following determinations were carried out on the blood samples: plasma recalcification time, plasma heparin tolerance, prothrombin activity and prothrombin consumption (thromboplastin activity), total antithrombin activity, the level of antithrombins II, III, and IV, activity of fibrinolysis, fibrinogenolysis, and antiplasmin, the fibrinogen level, and in some experiments the antithromboplastin activity [6].

EXPERIMENTAL RESULTS

In preliminary experiments in which blood samples were taken immediately after acoustic stimulation for 30 min, 1, 2, and 5 h, and for 2, 5, and 10 days the maximal changes were observed after exposure for 30 min: a decrease was observed in the fibrinogen level (0.33±0.02%, control 0.48±0.10%; $P < 0.05$), the fibrinolysis activity (1.7±1.2%, control 17.2±5.2%; $P < 0.05$), and the fibrinogenolysis activity (19.7±5.8%, control 39.6±5.7%; $P < 0.05$), and the recalcification time was shortened (12.5±6.5 sec, control 105±7.5 sec; $P < 0.05$).

The results given in Table 1 show that a tendency toward hypercoagulation occurred 15 min after the beginning of exposure to sound: thromboplastin activity was increased, the antiplasmin level was raised, while the total antithrombin activity, the level of antithrombins III and IV, and the activity of antithromboplastin and fibrinogenolysis were lowered. Similar changes were discovered after exposure to sound for 30

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TABLE 1. Clotting Power of the Blood in Rats Exposed to Sound (94-96 dB, 2 kHz) for 15 and 30 Min

Index determined	Control	Duration of exposure to sound	
		15 min	30 min
Recalcification time (in sec)	94,6±6,6	89,0±10,5 $P>0,05$	90,8±4,5 $P>0,05$
Plasma heparin tolerance (in sec)	289±30	217±24 $P>0,05$	271±19 $P>0,05$
Prothrombin consumption (in sec)	36,2±2,6	54,2±7,2 $P<0,05$	46,4±1,6 $P<0,05$
Prothrombin time (in sec)	14,2±0,2	14,6±0,2 $P>0,05$	14,8±0,2 $P>0,05$
Antithromboplastin activity (in sec)	5,9±1,2	2,8±0,8 $P<0,05$	2,1±0,6 $P<0,05$
Antithrombin activity (in %)	130±6	99±10 $P<0,05$	95±10 $P<0,05$
Antithrombin II level (in sec)	12±0,6	8,7±2,3 $P>0,05$	7,6±1,8 $P<0,05$
Levels of antithrombins III and IV (in sec)	47,6±3,0	26,0±4,7 $P<0,05$	30,8±5,9 $P<0,05$
Fibrinogen level (in %)	0,41±0,01	0,39±0,007 $P>0,05$	0,32±0,007 $P<0,05$
Fibrinolysis activity (in %)	6,6±2,8	5,3±1,2 $P>0,05$	5,2±1,8 $P>0,05$
Fibrinogenolysis activity (in %)	33,1±3,3	8,2±1,8 $P<0,05$	11,7±2,5 $P<0,05$
Antiplasmin activity (in %)	80±13,7	137±7,0 $P<0,05$	130±10,4 $P<0,05$

min, and as in the preliminary investigations they were accompanied by lowering of the fibrinogen level. The lowering of the fibrinogen level accompanying an increase in clotting activity of the blood can be tentatively regarded as the result of partial fibrination due to the lowering of antithromboplastin and antithrombin activity.

A study of the dynamics of changes in the blood clotting system 30 min after the end of exposure to sound for 30 min showed that the tendency toward hypercoagulation was even stronger than immediately after exposure: the previous changes persisted, no fibrinolysis could be detected whatsoever (zero level), and the heparin tolerance was increased, which was not observed immediately after exposure for 30 min (Table 2). The same picture was observed also 1 h after exposure. The indices in the experimental animals 1.5 h after the end of exposure to sound were close to the control values, but the fibrinogenolysis activity was considerably higher than initially and a tendency toward activation of fibrinolysis was observed.

The experiments in which the animals were exposed to sound continuously for 5 h showed that the tendency toward hypercoagulation which developed during the first 30 min had disappeared by the end of the first hour. By the end of the second hour the opposite tendency was observed: a tendency for the recalcification time to increase (104 ± 7.0 sec, control 87±4.4 sec; $P < 0.05$), for a decrease in the heparin tolerance (278±31 sec, control 210±15 sec; $P = 0.05$), and for activation of fibrinolysis (17.3±2.9%, control 5.4±2.6%; $P < 0.05$). After exposure to sound for 5 h the values obtained with the experimental and control animals were practically identical.

During exposure of the rats to sound for 5 h daily for 10 days, at the end of the second day signs of an increase in clotting activity of the blood were again found: a decrease in the recalcification time (102±7.2, control 125±6.5; $P < 0.05$) and an increase in the heparin tolerance (229±15 sec, control 401±43 sec; $P < 0.05$). As earlier, these changes were accompanied by lowering of the fibrinogen level (0.38±0.1%, control 0.57± 0.05%; $P < 0.05$). By the end of the 5th day of exposure to sound the recalcification time was shortened (86±3.3 sec, control 102±4.9 sec; $P < 0.05$), whereas the remaining indices were close to the control value. After exposure for 10 days to sound, no changes whatever were observed.

These results suggest that in the first 15-30 min of exposure to sound the coagulating power of the blood was increased, presumably as the result of lowering of the level of the antithromboplastic and antithrombin components and raising of the antiplasmin level. The tendency toward hypercoagulation later disappeared rapidly, to be followed by activation of the fibrinolytic system. The disappearance of signs of hypercoagulation took place somewhat faster if exposure to sound continued than if it was discontinued. At the same time, with more prolonged exposure to sound (for 2 days), the changes were repeated, a tendency toward hypercoagulation being slowly replaced by restoration of the normal values of the indices studied.

Analysis of these data suggests the following mechanism for development of depression of the anticlotting system occurring during prolonged (more than 4 months) exposure to sound. During acoustic stimulation the clotting power of the blood is periodically increased, evidently through activation of the production of adrenalin, ACTH, and corticosteroids – hormones stimulating blood clotting [3, 4]. The hypothesis of increased production of these hormones is based on information showing that their levels are increased during exposure to factors evoking a stress reaction, including exposure to sound [5].

TABLE 2. Clotting Power of Blood of Rats 30 Min and 1 and 1.5 h after Exposure to Sound for 30 Min (94-96 dB, 2 kHz)

Time of taking blood		Recalcification time (in sec)	Heparin tolerance (in sec)	Fibrinolysis activity (in %)	Fibrinogenolysis activity (in %)	Fibrinogen level (in %)
30 min	C	138±15,4	330±11,5	12,0±2,8	30,1±5,0	0,45±0,02
	E	123±5,0 ($P<95\%$)	247±9,2 ($P>95\%$)	0,0 ($P=100\%$)	20,9±7,2 ($P<95\%$)	0,29±0,01 ($P>95\%$)
1 h	C	138±15,4	330±11,5	12,0±2,8	30,1±5,0	0,45±0,02
	E	98±5,0 ($P>95\%$)	381±71 ($P<95\%$)	0,0 ($P=100\%$)	15,1±3,1 ($P>95\%$)	0,38±0,02 ($P>95\%$)
1,5 h	C	102±4,9	336±43	6,6±3,8	31,3±2,7	0,43±0,01
	E	108±5,3 ($P<95\%$)	281±27 ($P<95\%$)	11,6±4,5 ($P<95\%$)	75,1±10,1 ($P>95\%$)	0,28±0,04 ($P>95\%$)

Note. C and E denote control and experiment, respectively.

A periodic increase in clotting activity, accompanied by increased thrombinogenesis above the physiological level, in accordance with Kudryashov's concepts [2], must cause periodic activation of the anticlotting system and, in particular, of the fibrinolytic system as one of its effector mechanisms. Prolonged exposure to sound, repeated daily, by maintaining the anticlotting mechanism in a state of permanent stress, can probably ultimately cause its exhaustion, and in previous experiments [1] this was manifested by lowering of the thrombin tolerance.

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