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The role of catecholamines in preschool children in the neurotic development pathogenesis

The clinic of neurosis is diverse, but common symptoms are fears and anxiety, depression, mood swings, obsessions and other manifestations. In addition, it is believed that mental trauma, causing an emotion of fear or fright affect, can lead not only to cardiovascular, but also to various other violations of the functions of internal organs. All higher forms of human behavior are associated with the vital activity of nerve cells synthesizing catecholamines. Neurons use catecholamines as neurotransmitters (mediators) that carry the nerve impulse. From the activity of synthesis and isolation of catecholamines, such complex processes as the memorization and reproduction of information, aggressive reaction, mood, emotionality, etc. depend. The highest level of catecholamines (per unit of body weight) in children. The article evaluates the results of excretion of catecholamines in preschool children with different mental status. The study has found differences in their metabolism in children with neurotic manifestations and healthy. Biochemical indicators of biological fluids reflect the characteristics of the state of biochemical systems of the brain, in particular, they are indicators of the activity of the sympathetic-adrenal system. This suggests that the evaluation of excretion of catecholamines can be used as a diagnostic method for this disorder.

Key words: preschool children, neurosis, anxiety, catecholamines, dopamine, norepinephrine, adrenaline, neurotransmitter, sympathetic adrenal system

In the last decades of the 21st century, the problem of a significant increase in the number of children with mental and somatic disorders has become especially acute. There are neurotic states, caused by the impact of a variety of psychotraumatic factors. This is due to the growth of scientific and technological progress and related changes in all areas of human life, on the one hand, and the improvement of psychophysiological adaptation, on the other. In this regard, and in the structure of the incidence of the population, there have been shifts towards an increase in the specific gravity of diseases, in the emergence of which an essential role is played by the neuropsychic overvoltage factor. Among such diseases are neuroses. Among the most vulnerable age groups in this regard, preschool and primary school children are confidently leading the way. The consequences of a timely unrecognized disorder in the future can be firmly fixed and will determine not only the state of neuropsychiatric and psychosomatic health [1, 2], but also the features of personality development [3], affecting all levels and forms of adaptation (mental, social, professional) [4]. A.I. Zakharov points out deviations in the neuropsychological development of children in 33 % who attended kindergarten [5].

Neurosis is a complex and, on a number of aspects, a debatable problem. Analysis of the scientific literature indicates that research in the field of neuroses is not of a complex nature and, as a rule, leans either on psychological methods [6, 7] or on medical [8, 9] methods of diagnosis and interpretation of data. The spectrum of clinical forms of neurosis in childhood is very wide, diverse, but not all forms are well known even to specialists. An important circumstance that makes us turn to this topic is the significant age-specific originality of the clinic of this condition, ignorance of which leads to diagnostic errors. In the modern scientific literature there are virtually no works devoted to the analysis of physiological changes in the child's organism

with neurosis. The importance of studying these conditions is due not only to their high prevalence, but mainly to the fact that in childhood, neurosis can remain hidden for a long time, or manifest as a symptom of a physical malaise [10].

Assessing the state of the problem of neuroses in general, it should be recognized that pathogenesis mechanisms remain the most vulnerable place in the whole problem. It is possible that the way to overcome this difficulty is that neurosis must be viewed not in parts, not in individual symptoms, but as a disease of the whole organism. The child's body for a variety of mental trauma and biologically strong agents and harmful effects can respond with a nonspecific reaction called stress [11]. With neuroses, the functional activity of a wide variety of organs and substances is changing, resulting in disturbances in the cardiovascular, respiratory, digestive and other systems.

Neurotransmitters play a significant role in the response to external influences and disruption of homeostasis [12]. Catecholamine innervation affects the main centers of higher nervous activity: the center for control and inhibition of motor and emotional activity, programming activity, attention system and operational memory. It is known that catecholamines perform the function of positive stimulation and are involved in the formation of a stress response. Proceeding from this, it can be considered that catecholamine systems participate in the modulation of higher mental functions and in the violation of catecholamine metabolism, various neuropsychic disorders can arise. These reasons cause the need to study data on the mechanisms of development of pathological processes of the child's body in neurosis, namely: determining the level of catecholamines in a biological fluid in preschool children with various neurotic states.

Materials and methods

A study was carried out in the kindergarten nursery № 15 «Akku», a kindergarten «Tolagay» in Karaganda. Based on the results of primary research, a group of 127 children was selected, who later participated in in-depth studies. The entire sample was divided into four groups. There are 22 children with the established diagnosis — neurosis, 18 children with pre-neurological status, 40 — with a high degree of anxiety, 48 children — normally developing. On the basis of gender, the study involved 55 girls and 72 boys. The number of children in the main groups was as follows: in the neurosis group — 18 girls, 13 boys; in the group of predneurosis — 8 girls, 10 boys; in the group of anxious children — 17 girls, 23 boys; in the group of normally developing children — 24 girls, 24 boys. The age of the children ranged from 4 years to 5 years 5 months. The indicators of the physical development of children were within the limits of the age norm. The body weight of children 4 to 5 years was 15.2 ± 1.3; from 5 to 5.5 years — 21.4 ± 1.1. The average height of children from 4 to 5 years is 103 ± 0.9; from 5 to 5.5 years — 108.4 ± 2.1.

The study was conducted by standardized sets for enzyme immunoassay. Such sets as Elisa Kit for Dopamine (DA), Elisa Kit for Noradrenaline (NE), Elisa Kit for Epinephrine (EPI) are designed for 96 assays with any type of biological fluids. For the analysis, an EIA station was used: Microplate reader — Zenyth 340st Anthos, a shaker-thermostat — ELMI ST3, washer — anthos fluido. The concentration of epinephrine, norepinephrine, and dopamine was expressed in mol/d. The calculation used the program Statistica V.6.1, specifically designed for statistical calculations, including in the natural sciences. Given the presence of four groups, to solve the problem of detecting differences in these parameters, the best option was Fisher's variance analysis or F-criterion. The reliability of the parameters studied was assumed to be $p < 0.001$. The description of the quantitative characteristics is carried out with the help of the arithmetic mean of the plus-minus error of the mean value.

Based on the results of single-factor analysis of variance analysis, the following results were obtained below.

Results and its discussion

In the study, the average statistical indices describing the level of catecholamines in children of different groups (neuroses, prednevroses, anxiety states, and norm) were determined. When analyzing the differences in the Dopamine scale, the values of $F = 3209.73$ at $p = 0.001$ were obtained. The graphical analysis of the differences presented below clearly demonstrates its focus.

Figure 1 clearly demonstrates that the average values for this hormone are the highest in the group «Norm», gradually decrease when going to the groups «Alarming states», «Predneurose» and finally reach their minimum in the group «Neuroses». In this case, it makes sense to note a small spread of values and a high density of results, which certainly increases the accuracy of the measurement.

In the second parameter, the level of norepinephrine F = 2460.75 at p = 0.001, the opposite situation can be observed (Fig. 2).

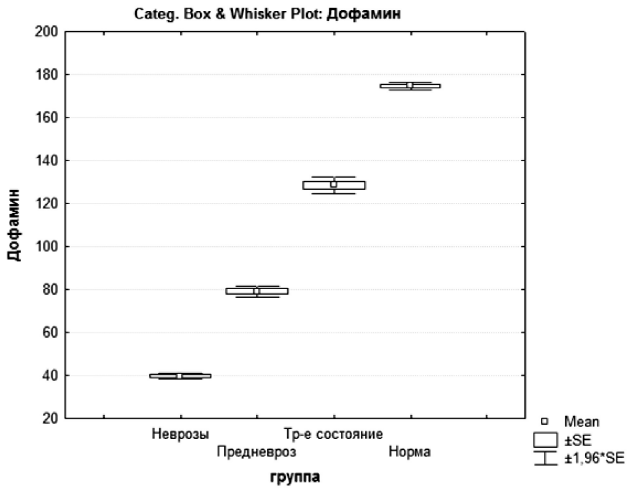

Figure 1. Descriptive characteristics of the parameter «Dopamine»

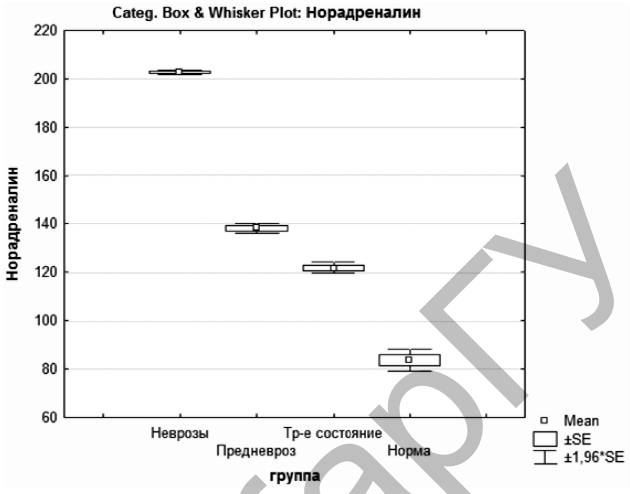

Figure 2. Descriptive characteristics of the parameter «Noradrenaline»

With a significant gap, according to the average indices, the group «Neuros» leads, then, after a strong «failure», the norepinephrine rates decrease smoothly, reaching a minimum on the «Norm» group. As in the previous case, one can note a high density of indicators and a small spread in the values of groups.

According to the third indicator of the level of hormones — Adrenaline F = 1785.84 with p = 0.001, a similar situation was found (Fig. 3).

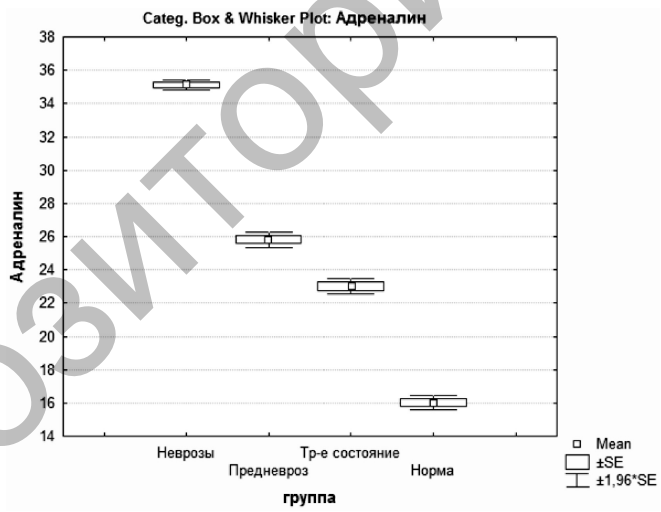

Figure 3. Descriptive characteristics for the parameter «Adrenaline»

As in the previous case, the highest level is observed in the group «Neuroses» after which it drops sharply and having a clear tendency to decrease reaches a minimum on the «Norm» group.

The diagnostic value of these physiological studies allows us to state that the secretion of epinephrine and noradrenaline rises sharply in anxiety and fear in pre-school children with neuroses, predoneuroses, and anxiety. From the physiological point of view, they do not differ from each other, the difference consists only in the fact that anxiety causes activation of the organism before the expected event occurs, which is why the children in the group «Anxiety» in terms of adrenaline and noradrenaline are not much inferior to the group of «Predneuroses».

W.B. Cannon's studies of the emotion physiology [13] showed an increase in the amount of adrenaline in the blood in emotional states (fear, anger, etc.), an excess of which in turn causes a number of somatic changes in the body. An increase in the amount of adrenaline occurs when emotions are caused by the action

of both conditioned reflexes and unconditioned reflex stimuli. However, prolonged exposure to high concentrations of adrenaline leads to increased protein metabolism, which leads to a decrease in muscle mass, loss of body weight, and often to exhaustion. This explains the asthenic constitution of neurotic children. In addition, the predominance of adrenaline in the body destroys the heart, kidneys. The child is in a state of constant nervous over-excitation, sometimes inadequately perceives the emerging situation. In this case, often increases blood pressure, which can lead to vegetative-vascular dystonia.

When a high concentration of noradrenaline and epinephrine combine, a strong muscular tension arises, which can lead to a physiological response, such as a tremor which is caused by the excitation of β2-adrenoreceptors, which is enhanced the contractile activity of skeletal muscles. This reaction is typical for both neurotics and children with anxiety. It appears in the trembling of the chin, lips, and limbs in a stressful situation.

Dopamine is a neurotransmitter, as well as a hormone formed from L-tyrosine [14]. It is a precursor in the synthesis of noradrenaline and epinephrine. As a representative of catecholamines participates in the basic metabolic processes of the body, the formation of a common adaptation syndrome and through the activation of the hypothalamus-pituitary-adrenal system promotes metabolic and hemodynamic adaptive reactions [15]. The excretion of dopamine in the urine in our study is significantly reduced in the Neurosis group by 43.6 %. When dividing children into groups according to various clinical signs, there were also statistically significant differences. Thus, the level of dopamine was significantly lowered in the Predneuroses group by 13.1 %. In the group «Anxiety» was found low numbers of the norm.

The results of the study of catecholamines of older children (middle school age, adolescents), having neurosis, increased anxiety, etc., are somewhat contradictory. The level of adrenaline, noradrenaline or dopamine (and sometimes all three hormones at once) did not increase, and in some cases even decreased significantly, despite the fact that it was already low initially [16]. Presumably, in a state of chronic stress, since older children, the adrenal glands are functionally depleted and are no longer able to adequately react and produce these hormones in the required amount.

The results allow us to conclude that psychoemotional stress in preschool children with neuroses, under the influence of impulses coming from the limbic system, releases corticotropin releasing hormone in the hypothalamus), which stimulates the activity of the pituitary gland. The pituitary gland secretes adrenocorticotropic hormone, which activates the work of the adrenal glands — the main source of catecholamines (epinephrine and norepinephrine) with a parallel decrease in dopaminergic activity.

This is accompanied by activation of the sympathoadrenal system and changes in the functioning of both internal organs (heart, lungs, gastrointestinal tract) and behavioral disorders. Depressed and anxious which are not characteristic of children, in children with neuroses are explained by a decrease in dopamine activity and an increase in norepinephrine and adrenalin neurons.

The magnitude of stress is estimated by the level of increase in adrenal hormones. In children with preneuropathic condition, a significant decrease in dopamine is observed, an increase in epinephrine and norepinephrine reaches a neurotic level in terms of severity.

Anxious state has common biochemical pathogenetic mechanisms with neurosis. Despite close to the norm of dopamine, a significant imbalance in the direction of increased adrenaline and norepinephrine, which is indicated a significant risk of neurosis in the future.

From the above it follows that to understand the mechanism of neuroses is very important (no less than the unfolded stage) its initial, more latent period. It is characterized not so much by disturbances in individual functional systems of the body, as by changes in the interaction of different systems, i.e. the violation of correlations between individual systems is the first reliable criterion for developing neurosis.

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З.Я. Олексюк, Б.Д. Дахбай, М. Даниленко

Мектеп жасына дейінгі балалардың невротикалық даму патогенезінде катехоламиндердің рөлі

Невроздың клиникасы көптүрлі, алайда олардың жалпы әрі ортақ симптомдарға қорқу, алаңдау, үрей, депрессия, көңіл-күйдің жиі ауысуы, жалықтыратын ойлар жатады. Сонымен қатар психикалық жарақаттан болатын қорқу эмоциясы мен үрей аффектісінен жүрек-тамырлы жүйесінің жұмысы ғана емес, жалпы ішкі мүшелерінің функцияларының бұзылыстарына әкелуі мүмкін. Адамның мінез-құлқының барлық жоғары нысандары катехоламиндерді синтездейтін жүйке жасушаларының өмірлік белсенділігіне байланысты. Нейрондар катехоламиндерді жүйке импульсін алатын нейротрансмиттерлер (медиаторлар) ретінде пайдаланады. Катехоламиндердің синтезі мен оқшауланыунан, ақпараттың есте сақтауы мен көбеюі, агрессиялық реакциялар, көңіл-күй, эмоционалдық және тағы басқа күрделі процестерге байланысты. Балаларда катехоламиндердің ең көп деңгейі (дене салмағының бірлігіне) байқалады. Мақалада мектеп жасына дейінгі әртүрлі психикалық статусы бар балалардың катехоламиндердің экскрециясына баға беріледі. Зерттеулер көрсеткендей, сау және невротты балалардың метаболизм қатарындағы ерекшеліктер болады. Биологиялық сұйықтықтардың биохимиялық көрсеткіштері бас мидың биохимиялық жүйелер күйінің ерекшеліктерін сипаттайды, ол симпатолы-адреналды жүйенің белсенділігінің бағасы болмақ. Катехоламиндердің экскрециясын бағалау берілген бұзылыста диагностикалық әдіс ретінде қолданыста болуын дәлеледейді.

Кілт сөздер: мектеп жасына дейінгі балалар, невроз, алаңдаушылық, катехоламиндер, дофамин, норадреналин, адреналин, нейромедиатор, симпатолы-адреналды жүйе.

З.Я. Олексюк, Б.Д. Дахбай, М. Даниленко

Роль катехоламинов у детей дошкольного возраста в патогенезе невротического развития

Клиника невроза многообразна, но общими симптомами считаются страхи и тревожное состояние, депрессия, перепады настроения, навязчивые идеи и другие проявления. Помимо этого, принято считать, что психические травмы, вызывающие эмоцию страха или аффект испуга, могут вести не только к сердечно-сосудистым, но и к различным другим нарушениям функций внутренних органов. Все высшие формы поведения человека связаны с жизнедеятельностью нервных клеток, синтезирующих катехоламины. Нейроны используют катехоламины в качестве нейромедиаторов (посредников), осуществляющих передачу нервного импульса. От активности синтеза и выделения катехоламинов зависят такие сложные процессы, как запоминание и воспроизведение информации, агрессивная реакция, настроение, эмоциональность и т.д. Самый высокий уровень катехоламинов (на единицу массы тела) — у детей. В статье оцениваются результаты экскреции катехоламинов у детей дошкольного возраста с различным психическим статусом. Исследованием установлены различия в их метаболизме у детей здоровых и с невротическими проявлениями. Биохимические показатели биологических жидко-

стей отражают особенности состояния биохимических систем мозга, в частности, являются показателями активности симпато-адреналовой системы. Это позволяет предположить, что оценка экскреции катехоламинов может быть использована в качестве диагностического метода при данном расстройстве.

Ключевые слова: дошкольники, невроз, тревожность, катехоламины, дофамин, норадреналин, адреналин, нейромедиатор, симпато-адреналовая система.

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