

STRESS-PROTECTIVE ACTION OF THYMUS PEPTIDES CONCERNING AGING RATS

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СТРЕСС-ПРОТЕКТОРНОЕ ДЕЙСТВИЕ ПЕПТИДОВ ТИМУСА ПРИ СТАРЕНИИ У КРЫС

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The survey objective is to check stress-protective action of thymus peptides concerning aging rats, experimentally. Methods used to study anxiety state were applied in tests with 18-months rats. It was found that thymus peptides in elevated plus maze (Thymosin fraction 5 (0.5 mg/kg) and Thymulin (0.15 mg/kg)), and anxiolytic Diazepam (0.5 mg/kg) increased the motion activity in open arms, and number of positions onto hind legs in the light part of dark-light chamber. Influence of thymus peptides on the emotional stress associated with the failure of formed conditioned response of active avoidance was studied among aging rats. Within the control the failure caused a sharp decline in avoidance reactions and other demonstration of emotional tension. Thymus peptides and Diazepam prevented negative consequences on avoidance learning reactions. Thus, thymus peptides have demonstrated effect comparable to Diazepam in used models conditions. In avoidance learning model thymus peptides entirely prevented the consequences of emotional stress in ageing rats.

Keywords: thymus peptides; emotional stress; stress-protective action; Thymuline; Thymozine.

Цель работы состояла в экспериментальной проверке стресс-протекторного действия пептидов тимуса при старении у крыс. В опытах на крысах в возрасте 18 мес использованы методики, применяемые для изучения состояния тревожности. Установлено, что в приподнятом крестообразном лабиринте пептиды тимуса (тимозин фракция 5 (0,5 мг/кг) и тимулин (0,15 мг/кг)), и анксиолитик диазепам (0,5 мг/кг) увеличили двигательную активность в открытых рукавах, а в светло-темной камере — число стоек в ее светлом отсеке. Изучено влияние пептидов тимуса при старении у крыс на эмоциональный стресс, вызываемый с помощью сбой выработанной условной реакции активно-го избегания. В контроле сбой вызвал резкое уменьшение реакций избегания и другие проявления эмоционального напряжения. Пептиды тимуса и диазепам предотвратили указанные негативные последствия сбой на воспроизведение выработанного навыка. Таким образом, пептиды тимуса оказали сопоставимое с диазепамом влияние на поведение в условиях использованных моделей. В модели сбой реакции избегания пептиды тимуса полностью предотвращали последствия эмоционального стресса у крыс при старении.

Ключевые слова: пептиды тимуса; эмоциональный стресс; стресспротекторное действие; тимулин; тимозин.

Introduction. Lately the bidirectional interaction of neuroendocrinal and immune systems has been studied dynamically, and the mechanisms give a possibility to optimize the therapy of some diseases both within the norm and upon aging. The mnemotropic and stress-protective action of the thymus polypeptides Tactivin drug was currently detected [3, 5]. As it shown in further studies, the underlying mechanism of such drug effect is activation of serotonergic and in a less degree, noradrenergic system [4]. However, it is still unknown which of three stages of adaptation process, resulting from the stress condition (alarm reaction, resistance phase, exhaustion phase), affect thymus peptides. The survey objective is to check stress-protective action of

thymus peptides concerning aging rats, experimentally.

Material and methods. The study performed with 120 male rats Wistar weighing 300–350 g. The age of animals is 18 months. The study was performed in 4 experimental groups, per 30 individuals in each. Drugs were abdominally injected in animals in volume of 0.5 ml: 1 group — 0.9% solution NaCl (control), 2 — thymus hormone thymulin at a dose of 0.15 mg/kg, 3 — thymosin fraction 5 (Hoffmann-La Roche Inc., Switzerland) (0.5 mg/kg), 4 — reference anxiolytic Diazepam (0.5 mg/kg). To explore the influence of the substance the methods used to study anxiety state were applied: elevated plus maze (EPM), dark-

The influence of thymus peptides for conditioned response of active avoidance reproduced after sCRAA

Substance	Avoidance response, %				
	before sCRAA	after sCRAA			
	16–20	1–5	6–10	11–15	16–20
Control ($n = 30$)	92.0 ± 7.3	28.0 ± 7.3 [^]	76.0 ± 6.2 [^]	76.0 ± 4.5 [^]	80.0 ± 7.0
Thymosin fraction 5 ($n = 30$)	98.7 ± 1.3	99.7 ± 0.3*	98.1 ± 1.7*	96.5 ± 3.5*	98.4 ± 1.5*
Thymulin ($n = 30$)	99.5 ± 0.5	99.8 ± 0.2*	99.2 ± 0.7*	99.5 ± 0.5*	98.1 ± 0.9*
Diazepam ($n = 30$)	89.8 ± 6.4	85.1 ± 7.6*	81.2 ± 6.9	71.4 ± 5.5	89.9 ± 5.9

Note. * $p < 0.05$ regarding control, [^] $p < 0.05$ regarding average value before sCRAA.

light chamber (DLC). Additionally thymus peptides influence among aging rats on emotional stress was investigated associated with the failure of formatted conditioned response of active avoidance (sCRAA) [2].

All the experiments were conducted in accordance with Good Laboratory Practice, GLP, ГОСТ (All-Union State standard) 33647-2015 and with European Communities Council Directives, November 24, 1986, 86/609/EEC.

The statistical treatment of results was performed by means of non-parametric Wilcoxon criterion with computer program "Statistica 8.0".

Results and discussion. It was found that thymus peptides and Diazepam in elevated plus maze increased the motion activity in open arms, and number of positions onto hind legs in the light part of dark-light chamber. The grooming behavior was analyzed independently. I. Wishaw et al. separated 7 stages of grooming [7]. Stress impact show itself either in several stages drop-out or in sequence fault. Our tests demonstrate that clear consecutive grooming occurred only with thymus peptides in dark arms of EPM and in dark section of DLC, which reached final stages. In light section of DLC with thymus peptides grooming was sudden and nonconsecutive. Grooming was not seen within these tests with Diazepam. Therefore, increase of motion activity in EPM and DLC with thymus peptides was generated by exploratory activity, since the observed grooming in light section of DLC reflects the stress available among animals.

Influence of thymus peptides on the emotional stress associated with sCRAA.

The failure resulted in deep disorder of generated skill in first five presentations of control animals (Table) — number of avoidance reactions decreased 3.3 times. Under the influence of Diazepam reaction reproductive level immediately after sCRAA was 3 times higher that the control parameter.

With thymus peptides in first five presentations of conditioned signal after sCRAA the functional disorder of the generated skill was prevented and there was no failure. The positive influence of thymus peptides on avoidance reactions reproduction showed also in further set of presentations. Received results are comparable with data got with nootropic drugs [1].

Besides decreasing avoidance reactions after sCRAA among control rats the number of inter-signal reactions sharply decreased 3.3 times and number of reactions characterizing mental disturbance (jumps, chaotic running, vocalization), what indicated the increasing emotional tension of animals and developing emotional stress [6]. Thymus peptides and Diazepam prevented the appearance of generalized motion activity after sCRAA.

It is commonly known that stress interrupts problem solving, while its decrease removes the said influence. On the other side emotions and activation of generalized motion activity, which is shown as increasing intersignal reactions, reflect adaptive process, connected with mobilization of physical capacity in satiations threatening its entirety and with search for new solution under the altered circumstances, when the old is not effective anymore. As we can see, thymus peptides, not depressing the abovementioned adaptive process, prevent its excess performance, with the result that reproduction of the generated skill is not affected. Thymus peptides had an impact on behavior used models conditions comparable with Diazepam. In model sCRAA thymus peptides completely prevented the consequences of emotional stress among aging rats.

Conclusion. Therefore, the received results show that thymus peptides have discernable effect on higher integrative functions of brain. They ease emotional tension and improve adaptation in stressogenic conditions among aging rats, which means its stress-protective effect.

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