THE NEW ARMENIAN MEDICAL JOURNAL
Vol.10 (2016), No 1, p. 11-23

Review Article

PRENATAL STRESS AS A DISTURBANCE FACTOR OF BEHAVIORAL REACTIONS AND MEMORY IN POSTNATAL ONTOGENESIS

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Received 29/07/2015; accepted for printing 15/01/2016

Abstract

Prenatal stress problem, which is considered to be one of the factors promoting development of such diseases as Alzheimer's disease, Parkinson's disease, autism, epilepsy and others, has recently attracted more attention on behalf of researchers. The studies concerning the prenatal stress impact on behavioral reactions of the posterity are of utmost interest. There are numerous data testifying, that increased anxiety, tendency to depression, difficulty in gaining skills, disturbance of the organism adaptation ability, which in a number of cases is accompanied with decreased vitality and weight, are observed in the animals under the prenatal stress impact. Moreover, the mentioned changes are sex- and age dependent.

It should be noted, that changes under the prenatal stress impact in sexual behavior of the animals are also observed, which are manifested as sexual cycle dysfunction, preterm delivery in females, whereas in males - as libido suppression and sometimes inclination to the individuals of the same gender. The data showing that the mentioned alterations can also be accompanied with such statical changes as female masculinization and male demasculinisation and feminization are available. The impact of prenatal stress causes changes in nociceptive system as well: pain sensitivity increase, duration and strength of the pain response, as well as pain relief system dysfunction.

Many scholars explain the changes observed in prenatally stressed animals by the disturbance in the development of different parts of central nervous system, particularly, neurogenesis weakening, decrease in neuron amount, dysfunction of synaptic transmission and synapsis plasticity, as well as changes in the activity of different endocrine systems. The inclusion into pathologic process of hypothalamic-hypophyseal-adrenocortical and other hormonal systems, which are under its control is of great importance.

The involvement into pathologic process of other biologically important systems (cannabinoid, opioid, serotonin), which have regulatory effect on the different functions of the organism and undergo functional changes under the influence of stress factors action in prenatal period is also significantly important.

Keywords: *prenatal stress, posterity, behavior, postnatal ontogenesis.*

Prenatal stress problem and its impact on the organism development and behavior was determined only at the end of the last century. Prenatal period is the most important period in the organism development, as the organs and systems determining the adaptation mechanism to postnatal living conditions are formed at this time. The formation of new neurons, their differentiation, synaptic link formation between them takes place exactly in this period. Therefore, various stress impact on the pregnant woman, affecting the embryo or fetus, can lead to the disorder of central nervous system functional state, the consequences of which could be revealed already in postnatal period. These changes can be manifested as both behavioral reaction disturbance and pathology development in different organs and systems. There are numerous data testifying to perinatal stress im-

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pact on pregnancy and delivery as well as on its various postnatal manifestations in descendants.

The aim of present study is the generalization of the study results of prenatal stress impact on behavioral reaction and memory condition as well as their manifestations depending on duration, impact strength and animal gender.

Numerous data concerning prenatal stress impact on general state of the experimental animals in postnatal period, including behavioral reactions) are widely available [*Said N et al., 2015*]. It has been revealed, that the vitality and weight decrease caused by chronic prenatal stress is observed in the descendants [*Shiota K, Kayamura T, 1989*]. Some researchers explain low weight of animals by the decrease in the amount of insulin-like factor-1 both in the mother's organism and in the fetal one, as well as diminishing the number of cells, producing somatotropic hormone and prolactin, which are responsible for the organism growth and development. Types of the hypophyseal transcriptional factors PIT1 and PITX2 isoforms, necessary for normal development and functioning of the cells producing the mentioned hormones considerably decrease as well [*Gao P et al., 2011*]. As to behavioral reactions, they have been studied on various experimental animals by means of various research test methods. So, it has been determined that in Morris water maze as well as in other test studies the prenatally stressed mice showed the highest emotional activity, memory and skill gaining ability disturbance. Simultaneously, hippocampus volume diminishing, neurogenesis weakening, including astrocyte amount decrease in the brain of experimental animals have been revealed [*Gong Y et al., 2012*]. With this, anxiety was registered in the rats which had undergone prenatal stress at the age of 29-35 days in the open space, in swimming and other test-reactions. The sign of anxiety and panic in stressed animals is that they spend less time in the open space of the x-maze. Such behavior is explained by corticosterone high level, causing hyperactivity of the hypothalamus-hypophyseal-adrenal cortex system, regulating organism stress-reactions [*Salomon S et al., 2011; Schroeder M et al., 2013*]. Similar alterations in psychopathologic states, such as anxiety, as well as depression; organism adaptation ability decrease to the changing environmental conditions in the stress-undergone animals is also mentioned by other authors. They refer such behavioral shifts to the changes possibly originating in different neuronal structures of central nervous system [*Weinstock M, 2007; Bustamante C et al., 2010; Neigh G et al., 2010; Rice F et al., 2010; Sandman C et al., 2012*]. There is an opinion that these changes can be more expressed with age [*Hosseini-Sharifabad M, Hadinedoushan H, 2007; Talge N et al., 2007; Tjulkova E, Vataeva L, 2012*].

Hippocampus role is especially emphasized, as it is responsible for the conduction of the organism numerous behavioral and emotional reactions [*Cai Q et al., 2008*]. It has been established that prenatal stress causes the surface diminishing of the cell chromocenter of the fetal hippocampus as well as neuron amount decrease in its CA3 zone [*Dyuzhikova N et al., 2012*]. As it is known, there are pyramidal cells in the CA3 zone of the hippocampus, responsible for the motive reaction conduction [*Vataeva E et al., 2005; Hosseini-Sharifabad M, Hadinedoushan H, 2007*]. Education ability decrease developing under stress conditions is also associated with changes in the hippocampus.

Changes taking place in central nervous system under conditions of prenatal stress refer not only to the neuron quantitative changes, but also to the link formation between them. The data testify that under the impact of prenatal stress the amount of the frontal cortex and hippocampus neuron processes as well as the number of dendrite spinules is changed. As it is known, the latter ones determine contact level between the neurons, synaptic conductivity, ability education and skill gaining. Some scholars connect spatial memory decrease revealed in stressed animals by means of Morris water maze with the decrease of dendrites' length and amount in pyramidal neurons of hypothalamus specific zones [*Van den Hove D et al., 2006; Martínez-Téllez R et al., 2009; Lui C et al., 2011*]. Such changes are noted both in males and in females [*Mychasiuk R et al., 2011a; 2012*].

It has also been proved that more prolonged fear feeling accompanied with corticosterone high level and limbic and paralimbic cerebral system (amygdala, ventral hippocampus, striatum) high activity, which are responsible, as it is known, for anxious and panic behavior is observed in prenatally stressed animals [*Charil A et al., 2010; Sadler T et al., 2011*]. It is established, that behavioral changes in descendants of the stressed rats depend

on their housing conditions as well. Particularly, it has been determined that satisfactory conditions, provided during pregnancy can lessen the probability of anxiety formation and education process and memory disturbance in descendants [*Li M et al., 2012*].

It is necessary to take into account the impacting factor type and its strength and duration in stressogenic factor study. Stress stimuli of different power have different sometimes even opposite influence on the development and functioning of the brain in descendants. For instance, brain weight in males and females decreases under stress conditions of average power, and, vice versa, brain weight increase is observed in females under prolonged stress [*Uygur E, Arslan M, 2010; Mychasiuk R et al., 2011b*]. Simultaneously under average stress impact, sensomotoric ability development and locomotion decrease is observed, and under prolonged stress – locomotion is, on the contrary, activated. According to the data of the same authors, under stress condition of average strength DNA methylation takes place and it is inhibited under high strength stressogenic factor influence [*Kapoor A, Matthews S, 2008; Uygur E, Arslan M, 2010; Mychasiuk R et al., 2011b*]. As it is known, DNA methylation participates in gene expression, and, therefore, in DNA function alterations.

The experiments show that postnatal behavioral alterations are connected with the stressogenic factor impact period. For example, weakening of spatial memory revealed in Morris water maze is more expressed in guinea pigs, undergone stressogenic factor impact in the initial period of pregnancy comparing with those in the final one [*Kapoor A et al., 2009*]. Different manifestation degree of social behavior, anxiety and aggression in rats also depends on the impact period [*Patin V et al., 2005*]. There are literature data testifying that rat immobilization three times a day for 45 minutes during the last week of pregnancy considerably affects the synaptic plasticity of hippocampus in the descendants. With this, it is proved that probability of prolonged potentiation formation decreases, and, on the contrary, prolonged depression formation becomes more probable. The authors consider such alterations are caused by the increase of neurotrophic factor precursor (preBDNF) in the animal brain and decrease of their mature amount. According to the authors' data, the obtained alterations do not depend on the animal gender [*Yeh C et al., 2012*].

Behavioral changes, similar to those registered in schizophrenic patients, are also revaled in the posterity of the rats undergone to the stress impact in the pregnancy final terms [*Koenig J et al., 2002; Kofman O, 2002*].

Social behavior is also significantly changed in the animals that underwent prenatal stress. Thus, it is shown that the contact degree in male rats in the group of animals, exposed to prenatal stress is 76% lower than in those in the control group [*Campbell B et al., 1974; Horn G, 1987*]. Social behavior changes are also revealed prenatally stressed rhesus monkey. They display lowered contact degree, weakened adaptational ability, they become more sensitive to various stressogenic factors [*Clarke A, Schneider M, 1993*]. Similar results were obtained by other researchers as well, which show that in the result of prenatal stress the defense reaction enhances in the animals: latent period of contacting with other animals becomes more prolonged, their playing activity decreases, they become more cautious [*Takahashi L et al., 1992a*].

It is known, that behavioral reactions of the organism are determined by some biologically active agents, particularly, oxytocin, antidiuretic hormone, serotonin, catecholamines, sexual hormones, glucocorticoids, prolactin and others. It is shown, that the changes in animal behavior in postnatal period are connected with the synthesis disturbance of the abovementioned and other biologically active agents, and changes in the systems, regulating their synthesis, which take place during intrauteral development. For instance, pathological changes in oxytocinergic system caused by prenatal stress are observed in male rats. Particularly, mRNA amount, responsible for oxytocin synthesis, decreases in paraventricular nucleus of the hypothalamus, and in the central amygdala oxytocin receptor amount increases [*Lee P et al., 2007*].

Moreover, it is considered, that pathologic changes in prenatal stress undergone animals can be caused by insufficient production of neuroactive steroids (5α-, 5β-dehydroprogesterone, allopregnanolone, androsteron, androstenol, etc.) which enforce GABA-ergic inhibiting mechanisms, especially in the last period of pregnancy, inhibiting irritation processes. According to the researchers, cerebral cell mitosis disturbance and their necrocytosis can be probably connected with

this. Placenta also plays a great role in the process of neuroactive steroid synthesis, and it is exposed to morphofunctional alterations in prenatal stress [*Hirst J et al., 2009*].

There are numerous data, testifying the connection between behavioral changes and quantitative variations of glucocorticoids arising after stressogenic impact. Pregnant rats were exposed to light stress impact during the last week of pregnancy (three times a day, for 45 *min)*, after which behavioral reactions of their posterity and glucocorticoid level were studied. It turns out that, the control group of animals showed interest to the suggested new conditions, whereas experimental animals responded by the escape reaction and increased anxiety, which was accompanied with more prolonged corticosterone secretion. Moreover, a direct correlation between corticosterone level and escape behavior manifestation was revealed [*Vallée M et al., 1996*]. This correlation is also confirmed by other scholars, who determined the studied behavior in the animals in low level of this hormone [*Piazza P et al., 1991; Dachir S et al., 1993*]. It is also known, that inhibition of 11β-HSD2 placental enzyme, causes glucocorticoid catabolism is accompanied with high anxiety and depressive behavior in the posterity [*Wyrwoll C, Holmes M, 2012*]. These researches emphasize the fact that placental barrier is also of great importance for further development of the posterity [*Hirst J et al., 2009; O'Donnell K et al., 2009*].

The researches carried out on guinea pigs show that high concentration of glucocorticoid in pregnant females results in the stress response of the organism due to cortisol and motive activity of the second-generation posterity.

The amount of pro-opiomelanocortin and adrenocorticotrophic hormone, corticoliberin and its receptors decreases in the hypophysis of females of the second generation. An increase in glucocorticoid receptors in the hippocampus of males of the second generation is registered, and, on the contrary, in females' hippocampus a decrease in glucocorticoid and mineral corticoid receptors is registered. Thus, it can be concluded, that glucocorticoid amount increase in prenatal period can cause alterations in behavior and pituitary-hypothalamic system even in the posterity of the second generation [*Gong Y et al., 2012; Iqbal M et al., 2012*].

Treatment with synthetic glucocorticoid in prenatal period, which is used in medicine in mothers with preterm delivery, aimed at fetal lung development stimulation, can have an impact on pituitary-hypothalamic system of the posterity, resulting in sleep disturbance, anxiety, depression, memory infringement. All this gives the evidence of corticosterone importance [*Darnaudéry M, Maccari S, 2008; Emack J, Matthews S, 2011*].

It has been determined that prenatal stress impact on pituitary-hypothalamic system depends on animal age as well. If young animals display sensitivity increase to the feedback signals in hypophyseal-adrenal corticoid system, more adult individual the feedback system is less expressed [*Shamolina T et al., 2009*], which is the evidence of the regulatory mechanism imperfection in this system. Other researchers also report about connection between glucocorticoid high level in prenatal period and behavioral reaction disturbance [*Aghajafari F et al., 2002; O'Donnell K et al., 2009; Tollenaar M et al., 2011; Urizar G, Muñoz R, 2011; O'Connor T et al., 2013*].

Behavioral reaction dependence on glucocorticoid influence is not limited by the abovementioned connections. It has been proved that they can be due to glucocorticoid high concentration effect on sexual glands and gonadotrophic function of hypothalamic-hypophyseal system. So, under glucocorticoid effect the synthesis of gonadoliberin in hypothalamus, luteinizing and follicle-stimulating hormone in hypophysis, and sex hormones and cells formation process in testis and ovaries is weakened [*Montano M et al., 1991*]. All this has its impact on reproduction process, sexual behavior, as well as on general behavioral responses of the organism [*Tazumi T et al., 2005; Mandyam C et al., 2008; Whirledge S, Cidlowski J, 2010; Biala Y et al., 2011*].

Some researchers consider the alterations not only in hypothalamus-hypophyseal system, but in the systems, regulated by it, to be the main causes in the behavioral response disturbance in prenatally stressed animals. So, it is known, that the mentioned shifts can be the result of functioning disturbance of serotoninergic and adrenergic mechanisms (the number of mediator, receptor activity) which, as it is known, depend on glucocorticoid level [*Shamolina T, Pivina S, 2009; Ordyan N et al., 2009; 2010; Benekareddy M et al., 2011*]. The mentioned connection is manifested by the fact, that serotoninergic neurons of the midbrain

innervate the hypothalamus paraventricular neurons, which produce corticoliberin. In addition, the latter ones, together with glucocorticoids, in their turn, affect serotonergic neurons. Numerous behavioral disturbances, such as depression, anxiety, eating behavior disturbance, chronic fatigue are explained by the dysfunction of these systems [*Hanley N, Van de Kar L, 2003*].

It is known, that besides pituitary-hypothalamic system, functioning of which is so important for the organism survival under stress condition, the endogenic cannabinoid system, which is in interaction with it, also takes part in formation of emotional response of the organism to various stressogenic factors [*Schöpper H et al., 2012*]. That is why, the dysfunction of the latter system after the exposure to prenatal stress can also have an impact on the state of the organism behavioral reactions. The researches show that if pregnant rats are administered corticosterone *per os* in the dose of 100 *mg/kg*, which is equal to stress factor impact, the anxiety increase, motive activity decrease combined with cerebral metabolism disturbance (glutamate increase and taurine amount decrease in the hippocampus and inositol and N-acetate decrease in hypothalamus) are observed in their posterity. Combination of corticosterone-induced prenatal stress with medicamentous stimulation of endogenic cannabinoids production results in normal regulation of emotional response of the mature individuals of the posterity [*Macrì S et al., 2012; Ceci C et al., 2014*]. Moreover, there are data, that formation of endocannabinoid-receptor signal complex regulates corticosterone response, arising as a response to stress and that arachidonoglycerol is just that initial endocannabinoid which promotes restoration of pituitary-hypothalamic system activity, altered under stress impact [*Roberts C et al., 2014*]. It is also known that cannabinoid system together with its receptors takes part in recurrent inhibition of some neuromediators secretion. Insufficiency of these receptors results in anhedonia (inability to experience pleasure), anxiety, and memory weakening. It has also been proved that endocannabinoid-CB1 receptor activity increases during acute stress, though under conditions of chronic stress factor the number of these receptors decreases. Corticosterone concentration in blood serum increases under the action of cannabinoid-1 antagonist receptors [*Patel S et al., 2009; Hillard C, 2014*]. Thus, endogenic cannabinoid system activation inhibits pituitary-hypothalamic system activity and provides new opportunities in anxious state treatment.

There are data testifying that behavioral shifts manifested in prenatal stress can also be due to the changes in dopaminergic system [*Takahashi L et al., 1992b*]. Particularly, in prefrontal cortex of prenatally stressed animals dopamine amount increases and it decreases in sinistral cores of the striatum [*Fride E, Weinstock M, 1988; Alonso S et al., 1994*].

Literature data testify that behavioral shifts can depend on the gender of the posterity, born in rats exposed to emotional and pain stress in prenatal period [*Kinsley C et al., 1988; Zuena A et al., 2008; Brunton P, Russell J, 2010*]. Thus, it is shown that if anxiety prevails in behavioral shifts in prenatally stressed females, the males display bad orientation in space, weakening of the memory and ability to learn [*Sierksma A et al., 2012; 2013*]. The abovementioned manifestations depend on stressogenic factor strength, duration and the impact period. Some authors connect learning ability weakening in males with testosterone level decrease [*Weinstock M, 2011*]. This is also proved by the studies conducted on prenatally stressed male guinea pigs in which anxiety increase is accompanied with testosterone level decrease as well as cortisol level increase. Administration of testosterone in a certain quantity to the guinea pigs results in restoration of behavioral shifts [*Kapoor A, Matthews S, 2011*]. According to the opinion of other researchers the mentioned behavioral shifts developed under stress can be the consequences of not only decreased formation of testosterone together with aromatase (estrogen synthetase) having utmost importance in sexual behavior formation, but also corticosterone level increase in the fetal brain [*Weinstock M, 2007; 2011*].

There are data according to which prenatally stressed males can have not only behavioral, but also statical changes as well, particularly, feminization and demasculinisation. It has been proved, that the present phenomenon is accompanied with weakly active androstendione synthesis increase in adrenal cortex and, on the contrary, inhibition of more active testosterone formation in genital glands [*Ward I, 1972; Ward I, Stehm K, 1991*]. Statical changes can be observed in females as well, what is expressed by their masculinization [*Sachser N, Kaiser S, 1996*].

What concerns behavioral shifts in females, they manifest higher anxiety level and low motive activity during estrus after being exposed to prenatal stress, than the control group animals. The animals suffered prenatal stress later become more sensitive to social stress when they are kept during puberscence in densely populated groups. It is expressed by corticosterone concentration increase, as well as the sexual cycle disturbance. In prenatally stressed rats, kept in isolation, the sexual cycle is shortened with prolongation of the heat period, what, according to the opinion of some authors, increases the period of their fertilization [*Shamolina T et al., 2010*]. It is interesting that after transfer of prenatally stressed females out of the isolated conditions into the group of rats, the corticosterone level turns out to be lower than in non-stressed animals. Under the impact of the suffered prenatal stress not only sexual cycle duration and females' behavior is altered, but also the threat of preterm delivery and low weight posterity combined with different neurogenic pathologies arises [*Kalantaridou S et al., 2010; Vrekoussis T et al., 2010*].

As it has been mentioned, memory and the learning ability deficiency in females are less expressed than in males. There are different opinions concerning this issue. One of them states that such difference is due to placenta functional peculiarities in the process of fetus development of different genders. According to another opinion, females are resistible to stress-response than males, since females have to stay in stress conditions a longer period of time (e.g., necessity to take care after the posterity). There is no such problem for males [*Glover V, Hill J, 2012*].

At present prenatal stress is considered as a factor promoting various disease development, such as Alzheimer's disease, Parkinson's disease, autism, epilepsy and others [*Kinney D et al., 2008; Li J et al., 2008*]. So, chronic stress and stress dependent dysfunctions, such as depression, increase the probability of Alzheimer's disease development. The connecting link for the mentioned diseases is brain-derived neurotrophic factor. Maternal stress causes the formation of depressive phenotype, especially in females. They have decreased hippocampus brain-derived neurotrophic factor level, which isn't observed in males, though the receptor number in both genders remains unchanged [*Sierksma A et al., 2012*].

The connection between behavioral changes under prenatal stress impact and neurotrophic factor is confirmed by the fact, that the changes previously observed in posterity can partially disappear when the latter is used. For instance, under prenatal stress impact males manifest inhibits sexual behavior while choosing a female, in some cases they prefer the individual of the same gender [*Kuznetsova E et al., 2006; Meek L et al., 2006*]. It turns out that behavior restoration after such disturbances is possible by means of brain-derived neurotrophic factor use [*Popova N et al., 2011*].

Pain sensitivity, being one of the most important adaptation mechanisms to stress factors is manifested already in the first stages of ontogenesis. Along with this fine adaptation reactions connected with nociception, are formed in later stages of individual development. Though some original studies on tonic pain ontogenesis have recently appeared, the issue of prenatal stress impact on behavioral reaction formation connected with pain sensation hasn't finally been solved. It is known that various factors have their impact in nociceptive system development: neurotransmitters, neuromodulators, different medicamentous preparations as well as prenatal and postnatal stressogens. Data concerning pain sensitivity alteration in suffered prenatal stress are available in the literature [*Rokyta R et al., 2008*]. It is of utmost importance, as pain signals about present or developing pathological processes and pain sensitivity alteration can cause the disturbance of behavioral reaction. It has been proved that prenatal stress suffered animals become more sensitive to pain stimuli, which is manifested by latent period shortening of pain response [*Sternberg W, 1999*]. According to other data prenatal stress lowers pain sensitivity threshold in female rats, whereas males show no difference comparing with the control group animals.

Similar data were also obtained in the studies of formalin-induced pain type in the suffered prenatal stress rats. They display hypersensitivity to pain stimuli, prolongation of duration and pain response enforcement. It is explained by that, the inhibitory processes responsible for pain weakening are disturbed [*Butkevich I, Vershinina E, 2001*]. According to the authors' opinion, one of the development mechanisms of the increased pain response is dysfunctioning of serotonin system which, as it is known, is a part of anti-nociceptive defence of the organism. The evidence of this is that the use of

the inhibitors of serotonin reverse capture out of synaptic cleft in prenatal period can decrease stress manifestation and regulate nociception in posterity by means of serotoninergic and the activation of pituitary-hypothalamic system, combined to it [*Chen A et al., 2012; Knaepen L et al., 2014*].

It is determined that nociceptive sensitivity changes under the action of not only prenatal, but also under postnatal stressor impact, as well as in their combination. In postnatally stressed animals in pre-pubertal period the pain is accompanied by a corticosterone level significant increase compared with prenatally stressed animals. In combined action of prenatal and early postnatal stressogens corticosterone level under the pain stimuli is higher than in isolated prenatal stress but lower in comparison to the group of postnatally stressed animals [*Butkevich I et al., 2008; 2010; Said N et al., 2015*].

What concerns anti-nociceptive mechanisms, morphine anesthesia is more effective in prenatally stressed females than in those in the control group, whereas an opposite picture is observed in males. It is determined that under prenatal stress impact the opioid system receptor sensitivity can lower, particularly that of μ-receptors, what is reflected on endogenic and exogenic opiate impact efficiency [*Kinsley C et al., 1988; Insel T et al., 1990*]. According to the data of other authors, morphine-induced analgesia is enhanced in the animals exposed to stress factors immediately in pre- or postnatal period (perinatal stress), whereas if the stressor stimulus is used in both periods simultaneously the analgesia degree doesn't change.

As it is known the stress itself in its turn can cause analgesia effect. It has been proved that the efficiency of stress-induced analgesia is inhibited in the animals exposed to prenatal stress [*Sternberg W, Ridgway C, 2003*]. According to the authors' opinion, this can indicate the activity disturbance of adrenergic system which takes part in analgesic process formation.

It is interesting that prenatal stress impact on stress-induced analgesia also depends on the animal gender. The females suffered prenatal stress analgesia degree increase is observed comparing to the intact animals, whereas such difference isn't revealed in the males. The authors refer such different reactions with estrogen effect, as ovarian excision eliminates the difference in antinociceptive reaction in rats [*Sternberg W, 1999*].

Hence, under stressogenic factor action in pre- and postnatal periods the dysfunction of nociceptive and anti-nociceptive systems takes place and this is reflected in the organism behavioral reaction changes [*Rokyta R et al., 2008; Sandercock D et al., 2011*].

Conclusion

Thus, significant changes of behavioral reactions, such as anxiety, contact avoidance, depression, adaptation ability disturbance, skill-gaining, memory, sexual behavior disturbance, revealed by various tests are found out in the prenatally stressed animals. Moreover, dependency of the mentioned changes for gender and age of the posterity is observed.

Prenatal stress manifestations also depend on the type and stressogenic factor strength and its exposure period.

Behavioral changes of the prenatally stressed posterity are connected with neuron formation disturbance in different parts of the central nervous system, their number change, as well as synaptic links between them and the efficiency of their functioning.

The abnormalities formed in the prenatally stressed posterity are connected with the changes in the activity of a number of hormonal systems, especially pituitary-hypothalamic system, and others under its control. However, it should be taken into account that not only the abovementioned system has impact on the organism, but many other biologically active agents (opioids, cannabinoids etc.) as well, which possess regulatory effect on the different functions of the organism and undergo functional changes under the action of stress factors in prenatal period.

Changes in nociceptive system, which is known as one of the most important in determining behavioral reactions of the organism, are observed under the prenatal stress impact. It is established that the re is an increase in pain sensitivity, strength and duration of the stress response under stress impact, as well as changes in endogenic opioid system activity, which ishould be considered in stress-induced changes of some behavioral reactions.

Despite the abovementioned data, the researches on the study of the prenatal stress impact on behavioral reactions of the organism and their development mechanisms aren't systematized and are contradictory.

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