DOI 10.51231/2667-9507-2024-007-03-18-25

Vasopressin improves the production of a conditioned two-way escape reflex

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Abstract

Vasopressin (Lvp) is neuropeptide produced largely in the hypothalamus. Lvp is released from paraventricular nucleus (PVN) and supraoptic nucleus (SON) magnocellular terminals located in the neurohypophysis [1]. Upon entering the systemic blood supply, they exert endocrine actions including uterine contraction and milk ejection. Furthermore, Lvp released from terminals of parvocellular neurons of the PVN influences adrenocorticotropic hormone synthesis and release from the adenohypophysis and, thus, modulates corticosteroid hormone levels and stress response [2,3,4]. The neurohypophyseal peptide Lvp play an important role in the regulation of such processes as learning and memory. The participation of these peptide in the processes of memory and learning have been confirmed by investigations in which neurohyphopiseal extract has been employed [5,6]. It is yet unclear exactly what role vasopressin has in the organization, development, and replication of long-term memory traces. We investigated the effect of modest dosages of vasopressin on the rate of conditional bilateral escape reflex elaboration in rats weighing 250-300 g for this purpose. The experiment consisted of two groups of animals: control and experimental. During 12 days, 15 minutes before testing, experimental animals were given 4 g/0.2 ml lysine 8-vasopressin (Gedeon-Rixter) intraperitoneally. The equal

quantity of saline was administered into the control animals. We employed the T Student criteria for statistical data analysis. It was shown that in experimental group the indices of correct responses, as a latent period of reaction of active avoidance, significantly lagged behind the control group. The level of conditional reflex on active defensive escape was checked during three days in two weeks, 1 month and 2 months after such termination of experiment in both control and experimental groups of animals. However, through the first and second month breaks, the level of fulfillment of conditional reflex reaction at the experimental animals statistically significantly (P <0,01) exceeded those of control group animals. Therefore, vasopressin promotes preservation of a trace of memory and had anti amnesic effect.

KEYWORDS: vasopressin; conditional reflex; memory; rat

Introduction

Learning and memory are essential requirements for every living organism in order to cope with environmental demands, which enable it to adapt to changes in the conditions of life. An aversive stimulus is used to develop an active avoidance reaction. Aversive stimuli are associated with the release of stress hormones and neuropeptides. Neuropeptides affect not only attention, motivation, concentration, and arousal or alertness, but also anxiety and fear. Thus, they are involved in learning and memory processes. Despite certain successes, achieved in researches, accumulated actual data frequently had inconsistent character and required further specialization. Till now it is not finally found out, what role vasopressin can play in organization, formation and reservation of memory at all a stage of its reproduction. Originally, the assumption about a possible role of hypophyseal hormones, (especially vasopressin) in organization of memory, was studied by Wied et al [7]. The aim of this study was to find out a lysine 8 – vasopressin role in process of consolidation, preservation and reproduction of long-term memory trace. Therefore, the influence of small doses of vasopressin in dynamics of conditional two-way escape reflex elaboration were studied.

Methods

The experiments were carried out in adult male laboratory albino rats (n=40), weighing 250-300 g. For study of conditional defense reflexes the model of bilateral

escape reaction was used. The experimental cage represented a box (dimensions – 30x50x30 cm) made of transparent organic glass. The box was divided into two equal compartments by a 10 cm height partition. The floor of the cage was made from metallic rods, by means of which a threshold electrical painful stimulation was rendered to the paws. The source of a conditional signal – 60 w electric bulbs – was placed in the center of the cage at a height of 60 cm, which illuminated the whole cage. If after presentation of a conditional signal the animal jumped in other compartment of the cage during 5 sec, the answer was considered correct and the animal fail of an electrical punishment, otherwise it was punished by an electrical current. Each experimental session was carried out 20 trails. During experiment the dynamics of elaboration and course of bilateral escape reaction were studied. The following indices were registered: duration of latent period of conditional signal; duration of latent period of conditional (bilateral escape reaction), and unconditional (escape) reaction. The general behavior of the animal was also observed.

For revelation of vasopressin influence on elaboration of conditional reflexes the experiments were carried out on two groups of animals. In experimental group (n=20) for 15-20 minutes prior to the beginning of experiments vasopressin (Lysine-vasopressin “Koch-Light, England) was administered intraperitoneally (4 mg/kg). In control group (n=20) for the similar time prior to the beginning of experiments same amount of saline was administered.

The degree of reproduction of the conditioned active-avoidance reflex was checked immediately, 2 weeks, 1 month, and 2 months after the end of the experiment in both the control and experimental groups of animals.

Results

It is shown that in the first day of experiment (20 couplings) the quantity of the correct answers in control group of animals reached 30%. In following days, this parameter grew and on the seventh experimental session (in limits of 140 couplings) critical level was reached. The indices of adequate reactions achieved 90%. This level was remained stable in further days also. After vasopressin administration the indices of correct responses of the animals did not exceed 5 %. In the subsequent days this parameter was gradually increased, but nevertheless much lagged behind from those at control group of the animals. The critical level by the experimental animals was achieved only for the 10-th day (200 couplings). At further stages of experiment quantity of correct reactions of experimental group did not give any difference (Fig.1).

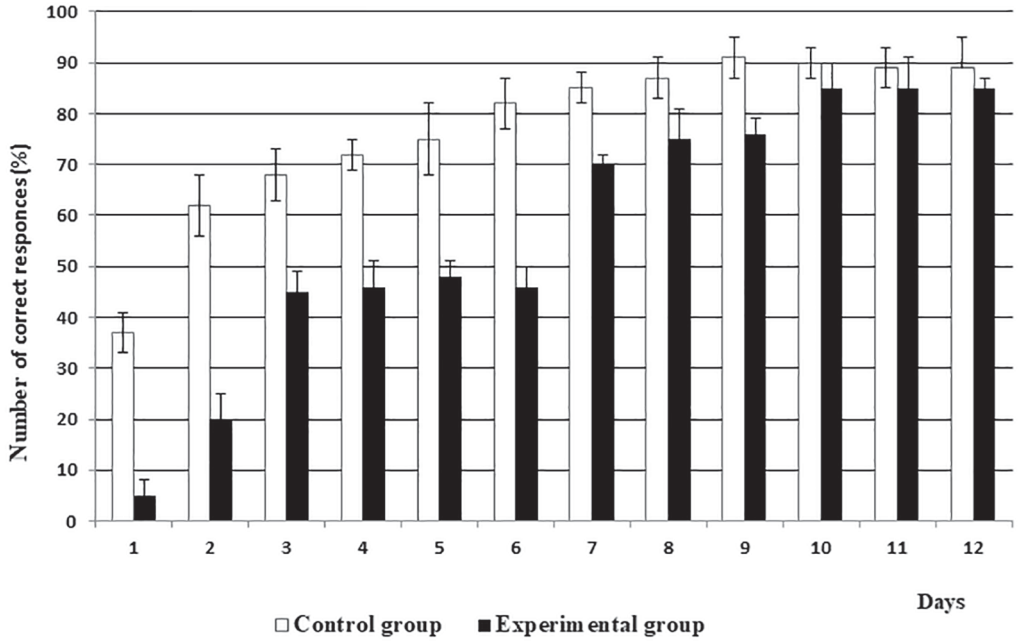

Fig.1. Effect of vasopressin on bilateral escape conditional reflex in rats.

During 12 days of elaboration of active defense reaction were revealed significant differences in the latent period of conditional reaction in control and experimental groups. In particular the latent period of conditional reaction changed in range of 1.9 – 2.4 sec and on the average made 2.1 sec. The minimal value of a similar parameter in experimental group of the animals has made 2.9 sec, and maximum – 3.6 sec. In general, during all period of elaboration of conditional reaction, latent period in experimental group of the animals statistically significant (P <0,05) exceeded those of control group of the animals. (Fig.2).

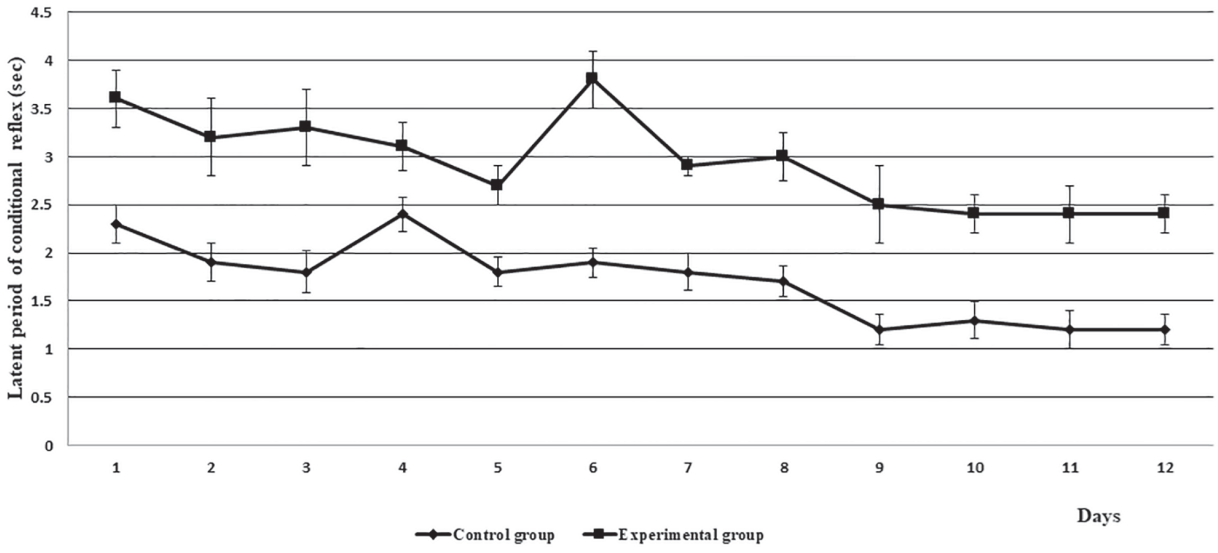

Fig.2. Latent period of bilateral escape conditional reflex in control and experimental groups.

The distinction between those two groups of the animals was marked also in latent period of unconditional escape reaction. In particular, during the first 9 days of elaboration of active escape defense reaction, latent period of escape in experimental group statistically significantly exceeded those in control group. During the three last days of experiments this distinction was kept, but statistically already was not significant. (Fig.3).

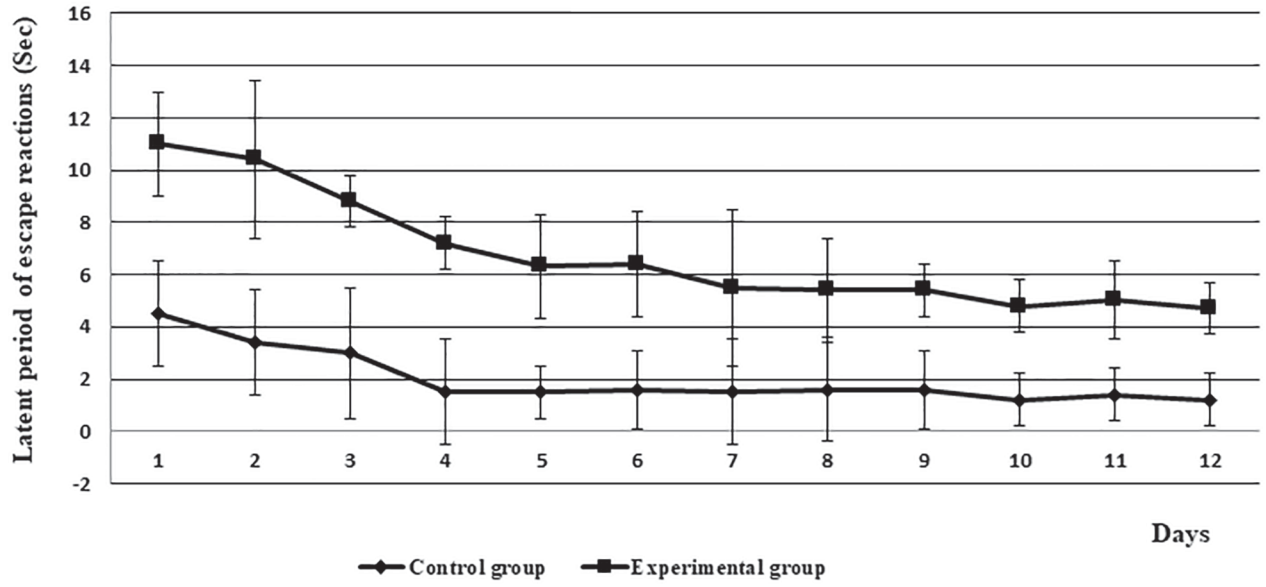

Fig.3. Latent period of unconditional escape reaction.

On basis of experiments it was established, that elaboration of adequate defense behavior for the animals' received vasopressin in comparison with the control animals much more couplings (80) were required.

As we mentioned above, the level of conditional reflex on active defensive escape was checked during three days in two weeks, 1 month and 2 months after such termination of experiment in both control and experimental groups of animals.

Two weeks after rest the distinction in a level of reaction on conditional reflex between the control and experimental animals was not found out. However, through the first and second month breaks, the level of fulfillment of conditional reflex reaction at the experimental animals statistically significantly ($P<0,01$) exceeded those of control group animals. In particular, on 20 conditional signals they adequately reacted 11 times (55%), and the conditional reactions were carried out on the verge of fortuity. At experimental group of the animals the level of the correct answers made 80-90%. (Fig.4).

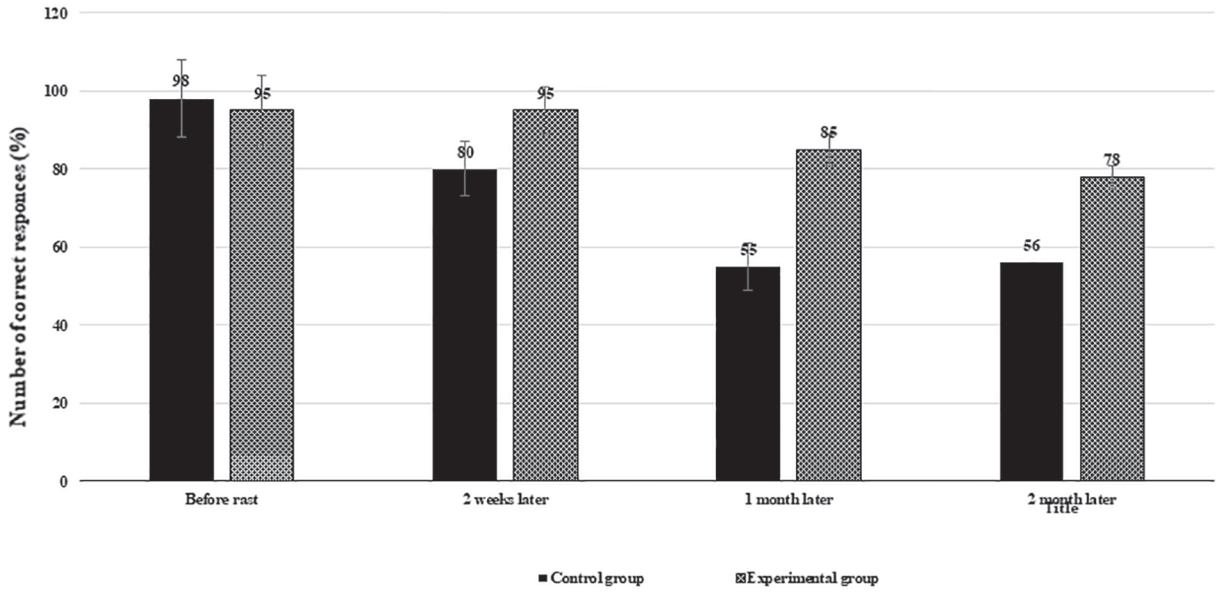

Fig.4. Effect of vasopressin on preservation and reproduction of active escape reaction. 1. Before rest; 2. Two weeks later; 3. One month later; 4. Two month later.

Discussion

We consider that such influence of lysine vasopressin on elaboration of conditional reflexes should be caused both by direct action of specified hormone on memory, and by alteration of motivational-emotional condition of the animal. The neuropeptide vasopressin might be affect motor performance in the early stage of formation conditional reflex (in order to maintain active avoidance extinction, the motor activity must be kept high) and this condition in its turn finds reflection during formation of memory [8,9,10]. Furthermore, vasopressin might be modulated the release of stress hormones such as epinephrine. In turn, catecholamines enhance memory consolidation. Vasopressin is co-localized with CRF in neurons from the paraventricular nucleus, which project to nuclei in the brainstem, involved in autonomic regulation [11-15]. These neuropeptides may act synergistically or in a concerted action aimed to learn to adapt to environmental demands. The effects induced by vasopressin is associated with central brain mechanisms which depends on the character of the reinforcing stimuli of the external environment.

The chronic administration of vasopressin promotes preservation of a trace of memory and its perfect reproduction.

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