ᲡᲐᲥᲐᲠᲗᲕᲔᲚᲝᲡ ᲛᲔᲪᲜᲘᲔᲠᲔᲑᲐᲗᲐ ᲔᲠᲝᲕᲜᲣᲚᲘ ᲐᲙᲐᲓᲔᲛᲘᲘᲡ ᲛᲝᲐᲛᲑᲔ, ტ. 3, №3, 2009
BULLETIN OF THE GEORGIAN NATIONAL ACADEMY OF SCIENCES, vol. 3, no. 3, 2009

Human and Animal Physiology

The Learning Ability According to the Rapidity of Elaboration of Conditioned Reflex Active Avoidance of Five Consecutive Generations' Offspring of Rat-Parents Crossbred in the State of Stable Information Pathology of the Higher Nervous Activity (Information Neurosis)

Felix Kalandarishvili*, Zaretta Khanaeva*, Tsiala Orjonikidze*, Ia Pantsulaia*, Mikhael Khananashvili**

** I. Beritashvili Institute of Physiology,Tbilisi*
*** Academy Member, I. Beritashvili Institute of Physiology, Tbilisi*

ABSTRACT. The indices of the elaboration of conditioned reflex of active avoidance in shuttle-box were studied in 5 consecutive generations of adult offspring (total quantity F1-F5 – 370) of initial eight pairs of white outbred rat-parents crossbred in the state of stable information pathology of the higher nervous activity (information neurosis). The information neurosis identical to that of initial parent rats was formed in offspring of all the generations before the sibling cross breeding. The estimation of good, average and poor learning ability was based on the indices of the rate of occurrence of the first conditioned response, as well as the sums of those during the first 5 days and the attainment of the learning criterion (80% of correct responses per day) during 10 days of learning. The connection of learning level with the indices of their behavior in the open field and in proconflict situation (modified Vogel test) was traced. Worsening of learning was revealed in the first two generations of offspring as compared to initial ancestral animals, which was most pronounced in the F2 - the generation with dominant poor learning (the ratio of poor- and good learning animals was 1.9:0.8). Beginning with the offspring of the third generation the process of change in the structure of the populations by learning was observed as an initial prevalence of the quantity of average-good learning rats in F3, equalization of the percent of good, average and poor learned rats in F4 and a sharp prevalence of the percent of good learned ones in F5. The fifth generation of the offspring with dominant good learning has two contrast subpopulations according to the quantity: good- and poor learned animals, in which the quantity of the former prevails by 5 times over those of the latter (the ratio 2:0.4). The offspring of the fifth generation also have the best indices of conditioned reflex at both stages of its formation. According to the data of testing in the OF and proconflict situation the unfavorable form of information psychogenic stress of rat-parents leads to stable changes in the emotional sphere of their offspring - to initially increased level of emotional tension, anxiety with high levels of excretory function and motor activity, high excitability followed by decrease of the threshold of the reaction to environmental influences and unequal to the strength of the latter with high stress response. Good learning is positively correlated with definite levels of increased emotional tension, anxiety; however, very high degrees of the latter - a pronounced fear with a high level of vegetative (excretory) tension - impedes the manifestation of the ability to accomplish the reflex of active avoidance. *© 2009 Bull. Georg. Natl. Acad. Sci.*

***Key words**: psychogenic stress, offspring, learning, emotional motor activity, stress-reactivity*

Introduction

A large quantity of experimental data based on different methods of genetic analysis on various types and species of animals showed that the peculiarities of conditioned reflex activity or the ability to form temporary connections, are hereditarily determined [1, 2]. Genetics of conditioned reflex - is primarily the genetics of the peculiarities of the nervous system, features of its main processes, which determine the character of the functioning of the CNS and its higher divisions processing the information and programming behavioral acts in response to the signals of the environment [1, 3]. The complex problem of the genetics of conditioned reflex, as well as of the HNA, involves the following questions: how the various forms of its variability, reversible and irreversible reconstructions of its hereditary basis in the individual and historical development of the organisms emerge and are realized; what their reasons and essence are .

Stress appears to be one of the most important factors of the increase of hereditary variability of the signs of the organism [1, 3-6]. The biological universality of stress phenomena and the important role of the mechanisms subjected to it in the formation of the resistance of the organism to the influence of the environment as well as in the origin of various pathological states [7-18], on the one hand, and well-known influence of stress-induced adaptive processes on the hereditary apparatus, on the other [1-3, 19], determine the enduring topicality of genetic investigations of the consequences of various forms (favorable and unfavorable) of parent stress on their offspring.

In our previous publications [20, 21] some results of multi-year investigations were presented, setting the task of genetic control of the influence of stable information pathology of the higher nervous activity (information neurosis) of rat-parents induced by stress on the behavior of their offspring in the line of consecutive generations. In adult offspring of the stressed rats the oriented-exploratory activity, emotionality, stress-reactivity as well as the ability to form defensive conditioned reflex of active avoidance according to the rate have been studied. The connection between the variability of behavior indices and the variability of the ability to form conditioned reflexes was also observed. To accomplish our task 5 consecutive generations of initial 8 pairs of offspring of ancestral rats crossbred in the state of information neurosis were grown.

Information neurosis - an experimental model of widespread information pathology of the higher nervous activity of people in conditions of their every-day life [16-18] was formed in animals according to the method of chronic uncontrolled psychogenic stress by M. Khananashvili and T. Domianidze [22] or of the so-called biologically negative “information stress” [17].

The results of the investigation of emotional-motor behavior in different test situations and at different stages of the experimentation in 5 generation offspring of stressed-rats were described by us earlier in detail [20, 21]. The data on the learning of these animals and the ratio between their indices and the indices of emotional-motor behavior 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 generation offspring (F1) - direct posterity of initial, 8 pairs of ancestral rats crossbred in the state of a strong chronic uncontrolled psychogenic stress with the following sibling cross-breeding four consecutive generations (F2-F5) were obtained with an overall number of 370 F1-F5 offspring. The offspring of all the generations were on maternal rearing and beginning with the 21^{st} day they were kept in blocks (3-5 offspring) in conditions strictly identical for all the generations maintaining a permanent cycle of day and night and giving them water and food *ad libitum*.

After the end of the stage of the investigation of behavioral signs and learning in the offspring of every generation, before their crossing, information neurosis was formed identical to that in the initial 8 pairs of ancestral rats. By means of this, a model of repeated stress in the continuous line of the generations was created.

Modeling of information neurosis. The method of chronic uncontrolled psychogenic stress proposed by M. Knananashvili and T. Domianidze [22], is based on the complication of information loading on the brain of the animal by means of “integration” of two independent conditioned reflexes of active avoidance (CRAA), preliminarily and consecutively elaborated (at different sound conditioned signals) in the modified shuttle-box (with three equal compartments). The “integration” of two CRAAs consists in the presentation of both conditioned signals with 30 sec intervals at random according to the scheme by Gellerman (1936) in one experiment. In such a situation the task of correct response appears to be difficult for the animal. During 20-25 sessions of such a psychogenic stress (deficiency of pragmatic information) a pronounced stable pathologic state of HNA with a high level of emotional tension developed in the animal.

The design of the apparatus, the procedures of consecutive elaboration of two CRAAs and their integration, as well as the procedure of testing of animal behavior in the open field (OF) and in "proconflict situation" (conflict test by Vogel, 1971, modified by Korda et al., 1986) are described in detail in our previous publications [20, 21].

The 10-day episode of the elaboration of the first CRAA (to 10 sec. exposure of conditioned sound signal - tone, 500 Hz and with addition of unconditioned painful electrocutaneous stimulation in the absence of avoidance reaction; 20 presentations with one-minute interval on every experimental day) was used, besides the goal of the "integration" at the formation of the neurosis: 1) to assess the ability of the animal to learning according to the rate of its formation and 2) as "average stress stimulation" for the determination of stress-reactivity.

Estimation of the learning ability was accomplished on the basis of the criteria elaborated by us according to which the animals giving 10 correct responses (i.e. of conditioned reactions or avoidances) one after another in one of the 5 experiments, while on the following days the animals displaying 80% and more of correct responses were estimated as good learning ones. The animals showing 10 correct responses one after another only after the 5^{th} experiment while in the following experiments they did not show more than 70% of correct responses were estimated as averagely learned animals. The animals giving no more than 50% of correct responses in all the 10 experiments were considered to be poorly learned animals. The number of combinations of conditioned and unconditioned stimulations which are necessary to evoke the first correct response, the sum of correct responses during the first 5 days of the experiment and achievement of the learning criterion (80% of correct responses) during 10 experiments were estimated.

The results were processed on average values and statistically estimated according to Student-test.

The scheme of experimentation. The study of learning ability and peculiarities of the behavior of the offspring of each of 5 generations began after attainment of puberty and was carried out according to a common scheme for all in the following sequence: 1. The assessment of initial, naïve status of the offspring, i.e. up to any special experimental impact - according to the level of exploratory activity and excretory function in the OF (and in addition according to the level of anxiety in Vogel's test); 2. The assessment of the ability to learn: 10 days of the first CRAA elaboration; 3. The determination of stress-reactivity of animals according to the indices of their exploratory activity and excretory function during the repeated testing in the OF after average stress (10 days of elaboration of CRAA, 200 presentations); 4. The elaboration of the second CRAA (with additional estimation of emotionality in the OF after it and according to Vogel's test); 5. The formation of information neurosis according to the above-described method; 6) Sibling cross-breeding. The cross breeding of offspring of each generation was carried out according to the signs of good, average and poor learning ability in all the possible combinations: $G_{♀}$ x $G_{♂}$; $G_{♀}$ x $A_{♂}$; $G_{♀}$ x $P_{♂}$; $A_{♀}$ x $G_{♂}$; $A_{♀}$ x $A_{♂}$; $A_{♀}$ x $P_{♂}$; $P_{♀}$ x $G_{♂}$; $P_{♀}$ x $A_{♂}$; $P_{♀}$ x $P_{♂}$ (G - good, A - average, P - poor learned female and male rats). The complete scheme of crossing was realized beginning from the F1.

The number of the animals in various generations subjected to the investigation was different, which was connected with the decrease of the ability to reproduce the offspring of stressed rats beginning with third generation to the subsequent one and poor survival of their offspring in the absence of evident signs of any somatic pathology. The cases became more frequent when the rats gave no offspring at all, or was not numerous if they did (2-3 individuals instead of the usual 8-12). At the same time the survival of newborn infant rats decreased, for example out of all the female rats only one rat had offspring - 2 infant rats (F6) who died on the second day. As a result in the F1 generation 82 offspring were retained out of 96 born, in F2 generation - 212 (out of 272 born), in F3 generation - 36 (out of 90), in F4 - 21 (out of 57) and in F5 - 19 (out of 39 born).

The results and discussion

Learning ability. The results of the estimation of the animals of each from F1-F5 generations according to the accepted criteria of good, average and poor learning ability are summarized in Fig. 1 and Table 1.

Among the offspring of F1 generation (n=82) good learning ability was observed in 23.07%, average - in 49.23%, poor - in 27.69% out of the whole population, which makes the ratio 1:2:1. Among the animals of F2 generation (n=212) good learning ability was seen in 20.25%, average - in 32.91%, poor - in 46.83% out of the whole population with the ratio 1:1.6:2.3. Among the animals of F3 generation (n=36) a good learning ability was revealed in 31.42%, average - in 40%, poor - in 28.57% out of the whole population with the ratio 1.3:1.6:1.1. Among the animals of F4 generation (n=21) the indices of good, average and poor learning ability were equal, the ratio - 1:1:1. Among the animals of F5 generation good learning ability was observed in 52.63%,

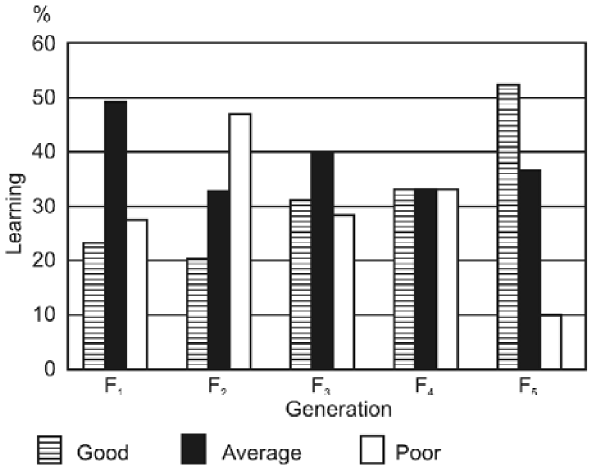

Fig. 1. Dynamics of the ratio of good, average and poor learning animals according to the rate of conditioned reflex active avoidance acquisition in the shuttle-box (10 days of training, 200 presentations) in different generation offspring.

Table 1.

Indices of good, average and poor learning of conditioned reflex active avoidance in the shuttle-box (10 days of training, 200 presentations) in different generation offspring (F 1 – F 5) and in initial ancestral group rats (Panc).

Generation; Group	Learning			
	good	average	poor	ratio
$P_{anc.}$	37.5	43.75	18.75	1.1:1.3:0.6
F1	23.07	49.23	27.69	1:2:1
F2	20.25	32.91	46.83	1:1.6:2.3
F3	31.42	40.00	28.57	1.3:1.6:1.1
F4	33.33	33.33	33.33	1:1:1
F5	52.63	36.84	10.52	2:1.5:0.4

average - in 36.84% and poor - in 12.52% out of the whole population, the ratio - 2:1.5:0.4.

In the initial ancestral group for all the G1-G5 rats (n=16, Table 1, $P_{anc.}$) where the animals were united by the randomization method, a good learning ability was revealed in 37.5% of the rats of the whole group, average - in 43.75%, poor - in 18.75%, the ratio being 1.1:1.3:0.6 (the indices are given in before stress state). Thus, the ancestral group is characterized by a distinct domination of average-good learning ability (with insignificant difference in the percent of the rats with average- and good learning ability, the ratio - 1.3:1) over the poor one. At the same time the percent of good learning animals exceeds approximately 2 times the percent of poor learning ability (ratio 1.1:0.6).

In the animals of F1 generation - the direct offspring of the initial group of ancestral rats a clear change of the population composition was observed according to the ratio of good, average and poor learning ability toward its worsening as compared to that in the parents. Average-poor learning prevails at the expense of a sharp decrease of the number of good learning animals with parallel considerable increase of the number of poor and partly of average learning ones. The animals of F2 generation - the direct F1 offspring - reveal a larger degree of worsening of learning: the quantity of the animals having a poor learning sharply increases at the expense of the decrease of the animals with good, as well as with average learning. It is possible to speak of the existence of two sufficiently contrasting subpopulations in terms of learning - animals with poor and good learning (Fig. 2), the number of animals of poor learning prevails twice that of with good learning (ratio 2.3:1). In terms of poor learning the second generation exceeds all other generations of offspring as well as the initial ancestral group of the rats.

However, beginning with the animals of F3 - direct offspring of F2 ones with dominant poor learning - a clear-cut pronounced process of reconstruction of the population composition is revealed in terms of learning: as initial predominance of average-good learning of F3 with the subsequent equalization of good, average and poor learning in F4 and finally, with a sharp domination of good learning in F5. The prevalence of average-good learning in F3 is observed at the expense of a considerable increase of good learning in parallel with no less pronounced decrease of poor learning (which, however, still considerably exceeds that of P_{anc}) and fairly noticeable increase of average learning.

Generation F5 suffers the most radical - as compared to both other generations of offspring and of the initial ancestral group - reconstruction of population composition in terms of learning. The percent of the animals with good learning sharply increases, while the percent of poor learners drops even greater. The percent of offspring of good learning is the highest in F5, while of poor learning is the least not only among all the F1-F5 generations of offspring but also as compared to the initial ancestral group. It is possible to speak of the formation of two pronounced contrast subpopulations in F5 according to learning: animals with good and poor learning (Fig. 2), where the number of the former 5 times exceeds that of the latter - the ratio being 2:0.4 (Table 1); pronounced domination of good learning is evident.

Thus, the dynamics of the changes in the composition of the populations in terms of learning ability in a continuous line of 5 generations offspring of rat-parents with information neurosis crossbred according to different levels of learning in all possible combinations has

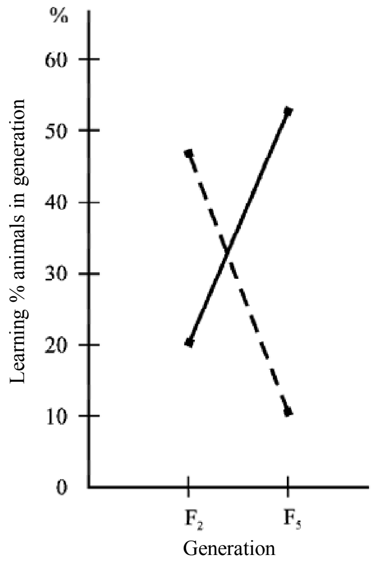

Fig. 2. Contrasting according to the ability of the conditioned reflex active avoidance acquisition in the shuttle-box (10 days of training, 200 presentations), the second and fifth generations.

shown that the first stage of this process (the first two generations) appears to be the worsening of this ability with the dominance of poor learning of F2; at the subsequent stage - (F3-F5) the ability of good learning improves, in F5 good learning becomes dominant. Besides, in F5 a reliable improvement of learning ability is observed as compared to initial animals ancestral to all the lines of the generations.

Proceeding from the presence of different stages of the formation of conditioned reflex - stages of generalization (simple and complicated summation reflexes according to Rusinov [23]) and specialization connected with various genetically determined neurophysiologic mechanisms [24] the peculiarities of the formation of CRAA were studied in the offspring of comparatively different generations according to the following 3 indices: 1) the number of combinations of conditioned and unconditioned stimulations necessary for inducing the first correct response; 2) the sum of correct responses during the first 5 days of elaboration of conditioned reflex; 3) the number of animals having attained the criteria of learning during 10 days of the elaboration of the reflex (Fig. 3, A-B; Table 2).

The maximal number of combinations (37.95) is observed in the animals of F2 generation, which corresponds to the end of the second day of learning, while the minimal number of combinations - in F5 generation which corresponds to the end of the first, beginning of the second day of learning. In other words, the rapidity of the first correct response, i.e. of conditioned reflex temporary connection in the animals of F5 exceeds approximately 2 times that of F2 (ratio 1.8:1). The ratio of the index in all the lines of F1-F5 from F1 to F5 makes 1.5:1.8:1.1:1.3:1.1, correspondingly (Fig. 3 A, Table 2). The least sum of correct responses (15.6), i.e. the greatest deficiency of avoidances was revealed in the animals of F2 in the first five days of training; the larger sum (39.2) - a maximal number of avoidances - in F5 with the ratio 1:2.1. In other words, in the first 5 days the animals of F5 are by half ahead of F2 in the ability of formation of CRAA. The dynamics of this index as a whole reveals a decrease of the reflex formation rate of F2 as compared to F1 as well as the subsequent improvement from F3 to F5 generations (Fig. 3, B; Table 2).

The number of the animals having attained the criterion of learning over 10 days of reflex elaboration (Fig. 3, C; Table 2) is considerably low in F2 generation as compared to F1 (ratio is 1.6:1); an improvement of this index is observed from the third to the fifth generation not only in comparison with F2, but also with F1 (the ratio 1.65:1:1.82:1.7:2.5 - F1-F5, respectively). At this stage of the completion of the specialization of con-

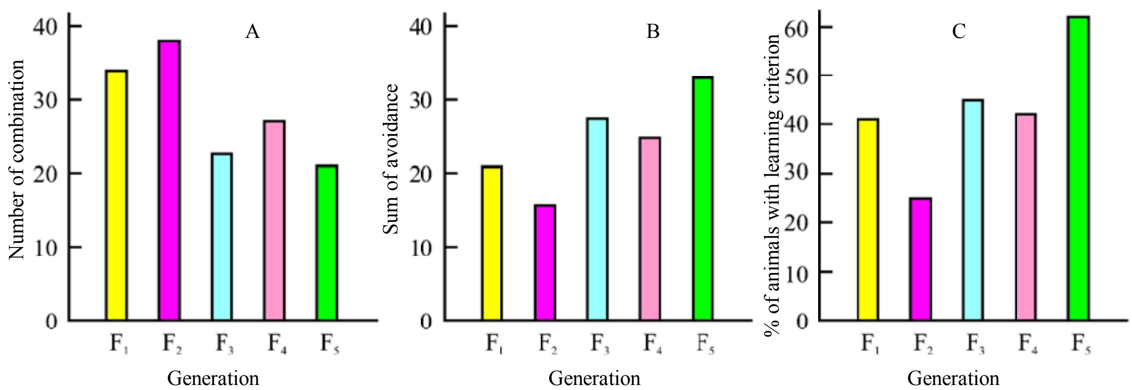

Fig. 3 A-C. Dynamics of formation of temporary connection at different stages of conditioned reflex active avoidance elaboration in the shuttle-box in different generation offspring.

A – The number of combinations of conditioned and unconditioned stimulations necessary for inducing the first avoidance response. B – Sum of avoidance reactions during the first five days of training. C – Percent of animals with attainment of the learning criterion over 10 days of training.

Table 2.

(to Fig. 3) Indices of formation of the conditioned temporary connection during 10 day active avoidance elaboration in various generation offspring (the same designations as in Fig. 3 A-C).

Generation / Index	F1	F2	F3	F4	F5	Ratio
A (number of combinations)	33.39	37.95	22.58	27.0	29.95	1.5:1.8:1.1:1.28:1.0
B (number of avoidance)	20.85	15.6	27.35	24.8	39.2	1.33:1.0:1.7:1.6:2.1
C (%of animals with learning criterion)	41.0	24.7	45.0	42.0	61.9	1.65:1:1.82:1.7:2.5

ditioned reflex connection the difference between F2 and F5 generations is more intensified (the ratio - 1:2.5) as compared to that at earlier stages of the elaboration (1:1.8 according to the rate of the first correct response appearance).

Thus, the difference in the character of the formation of conditioned reflex temporary connection in various generations of the offspring, manifested already at the very early steps of the stage of conditioned reflex generalization (Fig. 3, A; Table 2), is maintained (Fig. 3, B; Table 2) and intensified (Fig. 3, C; Table 2) in the course of the stage of specialization. The data of genetic researches suggest that the variations related to the genotype during the learning are revealed most at its initial steps [2, 24]. According to the results of the first two (as well as the first five) days of CRAA elaboration, the offspring of F1-F2 show considerable deficiency of avoidances - most pronounced in F2 as compared to F3-F5. This presupposes genetic conditioning of different levels of learning in different generations. F5 offspring have the best indices of CRAA formation at all its stages.

The rate of elaboration of active avoidance reflects the ability of the animals to activation of their behavior in response to escapable painful exposure. The deficiency of avoidances during CRAA formation revealed by F2 offspring with dominant poor learning points to their predominantly passive type of reaction to aversive impact; the best indices of avoidance behavior elaboration rate in F5 offspring with dominant good learning point to the prevalence of an active strategy of adaptation in them. Thus, in the line of F5 generation offspring a replacement of the strategy of their adaptive behavior to avoidance of aversive impact was observed: passive avoidance in F1 to active - in F5.

The genotypic changeability of the ability of forming conditioned reflexes is mainly due to the action of a great number of genes [1]. The dependence of the success of the formation of temporal conditioned reflex connection on such factors as the excitation level and summation ability of the nervous centers, the degree of general activation of the brain, functional state of the CNS, which in its turn are determined by tonic mechanism and related levels of motivational-emotional state are well documented in fundamental neurophysiological studies.

Emotional behavior. The results of study of the peculiarities of 5 generations of rats' offspring behavior with information pathology of the HNA in the OF (and additionally by Vogel test) in their initial status, as well as after test average stress impact (10-day procedure of learning of CRAA, 200 presentations) which are described in detail and illustrated earlier by us [20, 21] are summarized in table 3. The following are the main peculiarities revealed:

1. Essential distinctions of the first generation offspring according to the indices of their emotional-behavioral activity from all the other consecutive generations: they have the least indices of motor activity and excretory functions as compared to F2-F5, while the changes in their post-stress state are incomparably smaller than those of F2-F5. Their emotional reactivity (in terms of defecation) is manifested with significant increase of percent of animals' defecating in the OF after the stress, though the index of highly intensive defecation (5 and more boluses) is the least as compared to F2-F4. The post-stress change of locomotion consists in the weak tendency to an increase - by 4% from the initial, while the difference between the initial activity and that suffering decrease of post-stress activity totals 51.4% in F2, 59.7% - in F3, 83.9% - in F4 and 48.9% - in F5. The first generation of offspring was found to be the most stable, stress- resistant as compared to the consecutive generations.

2. The similarity of the offspring of all the subsequent F2-F5 according to both the type of their behavior in the OF in initial status and its change after average stress. A reliably increased level of emotional tension, anxiety coupled with a high defecation level and high

Table 3.

Indices of emotional-behavioral activity in open field in different generation offspring. A – Initial naïve status before beginning experiments. B – After test moderate stress (elaboration of the first conditioned active avoidance, 10 days, 200 presentations). I. Index of overall exploratory activity. II. Percent of the offspring of each generation having defecation. III. Percent of the offspring of each generation having 1-4 boluses in defecation. IV. Percent of the offspring of each generation having 5 and more boluses in defecation.

Activity \ Generation		F1	F2	F3	F4	F5
I	A	21.0	32.0	31.0	43.5	32.0
	B	22.0	15.5	12.5	7.0	17.0
II	A	14.3	37.0	72.0	43.0	50.0
	B	32.0	52.0	55.0	76.0	51.0
III	A	0	30.76	28.57	28.6	55.0
	B	40.0	46.15	16.7	17.2	49.0
IV	A	6.6	7.7	42.5	28.9	0
	B	0	30.76	50.0	48.5	1.0

motor activity, as compared to F1 is characteristic of their initial behavior. After the moderate stress a further increase of emotional tension, an expressed fear reaction coupled with a high defecation level (exceeding that of the initial) and pronounced suppression of locomotion are observed. The drastically increased initial motor activity of F2-F5 offspring as compared to stable F1, as well as more pronounced degree of its changes (i.e. reactivity) in the post-stress state and as a result - incommensurably larger than in F1 - scales of the motor component of behavioral response to stress impact of the same strength appear per se to be doubtless indices of the high level of excitability of the animals, of its low threshold and accordingly of the decrease of behavioral reaction threshold and of high stress-reactivity.

3. The phenomenon of progressive growth expression of the above-said peculiarities of the behavior from F2 to the subsequenr generations both in terms of the indices of initial and post-stress state with the maximum of their values in F4. Thus, the initial motor activity of F2-F3 exceeds that in F1 by 52% and 47%, respectively; the activity of F4 - the peak of growth - exceeds that in F3 by 39% and the activity of F1 by 107%. The activity of F5, although lower than that in F4, exceeds the index of F1 by 52%. After a moderate stress the motor activity of F2 in the OF drops lower than that in F1 by 29.5%, the activity of F3 is lower than the corresponding index of F2 by 13.6%, the activity in F4 is lower than that in F3 by 25% and lower in F1 by 68.1% - the peak of decrease. In the offspring of F5 an appreciable decrease of emotional tension level is observed in terms of all the indices as compared to F4 and F3, but at the same time it reliably exceeds that of F1 in their majority and is compared to F2 to a certain extent.

According to the results obtained in the F2-F5 offspring of stressed rats the increased motor activity along with increased defecation appears to be an index of increased emotionality in the initial status (reverse positive correlation of two parameters of OF). According to the data of more detailed researches with the control of the process of individual development [25-28] positive correlation of the defecation and locomotion indices in the OF in rats reflect their increased emotionality (combination of anxiety, fear and attempts to escape or an increase of exploratory behavior) and is noted in definite experimental conditions, primarily in animals preliminarily subjected to stress (including the perinatal period) [25-27] or in the offspring of female rats with experimental blockade of the hypophyseal-adrenal system [28]. Signs of post-stress state, described in the above mentioned studies, are found in the offspring of F2-F5 rats with information pathology of the HNA in their pre-stress, initial status before any special experimental exposures. At the same time, it is important that the degree of the expression of these signs increases from generation to generation. The difference between the generation offspring in our experiments consists in the difference of the number of previous generations of ancestors, crossbred in the state of information neurosis. This fact, as well as the identity of the conditions of early postnatal ontogenesis (including the “maternal medium” in the period of nursing), excepting any provocative neurotization of the influence on the offspring before the beginning of the experiments, at the same time the presence of significant difference in the level of emotionality both between F1, F2-F5 and, which is no less important, between F2-F5 themselves presuppose congenital conditioning of increased emotionality, anxiety of F2-F5, related to biologically negative information stress of the parents. The same conclusion was drawn on the basis of the experiments with drinking behavior of the offspring in “proconflict” situation of Vogel, revealing immanent anxiety of the offspring of F2-F5 in initial status and its increase after test stress exposure [21].

Initially increased anxiety, excitability with the decrease of reaction threshold to the impact of the environment determine the observed "discrepancy" of the value of response changes in emotional-motor activity to the real strength of the "stressor" which evokes them. This is indicated by the relatively hardly-changing behavior of stress stable F1 against the background of its incomparably considerable changes in F2-F5 and the difference between the latter in conditions of "novelty" in the OF at testing in naïve status, as well as pronounced quantitative difference in post-stress changes of behaviour between F1-F5 at the same strength of test stressor (10 days of elaboration of CRAA) during repeated testing in the OF, as well as pronounced avoidance reaction of F2-F5 of near-subthreshold strength of current - indifferent for intact animals in the proconflict test by Vogel [21]. Essentially adaptive responses of F2-F5 in all cases have the character of redundance and excessiveness. Such hypercompensatory reaction - according to the principle of A.A. Ukhtomski - is biologically expedient in the situation of pragmatic uncertainty [29]. However, it is ensured by surplus expenditure of energy resources of the organism, and on the whole by excess mobilization of adaptive mechanisms [10, 11]. The prolonged character of hyperadaptive reaction (strong and long acting stressors) may lead to stable disturbances of adaptive homeostasis and its diseases, to a decrease of the adaptive potential of the organism, to a lowering of viability and depression of the reproduction function. Hyperadaptosis as a disease of adaptation, is characteristic not only of ageing but, as emphasized by V.M. Dilman [10, 11] also of stress as well. As was noted above (materials and methods), the significant decrease of viability and depression of the reproductive sphere were observed precisely in the animals investigated by us, beginning with the third generation. The decrease of survival and depression of the reproductive function, induced by stress, are described for animals [30]. Disturbances of the reproduction function as a result of psychogenic stress have also been identified in human beings (both in men and women of childbearing age) [31].

Thus, as the results of this part of the investigation show pronounced information pathology of the HNA in rats, induced by chronic uncontrolled psychogenic stress, leads to stable changes in the emotional sphere of their offspring - to an increase of emotional tension, anxiety with increased vegetative function and motor activity, and high stress-reactivity. In the complex of the revealed peculiarities of the HNA of the offspring of the rats with information neurosis special importance attaches to their high general excitability and its low threshold as indices of high excitability of their nervous system, the observed peculiarities of their emotional-motor behavior being their phenotypic expression [21]. On the whole, the data obtained show that under the influence of an unfavourable form of psychogenic information stress of the parents, a high anxiety, easily excitable type of behavior with heightened vulnerability to environmental impacts is formed in their offspring. According to the present results two generations of ancestors with disturbances of adaptive behavior in the form of information neurosis induced by stress are quite enough for the formation of such a type of behavior.

The ratio of learning and emotionality behavior. A comparison of learning dynamics indices in the animals of F1-F5 (Fig. 1-3, Tables 1, 2) and emotional-motor behavior (Table 3) reveals complex ambiguous interrelations between them. The comparison of the learning of the offspring and indices of their initial behavior in the OF shows that definite degrees of increase of emotional tension, anxiety, excitability level (in terms of the indices of the excretory function and motor activity) positively correlate with the growth of the number of well-learning animals'. However, this is observed not in all generations, i.e. such a correlation is not rectilinear. Thus, the offspring of F2 with emotional tension increased, as compared to F1 (the percent of the animals with defecation in the OF is higher by 2.5, motor activity - by 1.5 than those in F1) have the poorest learning among all generations. However, in the offspring of F3-F4 against the background of further increased level of emotionality, anxiety (the percent of the animals with defecation is higher by 5 and 3 and with its high intensity - by 6 and 4, motor activity - by 1.5 and 2, respectively, than those of F2) a clear increase of the percent of well-learning animals is observed. In the offspring of F5, the level of anxiety and excitability of which is though lower as compared to F3 and F4, at the same time it remains high enough - according to the majority of the indices it exceeds F1 and to a certain extent is comparable with the most poorly learning F2, a drastic growth of the number of well-learning animals is found in evidence. Special note should be made that, as distinct from all the previous generations, F5 shows a decrease of the index of the highest degree of the tension in vegetative function, i.e. the index of highly intensive defecation - 5 and more boluses, however, according to the percent of the animals with defecation and to the percent having in it 1-4 boluses it reliably exceeds F1 and F2. Further analysis shows that it is the dynamics of the highest degree of vegetative tension (in terms of the difference of indices of highly intensive defecation in pre- and post-stress status) that reveals very close positive correlation with poor learning of CRAA in all the generations - their curves practically repeat each other (Fig. 4). At the same time the coordinated changes in this index and good learning (negative correlation) are observed not in all the generations. Thus, as compared to F3, F4 independently from reliable growth of the index of high vegetative tension also increases good learning (Fig. 4). However, at the same time it is evident that the most pronounced growth of good learning of F5 coincides with a sharp decrease of especially high degree of vegetative (excretory) tension. These data show that good learning is combined with increased anxiety; however, only definite degrees of emotional tension are favourable for learning, as its very high level, expressed fear (high vegetative tension) impede the manifestation of the ability to accomplish active avoidance.

The direct dependence between the levels of anxiety and capacity for learning is shown in many works [32-34], though the latest are performed with different experimental models. Our results completely agree with the data of V. Dennenberg's thorough investigations with detailed analysis of dependence between the value of various stress influences in early age in rats and the forming emotionality of an adult animal, as well as of its capacity to solve the tasks of varying difficulty, connected with the learning of avoidance of painful stimulation [25]. The author concludes that the high emotional reaction impedes the solution of moderate and difficult tasks. A similar study of P. Goldman [35] also leads to the conclusion that a very high level of emotionality impedes the performance of tasks connected with negative motivation.

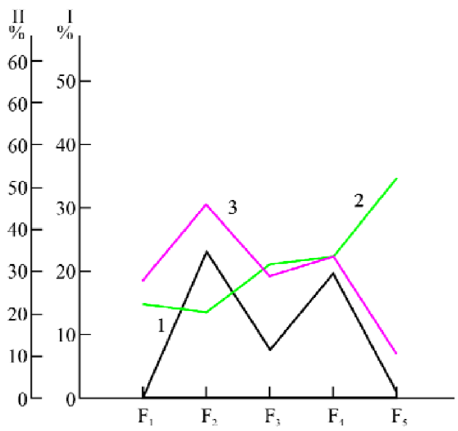

Fig. 4. Emotional stress-reactivity according to distinction of indices of high-intensity defecation (5 and > boluses) in open field in post- and pre-stress status (line 1, scale 1) and indices of good (line 2, scale II) and poor (line 3, scale II) learning of active avoidance in the shuttle-box (10 days of training, 200 presentations) in different generation offspring.

On the whole, the results of our investigation point to the fact that the manifestation of the individual capacity to form active avoidance is affected by both genetically determined motor activity and genetically determined level of emotionality towards defecation. The important question - the genetic variability of which of the behavioral features can affect the learning of animals has been investigated for a long time and remains topical to the present day. A genetic analysis of interrelations between the CRAA elaboration rate and the degree of emotionality in terms of defecation and motor activity was carried out by P. Broadhurst and G. Bignami, using the method of double selective experiment [36-38]. The results showed that there is a positive correlation only between the learning rate and motor activity, while between the learning rate and emotionality such a correlation is absent according to defecation index. Based on this, it was assumed that the rate of elaboration of defensive conditioned reflexes is under the control of other genes, as compared to those which determine the manifestation of emotionality in rats. The "special status" of the motor component of conditioned reaction was stressed by P.K. Anokhin: "the entire differentiation of an animal's behavior takes place due to motor analyzer" [1968]. The level of motor activity was chosen by L.V. Krushinski as simple but adequate and fairly trustworthy index of the state of general excitability of animals for the estimation of the excitability of the nervous system – one of the fundamental and universal features determining the level of functional state of any of its divisions and physiological mechanism related with them. The level of excitability which correlates with the level of motor activity in his physiological-genetic studies of dogs' behavior ultimately determines the manifestation and expression of the gene's activity determining separate behavioral acts. Comparative genetic analysis of excitability and motor activity ratio in rodents [1, 39] has shown that the connection of excitability with oriented-exploratory activity appears to be most invariant. At the same time the influence of excitability level on other forms of behavior may be species- and linear specific.

To date the existence of a genetic connection between the level of nervous system excitability and the ability to learn is proved by different methods of genetic analysis in animals of various phylogenetic levels [1, 40-46]. Thus, a high negative correlation between the threshold of excitability and rapidity of CRAA formation has been revealed in inbred mice [40]. Hybridologic analysis has proved a genetic connection between these features [41]. Genetic dependence on the signs of excitability and learning is revealed by methods of direct and reverse selections [42-44]. The selection of the lines of rats according to high and low rate of CRAA formation (KHA, KLA koltush lines of Fedorov-Lopatina) led to a distinction between these lines and the threshold of excitability of nervous system [42]. The choice of rats by the threshold of neuromuscular excitability (H and L lines, the selection of the laboratory of Professor N.G. Lopatina) also led to divergence of the lines, and in terms of ability - to CRAA formation [43, 44]. The gene controlling the thresholds of neuromuscular excitability in mice in its localization on chromosome map [45] appeared to be identical to the locus responsible for distinction in the rate of CRAA formation in the same mice lines [46]. Based on the results of their own long-term systematic investigations of genetic fundamentals of the HNA as well as on the totality of literary data, N.G. Lopatina and V.V. Ponomarenko underline that the genes responsible for the thresholds of neuromuscular excitability possess plural action and also take part in hereditary determination of the thresholds of excitability of peripheral and central divisions of the nervous system, a large complex of the characterization of excitation process, as well as the ability of conditioned reflex formation [1]. Furthermore, the authors come to the conclusion about the existence of hereditary determination of the level of functional activity of the nervous system or the general tonus of the CNS, underlining that the latter evidently appears to be the main physiological channel of gene influence on the behavior and general for animals of different phylogenetic level [1].

According to the results of our investigation, high excitability appears to be one of the important peculiarities of the HNA of the offspring of rat-parents with information neurosis and it positively correlates with the ability of forming CRAA, but, as was shown above, this correlation is not rectilinear. This is not a contradiction, since the state of high excitability is not identical to its optimal level, nor to the general optimal functional state of the brain. The dynamic balance of the processes of excitation and inhibition ultimately determining the efficiency of the brain as a whole, underlies the normal course of all the processes of the nervous system. The overexcited brain is a major source of behavioral and vegetative pathologies [47]. As M.M. Khananashvili notes [48], in the norm the brain itself regulates its general state in accordance with new conditions and by decreasing the level of excitability of nervous centers provides such a ratio of nervous processes which retains the optimal possibilities of the brain to solve its tasks. The mechanisms of the regulation and self-regulation of the general functional state of the brain are manifested in this [48]. In the light of the foregoing, it may be assumed that some decrease of the excitability level in the offspring of F5 as compared to F4-F3 (decrease of motor reactivity, decrease of especially high degree of vegetative tension) appear to be the expression of self-regulating processes of the brain forming optimal conditions for manifestation of their ability to learn active avoidance experience, i.e. to the improvement of their adaptation to specific stressor. At the same time it should be especially noted that according to the results of our investigation the improvement of the adaptation of animals to specific stressor aversive influence, observed in the line of the generation, in a certain sense has a restricted narrow- directional character and does not coincide with their general adaptability, if under the latter we understand the ability to survive and leave a viable posterity capable of reproduction. As noted above, beginning with F3 pronounced depression of the reproductive function and survival of the offspring of stressed rats have been revealed as one of the negative consequences of an unfavourable form of parent stress.

A number of results of this study concerning the general problem of biological expediency and compensatory significance of some manifestations in animal behavior in the formation process of HNA disturbances, and which are traditionally interpreted as harmful, as well as the question about the possibility of early identification of neurotization of the animal that is taking shape (particularly, the syndrome of deviation in the functioning of different systems [17, 18], e.g. of motor and vegetative systems) will be considered by us in a separate publication.

Conclusions

1. In the line of 5 consecutive generations of offspring in rats with information neurosis in the first two generations, the worsening of the ability to elaborate an active avoidance conditioned reflex was observed - most pronounced in F2 with dominant poor learning. In the subsequent generations this ability improves - in F5 good learning becomes dominant.

2. The difference in learning between various generations is revealed at the very earlier steps of formation of conditioned reflex connection, which presupposes its genetic conditioning.

3. Under the influence of an unfavourable form of psychogenic (information) stress of rat-parents a highly anxious, easily excitable behavior type with increased vulnerability to the impacts of the stressor is formed.

Two generations of ancestries having disturbances of adaptive behavior induced by stress are enough for its formation.

4. Good learning positively correlates with definite levels of anxiety, increased level of emotional tension; however, very high degrees of the latter - pronounced fear with high level of vegetative (excretory) tension - impede the ability to accomplish an active avoidance reflex.

5. The improvement of adaptation to specific aversive influence in the form of improvement of learning to active avoidance in the line of the generations does not coincide with general adaptability of the offspring. The pronounced decrease of the viability of animals and depression of their reproductive function, revealed from the third and increased to subsequent generations, appear to be one of the negative consequences of the unfavourable form of psychogenic information stress of their parents.

ადამიანის და ცხოველთა ფიზიოლოგია

აქტიური განრიდების პირობითი რეფლექსის ფორმირების სისწრაფის დასწავლა უმაღლესი ნერვული მოქმედების მდგრადი ინფორმაციული პათოლოგიის (ინფორმაციული ნევროზი) მდგომარეობაში შეჯვარებული ვირთაგვა-მშობლების ხუთი თანმიმდევრული თაობის ჰიბრიდებში

ფ. კალანდარიშვილი[*], ზ. ხანაევა[*], ც. ორჯონიკიძე[*], ი. ფანცულაია[*], მ. ხანანაშვილი[**]

** ი. ბერიტაშვილის ფიზიოლოგიის ინსტიტუტი, თბილისი*
*** აკადემიის წევრი, ი. ბერიტაშვილის ფიზიოლოგიის ინსტიტუტი*

შესწავლილია თეთრი უჯიშო ვირთაგვა-მშობლების საწყისი 8 წყვილის მოზრდილი ნაშიერების 5 თანმიმდევრული თაობის შთამომავლებში (საერთო რაოდენობა 370), რომლებიც შეჯვარებულები იყვნენ უმაღლესი ნერვული მოქმედების მდგრადი ინფორმაციული პათოლოგიის (ინფორმაციული ნევროზი) მდგომარეობაში აქტიური განრიდების პირობითი რეფლექსის ფორმირების მაჩვენებლები მაქოსებრ კამერაში. ყველა თაობის ნაშიერებში და-ძმათა შეჯვარებამდე ხდებოდა ინფორმაციული ნევროზის ფორმირება, რომელიც საწყის ვირთაგვებში ასეთის იდენტური იყო. კარგი, საშუალო და ცუდი დასწავლის შეფასება ეფუძნებოდა პირველი პირობითრეფლექსური პასუხის გამოჩენის სისწრაფის მაჩვენებლებს, მათ ჯამს პირველ 5 დღეში და დასწავლის კრიტერიუმის მიღწევას (განრიდების 80% დღეში) სწავლების 10 დღეში. დასწავლის დონე ედრებოდა ქცევის მაჩვენებლებს ღია ველსა და პროკონფლიქტურ სიტუაციაში (ვოგელის მოდიფიცირებული ტესტი). გამოვლენილია გაუარესება საწყისი ანცესტრალური ცხოველების — ნაშიერთა პირველი ორი თაობის — სწავლასთან შედარებით, უფრო მეტად გამოხატულია 2 თაობაში დომინანტური ცუდი დასწავლით (ცუდად და კარგად დამსწავლელი ცხოველების შეფარდებაა 1.9 : 0.8). მე-3 თაობიდან შეიმჩნევა პოპულაციის შემადგენლობის ცვლილების პროცესი F3 თაობაში საშუალოდ და კარგად დამსწავლელი ცხოველების რაოდენობის საწყისი პრევალირებით, F4 თაობაში კარგად, საშუალოდ და ცუდად დამსწავლელთა პროცენტის გათანაბრებით და F5 თაობაში კარგად დამსწავლელთა პროცენტის მკვეთრი სიჭარბით. მე-5 თაობას

დომინანტური კარგი დასწავლით აქვს რაოდენობის მიხედვით 2 კონტრასტული პოპულაცია: კარგად და ცუდად დამსწავლელი ცხოველები (შეფარდება 2:0.4). F3 თაობის ნაშიერები ამჟღავნებენ პირობითი რეფლექსის ფორმირების საუკეთესო მაჩვენებლებს მის ორივე სტადიაზე. ვირთაგვა-მშობლების ინფორმაციული ფსიქოგენური სტრესის არახელსაყრელ ფორმას მივყავართ მათი შთამომავლობის ემოციური სფეროს მდგრად ცვლილებებამდე - ემოციური დაძაბულობის გაზრდილ დონემდე, შფოთვამდე ექსკრეტორული ფუნქციისა და მოტორული აქტიურობის მაღალი დონით, მაღალ აგზნებადობამდე გარემოს ზემოქმედებაზე რეაგირების ზღურბლის დაქვეითებით და ამ უკანასკნელის ძალაზე არაადეკვატური სტრესული პასუხით. კარგი დასწავლა დადებითად კორელირებს გაზრდილი ემოციური დაძაბულობის შფოთვის განსაზღვრულ დონეებთან, თუმცა, ამ უკანასკნელის ძალიან მაღალი ხარისხები — გამოხატული შიში (ვეგეტატიური დაძაბულობის მაღალი დონით) — ხელს უშლის აქტიური განრიდების რეფლექსის განხორციელების უნარის გამოვლენას.

REFERENCES

1. *N.G. Lopatina, V.V. Ponomarenko* (1997), In: Fiziologiya povedeniya. Neurobiologicheskie zakonomernosti. Leningrad, 9-59 (in Russian).
2. *Z.A. Zorina, I.I. Poletaeva, Zh.I. Reznikova* (2002), Osnovy etologii i genetiki povedeniya. Moskva, 386 s. (in Russian).
3. *M.E. Lobashov* (1961), In: Issledovaniya po genetike. Sb.1. Leningrad, 3-21 (in Russian).
4. *D.K. Belyaev* (1979),Vestnik Akad. Med. Nauk SSSR, **7**: 9-14 (in Russian).
5. *A.L. Markel, P.G. Borodin* (1990), In: Ontogeneticheskie i genetiko-evolutsionnye aspekty neiroendokrinnoi regulyatsii stressa. Red. E.V.Naumenko, N.K.Popova, Novosibirsk 148-159 (in Russian).
6. *K.V. Sudakov* (1995), Zh. evol. biokhim., fiziol., **31**(4): 489-499 (in Russian).
7. *H. Selye* (1964), In: Nauka i chelovechestvo, Moskva, 89-91 (in Russian).
8. *H. Selye* (1977), In: Novoe o gormonakh i mekhanizmakh ikh deistviya, Kiev, 27-51 (in Russian).
9. *F.Z. Meerson* (1981), Adaptatsiya, stress i profilaktika. Moskva, 278 s. (in Russian).
10. *V.M. Dilman* (1981), Bolshie biologicheskie chasy. Moskva, 208 s. (in Russian).
11. *V.M. Dilman* (1987), Chetyre modeli meditsiny. Leningrad, 288 s. (in Russian).
12. *G.N. Kassil* (1983), Vnutrennyaya sreda organizma. Moskva, 225 s. (in Russian).
13. *B.S. McEwen, E.R. de Kloet, W.H. Rostene* (1986), Physiol. Rev., **66**:1121-1188.
14. *R. Sapolsky, L. Krey, B. McEwen* (1986), Endocr. Rev., **7**:284-301.
15. E.R. de Kloet (1991), In: Frontiers of Neuroendocrinol., **12**:95-164.
16. *M.M. Khananashvili* (1998), Vestnik Rossiiskoi Akad. Med. Nauk, Moskva, **8**: 13-16 (in Russian).
17. *M.M. Khananashvili* (2002), In: Rukovodstvo dlya vrachei i biologov. Moskva, 294-306 (in Russian).
18. *M.M. Khananashvili* (2007), Zh. patolfiziologii i eksperim.terapii. Moskva, **2**:2-6 (in Russian).
19. *R. Reff, T. Kofmen* (1988), Embriony, geny, evolyutsiya. Moskva (in Russian).
20. *F. Kalandarishvili, Ts. Orjonikidze, I. Pantsulaia et al.* (2008), Bull. Georg. Natl. Acad. Sci., **2**, 3: 121-128.
21. *F. Kalandarishvili, Z. Khanaeva, Ts. Orjonikidze, I. Pantsulaia* (2008), Bull. Georg. Natl. Acad. Sci., **2,** 4: 116-124.
22. *M.M. Khananashvili, T.R. Dovianidze* (1989), Sposob modelirovaniya nevroza. Avtorskii sertifikat. Moskva, №150674A1 (in Russian).
23. *V.S. Rusinov* (1987), In: Dominanta i uslovnyi refleks, Moskva, 5-47 (in Russian).
24. *J. Wilcock, D.W. Fulker* (1973), J. Comp. Physiol. Psychol., **82**: 247-253.
25. *V.H. Denenberg* (1964), Psychol. Rev., **71**: 335-354.
26. *A. Whimbey, V. Denenberg* (1967), J. Comp. Physiol. Psychol., **63**: 500-504.
27. *P.L. Broadhurst* (1975), In: Aktualnye problemy genetiki. Leningrad, 39-58 (in Russian).
28. *D.J. Smith, G.F. Joffe, G.F.D. Heseltine* (1975), Physiol. Behav., **15**: 461-469.
29. *P.V. Simonov* (1987), In: Fiziologiya povedeniya. Neirobiologicheskie zakonomernosti. Leningrad, 486-523 (in Russian).
30. *J.J. Christian* (1968), Colloq. Intern. Centr. Nation Recherche Scientif. (Paris), **173**: 289.
31. *S.L. Berga, T.L. Loucks* (2005), Minerva Gynecol., **57**: 45-54.
32. *P. Venault, G. Chaponthier, L.P. de Carvalho, et al.* (1986), Nature, **321**:864-866.
33. *R.W. Stackman, T.J. Walsh* (1992), Behav. Neural. Biol., **57**: 233-243.
34. *R.K. McNamara, R.W. Skelton* (1993), Psychobiology, **21**: 101-108.
35. *P.S. Goldman* (1965), Animal Behav., **13**: 434-442.
36. *P.L. Broadhurst, H.L. Eysenck* (1964), Emotionality in the rat: a problem of response specificity. Univ. of London Press, p. 205.
37. *G. Bignami* (1965), Anim. Behav., 13: 221-227.
38. *P.L. Broadhurst, G. Bignami* (1965), Behav. Res. Ther., 2: 273-280.
39. *A.I. Vaido,Yu. S. Dmitriev, D.A. Kulagin, M.Kh. Sitdikov* (1983), Genetika, 19:1446-1450 (in Russian).

40. *Yu.S. Dmitriev, A. I. Vaido* (1981), Genetika, **17**: 291-297 (in Russian).
41. *Yu.S. Dmitriev, A. I. Vaido* (1981), Genetika,**17**: 282-290 (in Russian).
42. *N. Dmitrieva, S. Gozzo, Yu. Dmitriev, M. Ammassari-Teule* (1984), Physiol. Psychol., **12**: 30-34.
43. *N.I. Dmitrieva, St. Gozzo, Yu.S. Dmitriev, N.G. Lopatina, V.G. Kassil* (1983), DAN SSSR, **272**: 1235-1238 (in Russian).
44. *N.I. Dmitrieva, St. Gozzo* (1985), Arkh. anat., **88, 2**: 5-10 (in Russian).
45. *Yu.S. Dmitriev* (1981), DAN SSSR, **261**: 203-206 (in Russian).
46. *A. Oliverio, B.E. Eleftheriou, D. Bailey* (1973), Physiol. and Behav., **2**: 497-501.
47. *L.V. Krushinskii* (1979), Fiziologiya cheloveka, **5**, 3: 500-509 (in Russian).
48. *M.M. Khananashvili* (1972), Mekhanizmy normalnoi i patologicheskoi uslovno-reflektornoi deyatelnosti. Leningrad, 223 s. (in Russian).

Received July, 2009