Effect of Transauricular Electroacupuncture on Stress-Induced Changes in Cognitive Function and Erosions of the Gastric Mucosa in Rats

A. Yu. Efimenko, D. R. Lachinova**, S. A. Radzievskii***, S. V. Kruglov*, I. M. Golovin**, and I. Yu. Malyshev**

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 139, No. 2, pp. 143-146, February, 2005
Original article submitted July 1, 2004

Transauricular electroacupuncture prevented stress-induced increase in the degree of anxiety and suppression of exploratory activity in rats. This procedure significantly accelerated decision-making process during acute stress in both control and prestressed rats. Transauricular electroacupuncture decreased the number and area of erosions by producing a pronounced antistress effect at the central and peripheral levels.

Key Words: *stress; cognitive function; gastric mucosal erosions; transauricular electroacupuncture*

Stress-induced damage to organs is an urgent problem of modern medicine. Long-term chronic stress and single exposure to acute stress induce structural and functional changes at the central (brain) and peripheral (heart, stomach, immune system, erectile function, *etc*.) levels. There are antistress defense systems in the organism. Negative feedback mechanisms suppress secretion of stress hormones glucocorticoids and catecholamines [13]. Stress-limiting systems are presented by the opioidergic, GABAergic, serotoninergic, antioxidant, and prostaglandin systems and heat-shock proteins HSP70 [15]. Stress-induced damage to organs occurs when the strength of stressogenic factors exceeds the potency of stress-limiting systems or activity of these systems decreases. Increasing the power of endogenous antistress systems would be most effective in preventing the development of stress-induced injury. The method of transauricular electroacupuncture (TAEAP) is of considerable interest in this respect.

Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow; *Vladimir State Pedagogic University; **M. V. Lomonosov Moscow State University; ***Russian Research Center of Rehabilitative Medicine and Balneology, Russian Ministry of Health, Moscow. ***Address for correspondence:*** igor.malyshev@mtu-net.ru. I. Yu. Malyshev

TAEAP is a method of reflexotherapy. The effect of TAEAP is determined by a reflex response to stimulation of a certain zone in the auricle and direct effect of electric current on brain centers responsible for activity of the stress-limiting system [6]. Published data show that TAEAP improves functional activity of the central nervous system [5,12] and produces changes typical of adaptation to stress. Stress exposure after TAEAP in rats did not elevate plasma corticosterone concentration (stress hormone), but increases the content of β-endorphin and met-enkephalin (stress-limiting transmitters) [7,8,10]. This treatment was accompanied by activation of other stress-limiting systems, including the GABAergic and serotoninergic systems and HSP70 [1,3,4,10]. TAEAP is considered as a method of adaptation to stress [9].

An important scientific and clinical question arises: whether the increase in the power of antistress systems during TAEAP can be realized into the ability of TAEAP to prevent stress-induced injury in central and peripheral organs. Here we studied the effect of TAEAP on stress-induced cognitive dysfunction in the brain and formation of erosions in the gastric mucosa. These changes are the most typical and serious consequences of stress.

0007-4888/05/1392-0176

MATERIALS AND METHODS

Experiments were performed on 45 male Wistar rats weighing 300-400 g. The animals were subjected to stress: closed cage with experimental animals was submerged into water (22°C) to a level of 10 cm below the upper edge of the cage for 30 min.

The cognitive function was studied in two behavioral paradigms: open field test and extrapolation escape test (EET).

The open-field test was conducted 1 h after stress. The rat was placed in the center of a chamber. The floor of this chamber was divided into squares. There were holes in the floor. Behavioral activity was recorded over 2 min. The degree of general anxiety was determined by changes in horizontal locomotor activity. The decrease in horizontal activity reflected the increase in anxiety. Exploratory activity of rats was estimated by the number of entries into the center of the field, peripheral and central rearing postures, and explored holes.

EET was performed 30 min after the open-field test. The rat was placed in a glass cylinder immersed in water (acute stress). The rat should dive under the lower edge of this cylinder to escape from it. The latency of the first locomotor reaction, number of jumps, and time to resultant diving reflected the start of searching the solution, effectiveness of problem-solving task, and rate of decision-making process, respectively.

The rats were killed 1 h after EET. The number and area of gastric mucosal erosions were evaluated.

Some rats were exposed to TAEAP before stress. Acupuncture needles were inserted into both auricles behind the external auditory canal. Electrical stimulation with spike pulses (amplitude 0.8-2.5 mA, duration 1.5 msec, frequency 3 Hz) was performed for 15 min using a Lasper CS-504 device. The procedure was performed daily over 12 days [9]. The amplitude of pulses was selected individually by the pain subthreshold.

Statistical treatment was performed using Statistica 6.0 software. Experimental data on the number and area of gastric mucosal erosions had a normal distribution. Intergroup differences were evaluated by Fischer's *F* test. Pairwise comparison of groups involved Schiffe test.

The data on behavioral activity did not fit a normal distribution and were analyzed by nonparametric Kruskal—Wallis test. Mann—Whitney test with Bonferroni correction was applied to perform pairwise comparison of groups. The differences were significant at $p<0.05$.

RESULTS

In stressed rats horizontal activity and number of vertical rearing postures in the open field decreased by 2 times (Table 1). These parameters characterize the degree of anxiety and exploratory activity, respectively. TAEAP had no effect on the open-filed be-

TABLE 1. Effect of TAEAP on Cognitive Functions in the Open-Field Test

Parameter	Control	TAEAP	Stress	TAEAP+stress
Horizontal activity	52 (34; 56)	42 (37; 54)	20 (19; 30)*	50 (35; 57)
Peripheral rearing postures	10 (8; 13)	12 (9; 17)	4 (4; 7)⁺	13 (7; 19)
Vertical rearing postures	1 (1; 2)	1 (0; 2)	0 (0; 1)°	3 (2; 5)
Number of entrances into the center	0 (0; 1)	0 (0; 1)	0 (0; 1)	0 (0; 1)
Hole exploration	2 (0; 2)	1 (0; 2)	0 (0; 1)	1 (0; 3)
Total exploratory activity	13 (11; 16)	17 (10; 20)	5 (4; 9)ˣ	18 (12; 24)

Note. Here and in Table 2: data are presented as median (lower quartile; upper quartile). *p*, level of significance in Kruskal--Wallis test. *p=0.0400, p=0.0304, and p=0.0008 compared to the control, TAEAP, and TAEAP+stress, respectively; ⁺p=0.0392 and p=0.0028 compared to TAEAP and TAEAP+stress, respectively; °p=0.0016 compared to TAEAP+stress; ˣp=0.0430, p=0.0159, and p=0.0028 compared to the control, TAEAP, and TAEAP+stress, respectively.

TABLE 2. Effect of TAEAP on Cognitive Functions in the Extrapolation Escape Test

Parameter	Control	TAEAP	Stress	TAEAP+stress
Start of solution search, sec	1 (0; 3)	2 (0; 3)	1 (0; 2)	1 (0; 2)
Effectiveness of problem-solving task	12 (7; 14)	7 (3; 8)	12 (5; 21)	12 (8; 14)
Rate of right decision-making process, sec	44 (22; 85)	17 (9; 33)*	58 (15; 81)⁺	26 (18; 31)

Note. *p=0.012 compared to the control; ⁺p=0.0392 compared to TAEAP.

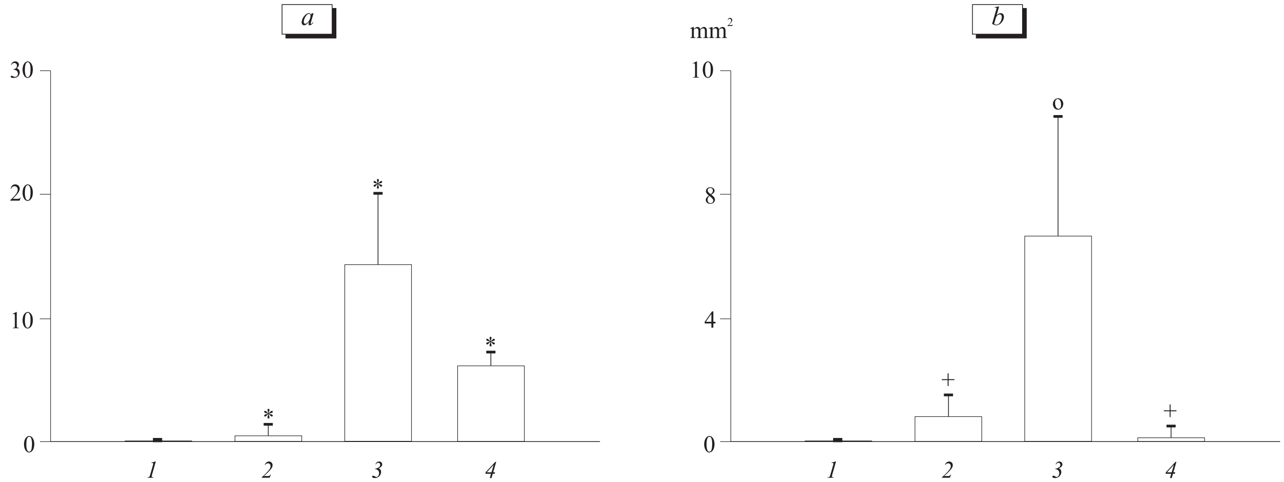

Fig. 1. Effect of TAEAP on the formation of stress-induced erosions in the gastric mucosa: mean number (ordinate, *a*) and area of erosions (*b*). Control (*n*=13, *1*), TAEAP (*n*=10, *2*), stress (*n*=11, *3*), and TAEAP+stress (*n*=11, *4*). $p<0.01$: *pairwise comparison of groups, number of erosions; +compared to stress; °compared to the control. *p*, level of significance in Fischer's *F* test.

havior, but prevented the increase in the degree of anxiety and decrease in exploratory activity of rats exposed to flood stress.

Prior exposure to flood stress did not modulate parameters of EET (Table 2). However, TAEAP significantly accelerated making decision in control and prestressed rats during acute stress (EET, Table 2).

Pretreatment with TAEAP improved the resistance of the gastric mucosa to stress (Fig. 1). After flood stress the mean number and area of erosions in rats exposed to TAEAP decreased by 2.4 and 73 times, respectively, compared to animals not receiving TAEAP. Therefore, TAEAP produced a potent antistress effect at the peripheral level.

It should be emphasized that flood stress impairs cognitive function "exploratory activity", but does not modulate cognitive function "rate of problem solving". A possible explanation is that stress factors have different effects on various cognitive functions. However, exploratory activity was studied in the open-field test, which simulates non-life-threatening stress. The rate of problem solving was estimated in EET, which is considered as a life-threatening situation. These data allow us to think of another explanation for the observed changes. Activation of antistress mechanisms and protection of cognitive functions determining animal survival have a biological rationale during acute stress. However, activity of several cognitive functions can decrease in the non-life-threatening situation.

TAEAP alleviates the central and peripheral damaging effect of stress. This treatment improves the ability of animals to solve problems under conditions of acute stress, prevents stress-induced increase in anxiety and decrease in exploratory activity, and reduces the severity of stress-induced gastric erosions.

The development of cognitive dysfunction under conditions of severe stress is associated with the effect of glucocorticoids in high concentration on hippocampal neurons. The formation of gastric erosions is primarily related to the effect of catecholamines in high concentration [13]. The antistress effect of TAEAP is probably due to inhibition of secretion of these stress hormones. This assumption is confirmed by published data that TAEAP strengthens the stress-limiting systems reducing the release of cortisol and catecholamines [1,3,4,7,8,10]. TAEAP probably improves the resistance of brain cells and gastric mucosa. However, this problem requires further investigations.

Our results form a basis for the use of TAEAP in clinical practice to improve cognitive function and prevent ulceration under conditions of stress overload. It should be emphasized that TAEAP is a validated procedure used to treat patients with various diseases [10,11,14].

REFERENCES

1. E. O. Bragin, Methodical, *Experimental, and Clinical Aspects of Reflexotherapy* [in Russian], Moscow (1985), pp. 104-156.
2. A. M. Vasilenko, *Lectures on Reflexotherapy* [in Russian], Moscow (2002).
3. R. A. Durinyan, *Physiological Bases of Auricular Reflexotherapy* [in Russian], Erevan (1983).
4. G. V. Kokurkin, *Reflexotherapy in Gastroenterology* [in Russian], Cheboksary (2003).
5. S. I. Kritskaya, I. A. Shchepelina, and A. P. Getmanov, *Vestn. OKB No. 1 g. Ekaterinburga*, Vyp. 4, No. 2, 45-47 (2002).
6. F. Z. Meerson, V. P. Pozharov, T. D. Minyailenko, *et al.*, *Byull. Eksp. Biol. Med.*, **115**, No. 4, 339-341 (1993).
7. F. Z. Meerson, M. G. Pshennikova, B. A. Kuznetsova, *et al.*, *Ibid.*, **117**, No. 4, 162-166 (1994).
8. E. V. Popkova, S. A. Radzievskii, L. M. Belkina, *Ibid.*, **124**, No. 10, 388-391 (1997).

9. S. A. Radzievskii, E. Ya. Vorontsova, L. M. Chuvil'skaya, *et al*., *Ibid*., **104**, No. 8, 151-153 (1987).
10. S. A. Radzievskii, *Acupuncture. Scientific and Practical Advances* [in Russian], Smolensk (1997), pp. 168-178.
11. D. M. Tabeeva, *Practical Manual on Acupuncture* [in Russian], Moscow (2001).
12. T. F. Filina, *Reflexotherapy of Cardiovascular Disorders. Collection of Scientific Researches of the Leningrad Medical Institute for Postgraduate Education* [in Russian], Leningrad (1988), pp. 84-89.
13. G. P. Chrousos and P. W. Gold, *J. Clin. Endocrinol. Metab*., **83**, 1842-1845 (1998).
14. D. L. Kirsch, *The Science behind Cranial Electrotherapy Stimulation: a Complete Annotated Bibliography of 106 Human and 20 Experimental Animal Studies Plus Reviews and Meta-analysis, a Current Density Model of CED, Side Effects and Follow-up Tables, All Indexes and Cross-referenced*, Edmonton, Alberta (1999).
15. F. Z. Meerson, *Adaptation, Stress and Prophylaxis*, Berlin (1984).