Effects of Alternative Social Experience on the Sexual Function of Male Mice

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The relevance of the social contact test "Wall" for evaluation of sexual motivation of male mice was tested and confirmed. Motivation of C57BL/6J male mice with alternative social experience (winners and victims in 10 and 20 daily male-male confrontations) was evaluated. Elevated primary sexual interest was detected in aggressive animals after 10 confrontations, while in submissive animals this interest was decreased; however after 20 confrontations sexual motivation in both groups was characterized by rapid exhaustion and low basal level of testosterone. Hence, the sexual function of male mice is inhibited under conditions of long social conflicts irrespective of previous experience of victories or defeats in male-male confrontations.

Key Words: *social stress; aggressiveness; sexual motivation; testosterone*

Sexual dysfunction involving virtually all components of response to a sexual stimulus (motivation and stimulation processes, copulatory behavior, gonadal endocrine response, *etc*) is a highly prevalent consequences of social stress in animals. For example, long-term social isolation stress provokes inability to copulation in male mice [7]. Studies on the resident-intruder model showed disorders in copulatory behavior in males exposed to attacks of aggressive partners over 5 days [5] in contrast to increased sexual activity of aggressive males [6]. Some authors suggest disorders of sexual function in aggressive socially successful males as well [2]. However, today there is no universal unambiguous concept of changes in the sexual system functioning in males under the effect of alternative social experience.

We tested the reveancy of the social contact test "Wall" for studies of sexual motivation of male mice, investigated primary motivation phase of male sexual behavior during acquisition of contrast social experience (winners and victims in male-male confrontations), and evaluated endocrine markers of the function state of the reproductive system in these animals.

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MATERIALS AND METHODS

Experiments were carried out on adult 2.5-3-month-old CBA/Lac and C57BL/6J mice (24-28 g). The animals were kept under standard vivarium conditions.

In the first experiment we studied the possibility of using the social contact test "Wall" [3] for evaluation of the sexual motivation in male mice. A receptive CBA/Lac female, in which estrus was induced by injection of chorionic gonadotropin (10 U, Prophazi, Serono) 24 h before experiment, was put into the free compartment of a cage divided into 2 parts with a transparent wall with holes, with a male of the same genotype behind the wall. These conditions allow the male see and perceive the female, but prevent physical contact. Male behavior was recorded using Etograf semiautomated device, which measured the number of excursions to the wall and time spent near the wall in reaction to the receptive female. The behavior near the wall was recorded during 10 min, after which the wall was removed and the next 20 min the parameters of male sexual behavior were recorded: number and duration of sniffing at the female and number and duration of copulations.

In the second experiment sexual motivation of C57BL/6J males with chronic experience of victories or defeats over 10 and 20 days was studied in this test.

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These animals were selected using the sensory contact model [3], which helps to distinguish animals with contrast social behavior: aggressive (winners) and submissive (victims) males. Sexual motivation of model animals was evaluated after 10 and 20 days of social confrontations. Intact males, placed into individual cages 5 days before the experiment in order to cancel the effect of previous living in a group, served as controls.

After the last fight the mice with alternative social experience were placed into new cages and their sexual motivation was evaluated after 24 h: at first the behavioral reaction of the male to the empty compartment of the cage was recorded for 5 min, then a female (in estrus) of the same strain was placed into this empty compartment. Behavioral reaction to the female was monitored over a 30-min interval during four 5-min periods (2 periods at the beginning and 2 at the end of the interval) by recording the number of excursions to the wall and time spent near it.

Basal testosterone level in the peripheral blood plasma of model males 24 h after the last of 10 (T10) and 20 (T20) daily male-male confrontations was measured by radioimmunoassay using ^{3}H-testosterone (Amersham) and highly specific antisera; the males were left alone in new cages over these last 24 h.

Experimental groups of animals were compared using nonparametrical Wilcoxon—Mann—Whitney test and paired Wilcoxon test. Each experimental group consisted of 9-12 animals.

RESULTS

Experiment 1 showed positive correlations between behavioral parameters in the Wall test and parameters

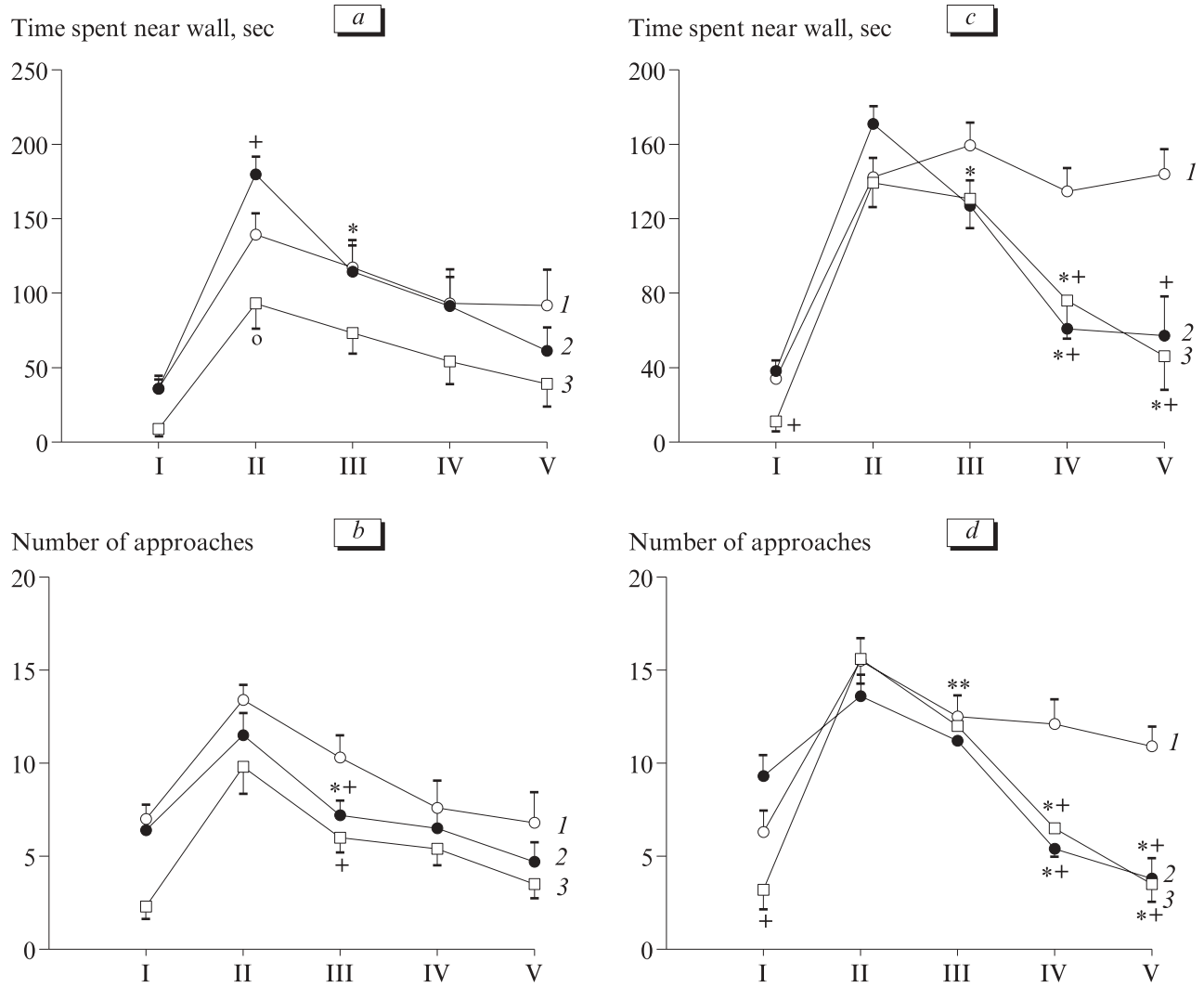

Fig. 1. Behavioral reaction to an estrous female in C57BL/6J male mice of alternative social status after 10 (*a*, *b*) and 20 (*c*, *d*) days of confrontation. Abscissa: time intervals of 4 testing periods from the moment of appearance of the female: 1) empty compartment; II: 0-5 min; III: 5-10 min; IV: 20-25 min; V: 25-30 min. *1*) control males; *2*) aggressors; *3*) victims. $p<0.05$ * compared to previous testing period in the same group of animals; + compared to the control; ° compared to aggressors during the same period.

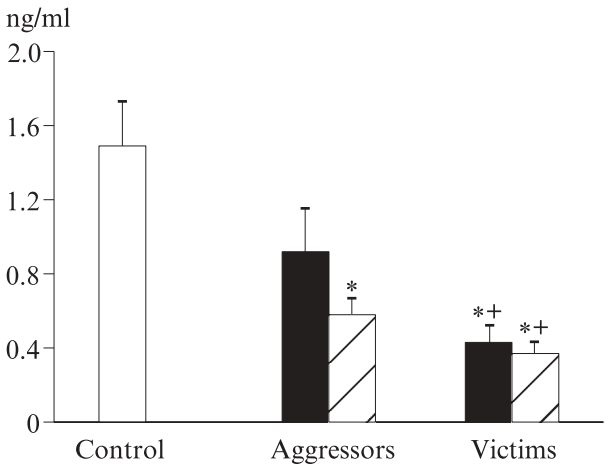

Fig. 2. Basal blood testosterone level in male mice during acquisition of alternative social experience of victories or defeats. Light bar: control; dark bars: model males in 10 daily confrontations; cross-hatched bars: males in 20 daily confrontations. $p<0.05$ * compared to. control; + compared to. respective group of aggressors.

of sexual behavior of males after removal of the wall: the time spent by the males near the wall correlated with the duration of sniffing before copulation (R=0.61,p=0.02) and duration of copulation (R=0.98, $p<0.005$); the number of male's approaches to the wall correlated with subsequent number of approaches to the female (R=0.53, p=0.05).

It was previously shown [3] that the behavior of a male near the wall separating it from another male correlated with parameters of aggressive behavior after removal of the wall. However the analogous reaction of the male to the female behind the wall as a reflection of male's sexual motivation is not proven, though it is known that these test conditions provoke elevation of blood testosterone in male [4]. This latter fact is an indirect (but not direct) evidence of the male's motivation behavior. The positive correlations between behavioral reaction of males to an estrus female in a situation of sensory contact and subsequent sexual behavior of the male observed in our experiment prove that it is adequate to interpret the results of the wall test in terms of sexual motivation.

In experiment 2 sexual motivation and basal testosterone level were studied in male mice with alternative social experience. The reaction to an empty compartment was, as expected, lowered in victims of social conflicts in comparison with controls and aggressive males (duration and number of excursions to the wall; Fig. 1, *a*, *b*). The appearance of an estrous female in the neighboring compartment of the cage activated the behavior of animals of all groups (time near the wall: T<1, $p<0.01$). Primary reaction to the female was more intense in aggressors than in intact animals. By contrast, submissive animals spent significantly less time near the wall behind which a female was placed in comparison with aggressors and there was a trend to a lower value in comparison with the controls (U=29, p=0.067).

Hence, previous experience of victories and defeats in male-male confrontations in general did not prevent the development of sexual motivation in male mice. Judging from lengthening of the time spent by winner males near the wall, it seems that the experience of victories promotes the development of more intense behavioral reaction to the female. This conclusion is in line with published data on increased sexual activity of aggressive animals [6].

Further measurements of motivation parameters from one testing period to another showed that sexual motivation of intact mice is stable in time: the time spent near the wall as a reaction to the female was the same during all testing periods. In aggressors the time spent near the wall decreased during the 2nd period in comparison with the 1st and by the end of the test did not differ from the control. In victims the interest to the female was constant, initial differences in comparison with aggressors leveled by the end of the test. The number of approaches to the wall gradually decreased during the test in animals of all groups (difference between periods 1 and 4: T<8, $p<0.05$), which, however, can reflect motor, but not motivation component of their behavioral reaction.

The initial reaction to the female in model animals exposed to 20-day social stress did not differ from the control (Fig. 1, *c*, *d*). However, it gradually decreased from one testing period to another. The total time spent by aggressors near the wall decreased starting from the 2nd testing period, in victims it decreased starting from the 3rd period, the difference in comparison with the controls was significant for this and subsequent periods. During the last testing period this value in model males was only 33% of the initial. The number of approaches to the wall as a reaction to the female rapidly decreased in model animals during the test: in aggressors starting from period 2, in victims from period 3. This parameter was significantly lower than in controls during the two last testing periods.

The basal plasma testosterone in model T10 and T20 males (Fig. 2) gradually decreased, being significantly lower in victims after 10 and in aggressors after 20 days of male-male confrontations in comparison with intact animals. The content of male sex hormone in victims was lower than in the respective group of aggressors for each point of measurements.

Hence, we observed dynamic changes in the sexual function of male mice during acquisition of contrast social experience. More intense initial reaction to the female in aggressive T10 males changed after 20 days of male-male conflicts. The functioning of the gonadal system decreased in submissive T20 males: testosterone level decreased and sexual motivation

rapidly faded. Inhibition of sexual function in submissive daily defeated animals could be expected. However, similar changes in the group of socially successful aggressive animals look paradoxical. This phenomenon can be explained by increased anxiety developing in aggressive males after 20 days of social confrontations [1]. The results improve our understanding of the processes essential for the functioning of the sexual system in animals exposed to social conflicts for a long time irrespective of their experience of victories or defeats.

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