Effect of Peptide Pro-Gly-Pro on Stress-Induced Behavioral Changes in Rats

G. N. Kopylova, S. E. Badmaeva, N. G. Levitskaya, G. E. Samonina, B. A. Umarova, and A. A. Guseva

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Tripeptide PGP in a dose of 1 mg/kg had a correcting effect on behavioral disorders in rats induced by stress exposure (forced swimming). PGP prevented the increase in anxiety and decrease in orientation and exploratory activity. Our results suggest that the effect of this peptide is realized via central nervous structures involved in organism's response to stress factors.

Key Words: *stress; behavior; regulatory peptides*

Tripeptide PGP belongs to the family of glyprolines [2,3] that prevent the development of various stress-induced disturbances. The peptide significantly decreased the area of injury in the gastric mucosa [1,5] and reduced reactivity and secretory response of mast cells to ulcerogenic stress [9]. The stress-induced microcirculatory disturbances in the mesentery were less pronounced after pretreatment with PGP [8]. Among a variety of mechanisms for the antistress effect of PGP, the central action of this peptide is least understood. Published data show that PGP crosses the blood-brain barrier [4] and directly affects central nervous structures involved in organism's response to stress factors.

Here we studied the central protective antistress effect of PGP during forced swimming.

MATERIALS AND METHODS

Experiments were performed on male outbred albino rats weighing 200-250 g. The model of stress included forced swimming in water at 22°C for 10 min. Orientation, exploratory, and locomotor activities of animals were studied in the open field and hole-board test [6,7]. Behavioral tests were conducted under non-stress conditions (quietness, red dim light). The degree of anxiety was estimated in an elevated plus-maze. The behavior of animals was assayed over 3 min. The pain thresholds were determined in the hot-plate test (licking of hindlimbs) [7].

The rats were divided into 3 groups, which included nonstressed animals (control I) and rats exposed to stress after pretreatment with physiological saline (control II) or PGP in a dose of 1 mg/kg (experiment). The peptide and physiological saline were injected intraperitoneally (0.5 ml per 200 g) 15 min before stress. The animals were tested 15 min after the treatment.

The results were analyzed using Statistica software.

RESULTS

Stress induced significant changes in the behavior of rats (Table 1).

We observed a significant decrease in total locomotor activity in the open field and hole-board test. The decrease in the number of explored holes and rearing postures reflects inhibition of orientation and exploratory activity. The degree of anxiety in the elevated plus-maze increased. Behavioral activity of rats in the light area of the maze decreased. The hot-plate test revealed a significant increase in pain thresholds. The observed stress-induced behavioral changes are consistent with published data [10,11].

Department of Human and Animal Physiology, Biological Faculty, M. V. Lomonosov Moscow State University. ***Address for correspondence:*** samonina@pisem.net. Samonina G. E.

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TABLE 1. Effect of PGP on Stress-Induced Behavioral Disorders in Rats

Index	Group		
	control I	control II	treatment
Open field			
n	26	27	27
Distance of running			
1st minute	34.35±1.60	21.2±2.7*	23.7±2.2*
2nd minute	16.20±1.62	9.70±1.27*	11.10±1.28*
3rd minute	11.0±1.4	7.10±1.16	7.50±1.15
Entries into the center of the open field	1.85±0.30	0.52±0.14*	1.10±0.22
Rearing postures	15.30±1.32	6.60±1.11*	9.6±1.4*
Hole-board chamber			
n	16	17	17
Distance of running			
1st minute	26.25±2.20	20.00±1.23*	18.5±2.1*
2nd minute	12.0±1.4	8.7±1.4*	9.6±1.6
3rd minute	10.40±1.35	4.20±1.04*	8.1±1.2+
Number of explored holes			
1st minute	4.40±0.45	1.76±0.43*	2.30±0.62*
2nd minute	3.06±0.70	1.30±0.43*	2.00±0.46
3rd minute	3.10±0.63	0.94±0.30*	1.9±0.5+
Rearing postures	14.0±1.6	7.9±1.2*	9.80±1.24*
Elevated plus-maze			
n	17	16	16
Total time spent in light, sec	34.5±5.6	23.0±5.8*	52.6±8.6+
Rearing postures in dark	9.3±1.1	4.0±0.5*	6.2±0.9
Rearing postures in light	1.53±0.53	0.13±0.08*	1.38±0.53+
Number of looking out from dark arms	5.5±0.7	2.5±0.4*	4.6±0.7+
Number of overhangs from open arms	4.70±0.65	2.10±0.45*	5.7±0.7+
Entries into light arms	1.2±0.2	0.70±0.17	1.50±0.23+
Number of transitions through the center	0.85±0.15	0.45±0.17*	0.93±0.20+
Hot plate			
n	10	10	10
Latency of hindlimb licking, sec	7.55±1.14	10.50±1.23*	10.00±0.95*

Note. *n*, number of animals. *$p<0.05$ compared to control I; +$p<0.05$ compared to control II.

Pretreatment with PGP decreased the severity of behavioral disorders in stressed animals.

The degree of behavioral changes in the open-filed test tended to decrease in stressed rats pretreated with PGP. However, no significant differences were observed between control II and stressed rats.

PGP had a stronger protective effect in the hole-board test and in he elevated plus-maze. In animals pretreated with PGP and exposed to stress the distance of running and number of explored holes decreased on the 1st and 2nd minutes, but returned to normal by the 3rd minute. They differed from control II rats, but were similar to control I animals. Behavioral characteristics of these rats in the elevated plus-maze corresponded to normal and differed from control II animals (Table 1).

PGP had no effect on the increase in pain thresholds in the hot-plate test.

Our results indicate that tripeptide PGP had a correcting effect on stress-induced behavioral disorders in rats. PGP prevented increase in the degree of anxiety and decrease in orientation and exploratory activity of animals. Our results suggest that the influence of this peptide is realized via central nervous structures in-

volved in organism's response to stress. These mechanisms probably mediate various antistress effects of PGP (*e.g.*, antiulcer activity).

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