Effect of Oxytocin on Neuronal Activity in Amygdaloid Nuclei in Stressed Rats

Kh. N. Mukhitdinova, L. G. Stamova, and M. M. Rasulov***

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 137, No. 6, pp. 641-643, June, 2004
Original article submitted January 26, 2004

The dynamics of impulse activity of amygdaloid neurons in response to intravenous injection of oxytocin were examined in acute experiments on random-bred albino rats. Oxytocin modified activity of amygdaloid neurons in intact and stressed rats. The dose-dependent effects of oxytocin were manifested in changes in the latency of neuronal responses and in rearrangement of their spike activity. The oxytocin-induced neuronal responses were less pronounced in cells with high baseline activity.

Key Words: *neuron activity; amygdala; oxytocin; stress*

Various nonapeptides, *e.g.* oxytocin (OT), exert central effects that underlie their use in sexual pathology for the correction of some types of impotence and frigidity. However, the effect of OT on activity of individual neurons received little attention. We previously showed that long-term sexual conflict deprivation in rats leads to stress associated with disturbances in the estrous cycle (shortening of diestrus and prolongation of estrus) and modification of behavior responses [1]. Taking into consideration the role of the limbic system (specifically, amygdaloid nuclear complex) in the formation of emotions and behavior, as well as the effect of OT on the function of reproductive system, we evaluated the effect of OT on spike activity of amygdaloid neurons during the development of sexual stress in rats.

MATERIALS AND METHODS

Experiments were carried out on mature female albino rats narcotized with nembutal (25 mg/kg). In estrous rats spike activity of neurons in the amygdaloid nuclear complex (A 5.0-7.3; L 4.52-5.5, H 2.2-3.0) was routinely recorded with glass micropipettes. Interspike intervals were measured and calculated automatically. After sacrifice, electrode localization was controlled by histological methods according to atlas [4]. OT (Gedeon Richter) was injected intravenously in doses of 1 and 5 U/kg. Experiments were performed from 10:00 to 16:00. In one experiment, the effect of single dose of OT on one neuron was examined. The effect of OT was significant, if it changed the parameters of spike activity by 30% and more. The baseline activity of the neurons was recorded for 10 min. The total recording time was 55 min. Emotional sexual stress was produced as described elsewhere [2]. The signs of stress were lengthening of estrous cycle (specifically, estrus phase), shortening of diestrus, and modification of behavior: disturbances in wakefulness-sleep cycle, prevalence of grooming and rearings, decreased number of runs *etc*. [2]. The estrous cycle was documented by cytological technique [3].

The rats were subdivided into two control and two experimental groups depending on the dose of OT. In control groups 1 (n=22) and 2 (n=21), OT was injected to non-stressed rats in doses of 1 and 5 U/kg, respectively. In experimental groups 3 (n=26) and 4 (n=29), OT was injected to stressed rats in doses of 1 and 5 U/kg, respectively.

Department of Physiology, Central research Institute, Abuali ibn Sino Tajik State Medical University, Dushanbe; *State Research Center of Elementorganic Chemical Technology, Moscow; **Lipetsk State Pedagogical University

0007-4888/04/1376-0563

RESULTS

In group 1 rats, 21 of 22 neurons (95.45%) responded with a latency of 10-35 sec. The discharge rate increased in 14 neurons, the discharge patterns changed (without changing discharge rate and with the formation of trains consisting of 5-10 spikes) in 6 neurons. In one neuron regularization of the discharge rhythm was observed. One neuron decreased the discharge rate 24 min postinjection. The changes induced by OT attained 220%.

In group 2 rats, OT induced short-latency increase in discharge rats in all neurons (n=21). The responses were pronounced and reached 60-350%. It is noteworthy that in both controls groups, reverse dependence between the responsiveness of the neurons to OT and their initial discharge rate was revealed: the greater the baseline discharge frequency, the smaller the changes induced by the peptide.

In group 3, in one neuron the inhibitory response appeared 20 min postinjection, while in others (n=25) the latency was shorter than 30 sec. Among these short-latency responses, 20 neurons were excited, 3 neurons were inhibited, and 2 neurons rearranged activity without changing the discharge rate. In this group, OT modified the discharges by 35-250%.

In group 4 rats, only short-latency responses were observed. Twenty-six cells responded by tachyrhythmia, and 3 neurons rearranged the discharge pattern without shifting the firing rate. In this group, OT produced 60-400% changes in impulse activity of the neurons.

To reveal possible plastic changes in the amygdaloid nuclear complex during the development of stress some statistical parameters of baseline activity of examined neurons were analyzed. In the control group, the distribution of the total set of interspike intervals was normal, the maximum probability density was 172.1 msec. The variational ranges of discharge frequency and interspike interval of all neurons were 0.5-16 Hz and 1750-10 msec, respectively. In 29 neurons the distribution of interspike intervals was approximated by normal logarithmic low (Table 1). The rhythm of discharges in other neurons cannot be characterized statistically.

In stressed rats the interspike intervals were characterized by normal distribution with maximum probability density about 183.7 msec. The variational ranges of discharge frequency and interspike interval were 0.3-18 Hz and 2300-9 msec, respectively. The interspike intervals of 13 neurons were distributed according to normal logarithmic low (Table 1). The rhythm of discharges in other neurons cannot be characterized statistically.

Thus, OT (1 and 5 U/kg) produced a pronounced neurotropic effect, which developed with different latencies and in most cases resulted in short-latency activation of the neurons. Probably, exogenous OT changed efficiency of aminergic synapses, which agrees with the current view [5] on the modulatory role of this peptide exerting its effect via monoamines.

The late reactions and recovery of the rhythm without changing the discharge rate probably attest to the dependence of the degree of OT neuronal action on functional state of the target cells. These reactions can be characterized by the parameters of stochastic distribution of the baseline firing activity of the neurons. However, the long-term latent reactions can also indicate the presence of cells controlling termination of the processes related to neurotropic effects of OT and/or to its action on myometrium in the amygdaloid nuclear complex.

However, spontaneous rhythmicity can reflect both periodic changes in neuronal activity and persistent tonic phenomena probably caused by the differences in the metabolism of various neurons or individual peculiarities in the neuron-glia system. In this case, potentiation of OT-induced neuronal response during the development of stress can indicate metabolic changes in the amygdala in stressed animals. This hypothesis is corroborated by the increase in the maximum probability density of interspike times and in the corresponding variational range in the stressed rats.

Thus, our data shed light on one of the elements of central action of OT mediated via its contact with neuronal membrane accompanied by modification of

TABLE 1. Effect of Oxytocin on Interspike Time Parameters of Neurons from Amygdaloid Nuclear Complex in Normal and Stressed Rats

Parameter	Control		Experiment	
	range	($M\pm m$)	range	($M\pm m$)
Mathematical expectation	93.2-947.3	207.3±24.5	97.1-941.5	181.1±19.2
Variance, %	37-326	106.2±16.4	46-331	139.1±18.2
Variation coefficient	0.21-1.31	0.7±0.1	0.23-1.56	0.93±0.12
Asymmetry coefficient	5.24-239.20	107.5±12.7	7.7-293.7	154.2±15.3

synaptic efficiency and metabolism in limbic system and amygdaloid nuclear complex during sexual stress.

REFERENCES

1. M. M. Rasulov, *Zdravookhran. Tadzhikistan.*, No. 5, 89-92 (1982).
2. M. M. Rasulov, *Zh. Vyssh. Nervn. Deyat.*, No. 3, 570-575 (1983).
3. O. N. Savchenko, *Sovr. Vopr. Endokrinol.*, No. 3, 151-167 (1969).
4. D. Albe-Fessard, F. Stulinsky, and S. Libouban, *Atlas Stereotaxique de Diencefali du Rat Blanc*, Paris (1971).
5. M. Linquette, *Bull. Biol. Pharmacol.* (Lille), **36**, 1-17 (1980).