Effects of Substance S-1 on Rats with Impaired Hearing

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Intraperitoneal administration of substance S-1 to male Wistar rats with impaired hearing markedly increased hearing acuity. Substance S-1 had no negative effects on hearing in intact animals.

Key Words: *deafness; serum; recovery*

Sensorineural hearing loss (SNHL) is a pressing otiatric problem. Clinical observations indicate that 5-7% people suffer from SNHL [1,10]. However, the efficiency of modern therapy of this condition does not exceed 50% [2,3].

We elaborated a new approach to SNHL correction based on the use of biologically active donor serum enriched with endogenous peptide bioregulators [5].

Our previous studies showed that biologically active donor serum contains considerable amounts of low-molecular-weight proteins (250-14,000 Da peptides).

Substance S-1 is lyophilized chicken serum obtained during electrical shock (alternating current, 220 W, 2-3 sec; patent application PCT/RU00/073) and containing proteins with similar molecular weights. Here we studied biological activity of substance S-1 in deaf rats.

MATERIALS AND METHODS

Experiments were performed on 42 Wistar rats weighing 240-260 g (Stolbovaya nursery). The reaction to acoustic stimulation was studied in a shuttle box [9]. After the rat was placed in the chamber, acoustic stimuli (7 kHz, 1-10 dB) were presented and transitions to the opposite compartment were counted.

In series I, the rats were preconditioned (10 sessions, 20 presentations each). Acoustic stimuli (2 dB for 5 sec) were presented. The rats developed a conditioned response (transition to the opposite compartment in response to sound).

After initial tests the rats were divided into 4 groups. In series II, rats of groups 1 (n=7) and 2 (n=7) were intraperitoneally injected with 1 ml distilled water for 5 days. Rats of groups 3 (n=14) and 4 (n=14) received 400,000 U streptomycin sulfate dissolved in distilled water for 5 days. One rat in group 3 died after streptomycin administration. This ototoxic dose of streptomycin is used for modeling deafness in animals [5]. Repeated tests demonstrated the ototoxic effect of streptomycin.

In series III, substance S-1 (100 mg/kg) dissolved in 1 ml distilled water was administered to group 2 and 4 rats 30 min before the experiment. The rats of groups 1 and 3 received an equivalent volume of physiological saline. The animals were subjected to final tests.

The results were analyzed by Student's t test.

RESULTS

In the initial test all rats displayed active response to acoustic stimulation (18.4±2.6 reactions, Fig. 1).

Treatment with streptomycin for 5 days markedly decreased the response to acoustic stimulation (Fig. 1): the mean number of reactions in group 3 and 4 rats decreased to 5.4±1.6 and 6.1±1.9, respectively (p<0.001). These changes were not observed in groups 1 and 2 rats.

Substance S-1 improved hearing in deaf rats by 44% (p<0.001, Fig. 1), while in rats receiving physiological saline hearing remained at a low level. These results indicate that substance S-1 possesses high auditory activity.

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Substance S-1 and donor serum contain compounds with similar molecular weights. Therefore, the increase in auditory sensitivity is associated with the effects of low-molecular-weight compode-monstrated revealed that peptide compounds have similar molecular weights. Donor serum is enriched with vasopressin, vasoactive intestinal peptide, and neurotensin [5]. Molecular weights of these substances and components of substance S-1 are similar. Published data show that the internal ear contains receptors for vasoactive intestinal peptide and vasopressin [6-8]. Hence, these compounds play a key role in the regulation of hearing. We hypothesize that endogenous peptides present in chicken serum improve auditory sensitivity in rats with impaired hearing.

It should be emphasized that substance S-1 had no negative effects on hearing in intact animals with normal hearing.

Our results indicate that substance P obtained from chicken serum possesses high auditory activity and improves hearing in rats with experimental deafness.

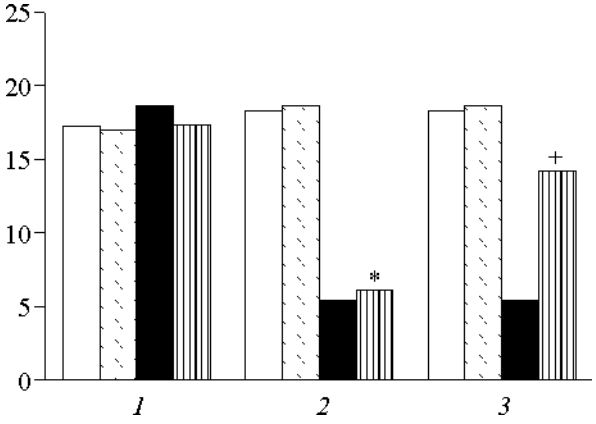

Fig. 1. Effects of substance S-1 on hearing in rats. Ordinate: mean number of reactions to acoustic stimulation. Light bars: distilled water in series *2* and *3*. Slant shading: distilled water and substance S-1 in series *2* and *3*, respectively. Dark bars: streptomycin and physiological saline in series *2* and *3*, respectively. Vertical shading: streptomycin and substance S-1 in series *2* and *3*, respectively. Series: initial test (*1*), deafness modeling (*2*), and evaluation of substance S-1-induced changes (*3*). $p<0.001$: *compared to initial tests; +compared to parameters before substance S-1 administration.

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