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High Anxiety as Typological Peculiarity of the Offspring of Rats with Chronic Uncontrolled Psychogenic Stress

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ABSTRACT. Five consecutive generations of the offspring (total number 300) of 8 initial pairs of rat-parents, crossbred in the state of chronic psychogenic stress with pronounced anxiety, were obtained. Before their sibling cross-breeding an information neurosis was formed in the offspring of all generations similar to that formed in the initial ancestry pairs of all lines. The peculiarities of emotional-behavioral activity of adult F1-F2 offspring have been studied both in their initial or naive status (i.e. before any special experimental influences) and after testing moderate stress (elaboration of conditioned reflex of active avoidance, 200 trials).

It has been established that uncontrolled psychogenic stress of rat-parents repeated in the line of genetically related generations appears to be a result of increased excitability, anxiety with high motor activity and defecations, high stress-reactivity with unequal strength of influence of greater stress response. To form phenotypically pronounced anxiety two generations of ancestry with stress induced by adaptation disorders in the form of information neurosis are sufficient. Manifestations of anxiety grow progressively from generation to generation. The offspring of rat-parents with information neurosis appear to be an experimental model of congenital predisposition to anxiety.

The anxiety of stressed rat offspring is discussed in the context of a whole complex of signs of their behavior and revealed peculiarities of their general nervous activity. Possible ways of the influence of information pathology of parents' behavior on the congenital peculiarities of higher nervous activity of their offspring are discussed. *© 2008 Bull. Georg. Natl. Acad. Sci.*

***Key words**: psychogenic stress, offspring, open field, Vogel's test, anxiety, excitability, inheritance.*

INTRODUCTION. Anxiety - one of the most widespread forms of unfavorable emotional reactions - underlies or forms the structure of many psychic and somatic diseases of human beings.

Expressed anxiety appears to be one of the main symptoms of a broad spectrum of different mental diseases ("panic disorder", "generalized anxiety disorder", "reaction to heavy stress and adaptation diseases", "mixed anxiety and depressive disorder", etc), united in modern diagnostic classifications in a large group - "neurotic and associated with stress and somatoform disorders" [1] in view of historical connection to the conception of neurosis or in a special class of "anxiety disorders" [2].

Current epidemiological data indicate that on the whole anxiety disorders highly prevail over other psychiatric problems both in hospital and adult and childhood general populations [3-7].

In the generally accepted polyfactorial etiology of anxiety (neurotic) disorders [1, 2, 7-10] together with the importance of direct psychotraumatic events, a significant role is assigned to the character of the patient's heredity (genotype and peculiarities of pregnant mother), character of postnatal effects of the environment (upbringing, every day-life conditions) in premorbid to typological personal traits. The latter may be considered either as predisposition to disease or not rarely as initiating its development. In the principles of diagnosis it is emphasized that, although a heavy stressor may induce a psychic disease in any human being, in cases when the etiological significance of extremely stressful event or prolonged unpleasant circumstances is not clear, the development of disease completely depends on the individual peculiarities of the patient's personality and often - on its particular sensitivity, i.e. vulnerability to the impact of diverse factors of the environment [1, 2, 7-10]. The cause of such particular vulnerability to environmental impacts more often appears to be anxiety as the initial peculiarity of the emotional sphere of the individual. It may be anxiety of any type, both reactive or state anxiety - increased fear of potential danger, recurring or increasing in corresponding situations and trait anxiety - characteristics of an individual psyche as a relatively stable tendency to perceive various situations as threatening (anxiety types according to Spielberg [11] and Lister [12].

Such a particular role of emotional anxiety state is determined by the reflective-evaluative essence of emotions themselves (a peculiar universal "measure of values" [13, p. 495], measure of the significance of developments), conditioning their exclusive role in the processes of perception, learning, memory and in the organization of the adaptive behavior of all higher animals.

In the etiology of anxiety disorders genetically conditioned predisposition is assessed as modest [7, 14, 15]. For example, in large twin (1033 pairs) study it has been established that the genetic factor plays an important but not prevailing role in the etiology of generalized anxiety disorder (the most widespread form of all anxiety disorders [3-7] with approximately 30% of hereditability as compared to 70% of major depression [14]; 22% of heredity is revealed according to the data of observations of 20 monozygotic and 29 heterozygotic pairs of twins [15].

As is known, prenatal effects of the maternal organism in an adult individual are major channels of congenital variability of traits of behavior (as of any other traits of the organism) i.e. the so-called maternal environment (maternal effect) which is determined not only by the genotype of mother but also by specific impacts on her organism during pregnancy [16-19]. In numerous animal experiments with various influences (emotional, physical stress, injection of hormones, mediators, surgical operations) on pregnant females changes in the level of emotionality of their adult offspring are demonstrated [20-23].

Similar results were obtained in our investigations on genetic control over expressed pathology of higher nervous activity of rat-parents, induced by stress in a continuous line of 5 subsequent generations of their offspring [24]. Adult offspring of stressed rats have revealed stable changes in behavior with a high level of emotional tension, fear, high stress-reaction. The evidence of observed peculiarities of behavior progressively increases from generation to generation. For the estimation of emotionality, level of the animals' anxiety, the methods of proconflict situation by Vogel were used along with the test of the open field (OF) (the results in detail were presented in our previous publication) [24]. The results of this part of our investigation are presented below.

MATERIAL AND METHODS. The investigation was carried out with 386 white outbred rats of both sexes, weighing 150-300 g.

From the first offspring (F1) of initial, eight pairs of parents in the state of strong chronic psychogenic stress (information neurosis) four consecutive generations were obtained by means of sibling cross-breeding (F2-F5) with an overall number of 370 F1-F5 offspring.

The offspring of all the generations were on maternal rearing and after 21 days they were kept in blocks (3-5 offspring) in conditions strictly identical for all the generations (according to age) maintaining a permanent cycle of day and night and giving water and food *ad libitum*.

After the investigation of the complex of behavioral signs in different test situations in the offspring of all the generations, before their crossing, information neurosis was formed, identical to that in the initial F1-F5 of 8 parent pairs of rats. By means of this, a model of repeated stress in the line of genetically related generations was created.

Formation of information neurosis was effected according to the original methods of avoidance of uncontrolled psychogenic stress, proposed by M. Khananashvili and T. Domianidze [25]. The method is based on the integration of two preliminarily elaborated conditioned reflexes of active avoidance (CRAA) in a modified shuttle-box (with three different compartments). Integration of CRAA consists in the presentation of both conditioned signals with 30 sec intervals in random order, according to the scheme by Gellerman (1936) in one experiment. In such a situation of integration with an uncertain time of signal presentation, the task of correct response appears to be unrealizable for the animal. During 20-25 sessions of such psychogenic (deficiency of pragmatic information) stress, a pronounced neurotic state with a high level of anxiety develops in the animal.

The design of the experimental apparatus, procedures of CRAA elaboration and their integration are described in detail in our previous publication [24].

The emotional behavioral activity of the offspring was assessed according to Hall's method of the open field (OF) and proconflict situation by Vogel. Registered in the OF during 5 min were: the number of crossed squares, penetration into the center, vertical standing, the number of head raisings, the number and duration of grooming reactions, the number of explored holes, urinations, defecations and boluses. The total data on horizontal and vertical activity were considered as an index of overall motor activity.

Emotionality and anxiety were also determined according to drinking behavior of rats in Vogel's proconflict situation test modified by Corda (Corda, Biggio, 1986). After 48 hr water deprivation the rat was placed in the cage where it was given an opportunity to consume water from an electrified drinking bowl. After each 3 sec of drinking act 0.3 mA current was supplied to the drinking bowl and the number of drinking acts was registered for 5 min. Such a current strength of electrical stimulation of oral cavity generally does not disturb drinking behavior and the rat, with a normal level of emotionality, after each electrical stimulus renews (resumes) the process of water consumption and during 5 min is able to accomplish approximately 50 swallowing acts. Such behavior is estimated as "the norm" of the given test. A sharp decrease of the number of swallowing acts testifies to the existence of anxiety and increased fear in animal.

The results were processed for mean values and statistically estimated according to Student's test.

Investigation of the peculiarities of offspring behavior of each of the 5 generations began after attainment of puberty and was fulfilled according to a common scheme for all. First of all the levels of emotionality, exploratory-oriented activity and defecations in the OF as well as the level of anxiety according to Vogel's proconflict test in an initial naïve status of the offspring, i. e. before the beginning of any special experimental influences were estimated. Then, to determine stress-reactivity re-estimation of these indices was carried out immediately after the influence of moderate stress. A 10-day episode of the procedure of CRAA elaboration (200 presentations) was considered to be a moderate stress. Reassessment of the indices of the behavior after elaboration of the first CRAA was accomplished according to the OF test, while after elaboration of the second CRAA - according to Vogel test.

At the termination of all the procedures of testing of behavior signs in animals of all the generations before the crossing "information neurosis" was formed by means of the integration of two CRAAs (according to the above-mentioned method).

THE RESULTS AND DISCUSSION. The results of the testing of 5 generations of offspring of rats with experimental information pathology of behavior in the OF were described in detail, documented and interpreted in our previous publication [24]. The main ascertained peculiarities (Table 1) are the following: I. Essential distinction of the first offspring from all other generations according to their emotional-behavioral activity:

Table 1.

% indices of emotional-behavioral activity of the different generation offspring in the open field

Activity \ Generation		F_1	F_2	F_3	F_4	F_5
I	A	100	152.3	147.61	207.12	152.3
	B	104.76	70.46	56.83	31.83	77.25
II	A	14.3	37	72	43	50
	B	32	52	55	76	51
III	A	6.6	7.7	42.5	28.9	0
	B	0	30.76	50.0	48.5	1.0

A - initial naïve status before beginning experiments.
B - after moderate stress (elaboration of the first two-way avoidance, - 200 trials).
I - Overall exploratory activity of the offspring of each generation. 100%-initial exploratory activity of F_1-offspring.
II - Percent of the offspring of each generation having defecation.
III - Percent of the offspring of each generation having 5 and more boluses.

in initial status they have the least indices of motor and excretory functions as compared to those of F2-F5, while their stress response is incomparably too small as compared to those of F2-F5. An increase of defecations without considerable changes in locomotion was revealed; the latter shows only a slight tendency to increase. The first generation of offspring proved to be more stable and stress-resistant as compared to all the consecutive generations. II. The existence of basic similarity in the offspring of all the consecutive F2-F5 generations according to the type of their emotional-behavioral activity in the initial status and the type of reaction to stress influence the combination of high level of motor activity and emotional tension - high defecation - is characteristic of their initial status. Response to moderate stress is manifested in drastic suppression of locomotion and also in greater tension of the excretory function. For example, after moderate stress, of the initial the motor activity of offspring totals 48.5% motor activity in F2, 40.3% - in F3, 16% - in F4 (sharper suppression); 53.12% - in F5. III. Manifestation of the phenomenon of progressive growth of expression of typological peculiarities of emotional-motor activity of the F2-F5 offspring from generation to generation, both in terms of the indices of initial status and their stress-reactivity. For example, the initial motor activity of F2-F3 exceeds by 52% that of F1 and by 47%, respectively; the activity of F4 exceeds by 39% that of F3 (and by 107% the activity of F1, peak of growth); however, the activity of F5 is lower as compared to F4, but it exceeds the indices of F1 by 52%. After moderate stress, the motor activity of F2 decreases by 29.5% as compared to F1; the activity of F3 is 13.6% lower as compared to the corresponding index of F2; the activity of F4 is 25% lower as compared to F3 (and 68.17% lower in F1; peak of reduction).

The sharply increased initial motor activity of F2-F5 animals - as compared to the stable F1 - as well as the more pronounced degree of its change in post-stress state and as a result the incomparably greater scales of the motor component of behavioral response to identical stress stimulation as compared to F1 - are doubtless indices of a high level of general excitability and its low threshold, high stress-reactivity, and correspondingly a high emotionality in the initial status of these animals.

The existence of initial increased emotionality, anxiety of F2-F5 is also corroborated by high level of their defecation at the first testing. Defecation is considered to be a stabler index of emotionality [26] and reflects more specifically the level of fear and anxiety in rats [27]. However, according to the results of our investigation, high motor activity appears to be an index of high emotionality along with high defecation. This is in good agreement with the known data on rat behavior in the OF [20, 26-30]. High motor activity, as an index of high emotional tension, is manifested first of all in animals which were preliminarily subjected to stress influence of strong or prolonged acting factors [26-30] or in offspring of female-rats with pharmacological or surgical blockade of the hypophyseal-adrenal system [20]. During testing (especially the first one) of these animals in the OF, increased emotion of fear together with increased defecation, may be reflected not in a decrease but, on the contrary, in an increase of motor activity, which is mostly interpreted as a combination of fear and attempts to escape or as intensification of exploratory-oriented behavior [20, 26-30]. The results of these and other well-known genetic investigations of Hall [31], Broadhurst, Bignami, Eysenck [26, 28, 29, 32], Royce [30], Whimbey, Denenberg [27] warranted the important conclusion about the genetic determination of signs of locomotion and excretory (defecation) levels of function by a complex polygenic system, the elements of which may be disturbed under certain conditions of the environment - stress, extreme impacts conditioned either by the existence of many variants of this system or variants of its functioning.

At the same time it is important that high motor activity in combination with high defecation (unusual positive correlation of these signs) as an index of high emotional tension is observed in our investigation in F2-F5 in the OF at their first testing in naïve status, thus reflecting the immanence of this peculiarity of emotional sphere in the offspring of stressed rats.

Basically similar characteristics of emotionality of stressed rats offspring, revealed in the OF, were also obtained in the investigations of drinking behavior in Vogel's proconflict situation.

Vogel's test was not used in animals of the first generation. Testing of F2, F3 and F4 revealed reliable disorders of their drinking behavior both in initial status and after stress impact (procedure of elaboration of the second CRAA), as well as the fact of growth of these disorders from the second generation to consecutive ones. For example, after elaboration of the second CRAA during testing (Fig. 1, Table 2) deviations in drinking behavior from the norm of the given test are the following for the offspring: 55.5% - in F2; 94.43% and 93.84% - in F3 and F4, respectively. A drastic reduction of drinking activity is also observed in F3 and F4 as compared to F2. Supposing that the number of swallowing acts in F2 offspring is 100%, then, as compared to them, in F3 and F4 a decrease of drinking behavior by 87.6% and 86.6% is noted, respectively, i.e. approximately 9 times.

The modification of Vogel's test, used by us, does not form a proconflict situation. Vogel's original method is based on conflict of high drinking motivation of water-deprived animals and aversive action of pain induced by electrical stimulation of the oral cavity during drinking with current sufficient to challenge a defense reaction of the animal with normal emotionality. This test, which is a model of anxious state, allows to assess the action of anxiolytics. Decrease of threshold current strength, supplied by Corda to the water bowl, does not disturb the drinking behavior of the animals in this model and does not hinder rats with normal emotional sphere to satisfy the thirst and fulfill approximately 50 swallowing acts during 5 min. In such a modified test it is possible to quantitatively estimate the "proconflict" action of anxiogenic substances or the "proconflict" effect of intrinsic anxiety, fear of animals, which provokes the suppression of water consumption, punishable with 0.3 mA current strength. In our experiments it reveals immanent anxiety of F2-F4 offspring and its intensification after stressogenic impact.

Table 2

Indices of drinking behavior of different generations of offspring after moderate stress (elaboration of the second two-way avoidance, 200 trials) in proconflict Vogel's test with 48 hour-long drinking deprivation.

Generation \ Indices	% index	Absolute index	Auth
F_2	100	22.15	$\pm$4.3
F_3	12.4	2.85	$\pm$0.7
F_4	13.4	3.08	$\pm$0.91

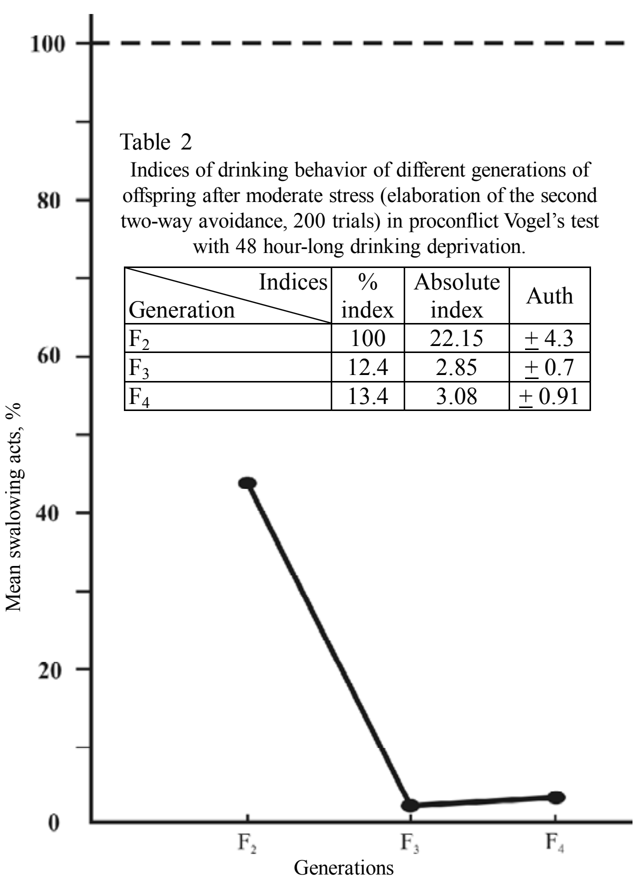

Fig. Dynamics of the proconflict Vogel's-test indices of drinking behavior of the offspring of different generations after moderate stress (elaboration of the second two-way avoidance, 200 trials). (Dotted line) drinking standart behavior.

Decrease of drinking activity in rats after the elaboration of the second CRAA in Vogel's test, as well as sharp change in the initial indices in the OF after the elaboration of the first CRAA presuppose pronounced anxiogenic impact of the learning procedure, which performs the function of "stress event" in the given tests. It should be noted that repeated assessments of behavior both in the OF test and Vogel's test in our experiments were carried out after 10-day episodes of CRAA elaboration, i.e. at the stage of practically well elaborated, automated motor habit. In the norm, in intact rats these stages of learning are not accompanied by pronounced emotional excitation and fear as distinct from early "emotional" or generalized stages [13, 33]. In view of this, emotiogenic effect of a practically accomplished process of learning with already mastered "routine" experimental situation [33, p. 23], at normal initial state of the animal's emotional sphere - should not be so considerable. Different degrees of emotional reaction of the offspring of various generations to one and the same strength of aversive stimulus in Vogel's test also testify to it (Fig. 1, Table 2). Data on animals' testing in the OF also point to this (Table 1): relatively little changing behavior of F1 against the background of dramatic changes in F2-F5 behavior at the same stressor, as well as the quantitative difference of stressor reaction between the four generations themselves. The observed "discrepancy" of the strength of emotional excitation of the animals and real danger of the stressor testifies to intrinsic increased emotional tension of the investigated animals, determining the decrease of the threshold of behavioral response. This appears to be a direct expression of the known principle according to which, the significance of the impact factor – its "extreme nature" - depends on the subjective estimation of the structure of the environment (Kitaev-Smyk, 1983).

Increased anxiety of F2-F5 offspring, manifested in their relatively stable tendency to perceive diverse situations as menacing (of "extreme nature" of the novelty of the situation in the OF, "extreme" threshold of current strength in Vogel's test, "extreme" routine situation of strengthening of the already elaborated CRAA) during the whole prolonged (approximately 3 months) period of learning of signs of their behavior undoubtedly appears to be one of their pronounced phenotypic peculiarities.

It is known that any phenotypic peculiarity of behavior, as well as the HNA phenotype, on the whole, is determined by the complex of main properties of the nervous system of the animal, created under the influence of the genotype and conditions of the environment [17, 19, 34-41]. Among them are: strength of main neural processes - excitatory and inhibitory, their balance, their mobility. The diversity of HNA types (characters, temperaments) is due to a diverse combination of these main properties of the nervous system [34-40]. Diversity of pathological states of the HNA or predispositions to this or that psychopathology arising in situations of a task difficult for the animal's nervous system (particularly, at neurosis – both experimental and clinical - which Pavlov considered first of all as disorders of adaptations of the organism) is determined by disorder ("functional overstrain") of these main processes – of their strength, balance and mobility [34-39].

In the complex of the identified typological peculiarities of the HNA in F2-F5 offspring, such are their initial high general excitability, its low threshold, high emotional tension in the form of anxiety with high locomotion and increased vegetative function, high stress-reactivity and their high excitability. As is of particular importance noted above, a sharp increase of their initial motor activity, more pronounced degree of its changes in post-stress state (high reactivity) as compared to stable F1, and as a result, their incomparably greater scale of the motor component of behavioral stress response to identical strength of influence.

Excitability is one of the fundamental and universal properties of the nervous system, determining the level of the functional state of any of its sections and related physiological mechanisms, identical for phylogenetically different animals [17, 19, 37-41]. Moreover, as shown by L. Krushinski, the level of excitability ultimately determines the manifestation and expression of gene activity, determining separate behavioral acts [37-39].

Continuing the investigations of HNA typologies and its genetic bases by I. Pavlov, , Krushinski – in order to assess the excitability of the nervous system - chose to analyse the state of the general excitability of animals by means of a simple but proving adequate and sufficiently reliable index - level of the motor activity of animals [37-39]. Level of excitability, which in the investigations of Krushinski on the genetic-physiological mechanisms of behavior correlated with the level of motor activity proved to be the modulator of the genetic manifestation of other signs of behavior. The conception of the genetic conditionality of such properties of the nervous system as excitability threshold, rate of neural impulses conduction, strength of the excitability process, its generalization, mobility of nervous processes - constitute one of the fundamental conceptions in modern genetics of the HNA [17, 19, 37-41].

From the view point of the above-said it should be assumed that the peculiarities of behavior of the offspring of stressed rats, observed in our experiments, their anxiety, with high motor activity and high stress-reactivity – represent a phenotypic expression of such a peculiarity of their nervous system as high excitability.

According to the results of the present investigation, for the formation of phenotypically pronounced variability of the sign of emotionality (in the given case of anxiety) in the offspring of stressed animals two generations of their ancestry with stress are sufficient - with induced disorders of adaptation in the form of information neurosis.

The identity of conditions of early postnatal ontogenesis (including the postnatal maternal effect), excluding any influences provoking neurotization in the animals studied in our experiments, at the same time existence of a considerable difference of emotional-behavioral indices in F1 and F2-F5 in their naïve status, as well as the phenomenon of the growth expression of the latter from generation to generation, point to congenital conditionality of the revealed peculiarities of behavior of the offspring of stressed rats. The latter may be primarily connected with the embryonic period of the stressed rat offspring's development – one of the most important and critical stages of ontogenesis, especially vulnerable to different influences, to which V.K. Fedorov paid attention in his genetic investigations [17].

It is known that the genetic program of neuron development and the nervous system on the whole (neurogenesis) is formed as the result of gene expression at an appropriate point of time and corresponding locus of tissue, under the influence of necessary concentration gradients of biologically active substances (hormones, growth factor, etc.) in the environment of the genome. Rigorous orderliness of this process determines not only the ratio of mediatory and hormonal products in each concrete period of development, but on the whole, also the formation of biochemical and morphological peculiarities of the brain (of separate structures and connections between them [20, 42, 43]. Genetic control over the development of the nervous system takes place as a reactive process in the form of continuous interaction of the genome with signals of the environment [16, 19, 41, 42]. At the same time the category of external influences of the genome involves the effects of products of gene expression of the differentiating neuron itself, as well as other neurons developing in parallel (distinguished by the pattern of gene expression) and glial cells of the whole developing organism [19, 42] and of surrounding natural maternal environment [16-19, 41, 42]. At the same time considerable channels of influence on neurogenesis (as well as on embryogenesis, on the whole) proved to be both cytoplasmatic and prenatal components of the maternal environment [16, 18, 19, 41, 42]. As shown above, the prenatal component of the maternal environment is determined by the genotype of the mother and specific influences (including pathogenic) on its organism during pregnancy [16-19] and before it – in the most important proembryonic phase of ontogenesis – in the period of gametogenesis [16]. Cytoplasmatic component or the so-called maternal effect is *per se* determined by paramount quantity of maternal cytoplasm in zygote with cytoplasmatic RNA and mitochondrial DNA pointing to the possible genetic nature of cytoplasmatic influences [16, 18, 19].

Besides, according to modern views, any individual experience of adaptation of the organism constitutes the main channels of influence on the regulation of gene activity in the nervous system not only in embryonic period but at any stages of ontogenesis [19, 41, 43]. It is known that biochemical agents of adaptive processes - corticosteroid hormones and\neuromediators – regulate gene expression in the brain [41, 44]. Changes in genome activity with corresponding reconstructions of cellular metabolism and neoplastic processes via reproduction of cellular structures and syngenesis induced by stress hormones in parent organism can be transmitted and fixed in the generations [19, 41, 43, 45].

Conclusions

1. Uncontrolled chronic psychogenic stress of rat-parents, repeating in the line of genetically linked generations, resulted in phenotypically pronounced anxiety of their offspring with high motor activity and stress-reactivity.

2. For phenotypically pronounced anxiety of the offspring to form two generations of ancestry with stress-induced disorders of adaptation in the shape of information neurosis are sufficient.

3. Manifestation of anxiety in stressed-rat offspring grows progressively from generation to generation.

4. The revealed peculiarities of behavior of stressed-rat offspring appear to be phenotypic expression of such a peculiarity of the nervous activity as high excitability.

5. Offspring of rats with information neurosis may be considered as an experimental model of congenital predisposition to anxiety.

ადამიანისა და ცხოველთა ფიზიოლოგია

მაღალი შფოთვა როგორც ქრონიკული არაკონტროლირებადი ფსიქოგენური სტრესის მქონე ვირთაგვების ნაშიერების ტიპოლოგიური თავისებურება

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ნაშრომში შესწავლილია 8 წყვილი ვირთაგვა-მშობლის 5 თანმიმდევრული თაობა (საერთო რაოდენობით 370), რომლებიც შეჯვარებული იყვნენ გამოხატული შფოთვის (ინფორმაციული ნევროზი) ქრონიკული ფსიქოგენური სტრესის მდგომარეობაში. ყველა თაობის ნაშიერებში მათ ახლო-ნათესაურ შეჯვარებამდე ავტორები აყალიბებდნენ ინფორმაციულ ნევროზს, რომელიც მსგავსია ყველა ხაზის წინაპართა თაობების

საწყის მდგომარეობასთან. ღია ველის და ვოგელის პროკონფლიქტური სიტუაციის მეთოდებით შესწავლილ იქნა F1-F2 ზრდასრული ნაშიერების ემოციურ-ქცევითი აქტიურობის თავისებურებები როგორც საწყის, ე.ი. რაიმე სახის სპეციალურ ექსპერიმენტულ ზემოქმედებამდე, ისე ტესტური ზომიერი სტრესის შემდეგ (აქტიური განრიდების პირობითი რეფლექსის გამომუშავება).

დადგენილია, რომ ვირთაგვა-მშობლების არაკონტროლირებადი ფსიქოგენური სტრესი გენეტიკურად დაკავშირებული თაობების რიგში გამოიხატება მათი შთამომავლობის აგზნებადობის ამაღლებაში, ემოციური დაძაბვის საწყის მაღალ დონეში, მაღალი მოტორული აქტიურობის შფოთვასა და დეფეკაციაში, მაღალ სტრეს-რეაქტიულობაში, რომელიც არაადეკვატურია ზემოქმედების ძალის მიმართ. ფენოტიპურად გამოხატული შფოთვის ჩამოსაყალიბებლად საკმარისია წინაპართა ორი თაობა, რომელთაც ჰქონდათ სტრესი, გამოწვეული ადაპტაციის დარღვევით ინფორმაციული ნევროზის სახით. შფოთვის გამოვლინებები პროგრესულად იზრდება თაობიდან თაობაში. ინფორმაციული ნევროზის მქონე ვირთაგვა-მშობლების შთამომავლები აღებულია შფოთვისადმი თანდაყოლილი წინასწარგანწყობის ექსპერიმენტულ მოდელად.

სტრესირებული ვირთაგვების შთამომავლების შფოთვა განიხილება მათი ქცევის ნიშნების მთელი კომპლექსის და მათი ნერვული სისტემის გამოვლენილი თავისებურებების კონტექსტში. ნაჩვენებია მშობლების ქცევის ინფორმაციული პათოლოგიის გავლენის გზები მათი შთამომავლების უმაღლესი ნერვული მოქმედების თანდაყოლილ თავისებურებებსა და ნერვულ სისტემაზე.

REFERENCES

1. International Classification of Diseases. Ten Revision (ICD-X) (1994), World Health Organization, Geneva.
2. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) (2000), American Psychiatric Association, Washington.
3. *G. Masi, M. Mucci, L. Favilla, et al.* (1999), Compr. Psychiatr., **40:** 210-215.
4. *W. Maier, M. Gaeniscke, H. Freyberger et al.* (2000), Acta Psychiatr. Scand. **101**: 29-36.
5. *R.C. Kessler* (2000), Psychiatr. Scand., (Suppt), **406**: 7-13.
6. *R. Kessler, M. Berglund, O. Demler et al.* (2005), Arch. Gen. Psychiatr., **62**: 593-602.
7. *J. Kay, A. Tasman* (2006), Essentials of Psychiatry, J. Wiley & Sons. Ltd., 1076.
8. *О.В. Кербиков, И.И. Озерецкий, Е.А. Попов, А.В. Снежневский* (1958), Учебник психиатрии, Москва, 367 с.
9. *С.Н. Давиденков* (1963), Неврозы, Ленинград, 271 с.
10. *А.В. Снежневский, Р.А. Наджаров, А.Б. Смулевич и др.* (1985), Справочник по психиатрии (под ред. А.В. Снежневского), Москва, 413 с.
11. *C. Spielberger, R. Gorsuch, R. Lushene* (1970), Manual for state-trait anxiety inventory. Cal.: Palo Alto.
12. *R.G. Lister* (1990), Pharmacol. Ther., **46**: 321-340.
13. *П.В. Симонов* (1987), В кн.: Физиология поведения. Нейробиологические закономерности, Ленинград, с. 486-523.
14. *K. Kendler, V. Neale, R. Kessler et al.* (1992), Arch. Gen. Psychiatr., **49**: 267-272.
15. *I. Skre, S. Torgensen, S. Lygren et al.* (1993), Acta Psychiatr., Scand., **88**: 85-92.
16. *П.Г. Светлов* (1965), В кн.: Проблемы медицинской генетики, Ленинград, с. 106-136.
17. *В.К. Федоров* (1971), Генетика высшей нервной деятельности. В кн.: Физиология высшей нервной деятельности, ч. II, Москва, с. 164-179.
18. *M. Carlier, M. Nosten-Bertrand, C. Michard-Venhee* (1992), In: Techniques for the genetic Analysis of Brain and Behavior: Focus on the Mouse. Techniques in the Behavioral and Neural Sciences" (Eds. Goldowitz D., Walsten D., Wimer R.) v. **8:**111-126, Amsterdam.
19. *З.А. Зорина, Н.Н. Полетаева, Ж.И. Резникова* (2002), Основы этологии и генетики поведения. Москва, 383 с.
20. *D.J. Smith, G.F. Joffe, G.F.D. Heseltine* (1975), Physiol. Behav., **15**: 461-469.
21. *M. Vallee, W. Mayo, F. Dellu et al.* (1997), J. Neurosci., **17**, 7: 2626-2636.
22. *Т. Авалиани, Р. Огурцов, В. Пузырева, О. Серьякова* (2000), Росс. Физиолог. Журн. им. И.М. Сеченова, **86** (12): 1565-1572.
23. *T. Fujioka, A. Fujioka, N. Tan, et al.* (2001), Neuroscience, **103**, 2: 301-307.
24. *F. Kalandarishvili, Ts. Orjonikidze, I. Pantsulaia, T. Mtskeradze, Z. Khanaeva* (2008), Bull. Georg. Natl. Acad. Sci., **2,** 3: 121-128.
25. *М.М. Хананашвили, Т.Р. Домианидзе* (1989), Авторский сертификат, №150674A1.
26. *P.L. Broadhurst, G. Bignami* (1965), Behav. Res. Ther., **2**: 273-280.
27. *A. Whimbey, V. Denenberg* (1967), J. Comp. Physiol. Psychol., **63**: 500-504.

28. *P.L. Broadhurst, H.L. Eysenck* (1964), Emotionality in the rat: a problem of response specificity. Univ. of London Press, p. 205.
29. *G. Bignami, D. Bovet* (1965), C.r. Acad. Sci., **260**:1239-1244.
30. *J.R. Royce* (1966), In: Handbook of multivariate experimental psychology (Ed. Gattel R.), Chicago, Rand McNallo, 670-680.
31. *C.S. Hall* (1934), J. Comp. Psychol., **18**: 385-403.
32. *П.Л. Бродхёрст* (1975), В кн.: Актуальные проблемы генетики, Ленинград, с. 39-58.
33. *Р.И. Кругликов* (1981), Нейрохимические механизмы обучения и памяти, Москва, 211 с.
34. *И.П. Павлов* (1923), Двадцатилетний опыт изучения высшей нервной деятельности (поведения) животных. Полное собр. соч., 1951, М.- Л., т. 3: 438.
35. *И.П. Павлов* (1926), Лекции о работе больших полушарий головного мозга. Полное собр. соч., т. 4: 451.
36. *А.Г. Иванов-Смоленский* (1952), Очерки патофизиологии высшей нервной деятельности. Москва, 296 с.
37. *Л.В. Крушинский* (1946), Изв. АН СССР, **1**: 69-81.
38. *Л.В. Крушинский* (1960), Формирование поведения животных в норме и патологии. Москва, 264 с.
39. *Л.В. Крушинский* (1979), Физиология человека, **5**(3): 500-509.
40. *В.К. Красуский* (1971), В кн.: Физиология высшей нервной деятельности, ч. II, Москва, с.180-194.
41. *Н.Г. Лопатина, В.В. Пономаренко* (1987), В кн.: Физиология поведения. Нейробиологические закономерности. Ленинград, с. 9-59.
42. *Р. Рэфф, Т. Кофмен* (1988), Эмбрионы, гены, эволюция. Москва.
43. *М.Е. Лобашев* (1961), В кн.: Исследования по генетике. Сб. 1, Ленинград, с.3-21.
44. *П.П. Голиков* (1988), Рецепторные механизмы глюкокортикоидного эффекта, Москва, 288 с.
45. *Л.Е. Панин* (1983), Биохимические механизмы стресса, Новосибирск, 233 с.

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