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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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INFLUENCE OF PROFICIENCY OF SYNTHETIC FOLIC ACID ON THE NEUROLOGICAL SYMPTOMS OF RATS

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Abstract.

It has long been known about the need for folic acid for the vital activity of both macro-and micro-organisms. It is necessary for the processes of methylation, nucleotide synthesis and also the formation of methionine and reducing the toxic effect of homocysteine. The addition of synthetic folic acid to the diet of pregnant women, as well as at the stage of pre-pregnancy preparation, significantly reduces the risks of fetal neural tube defects, heart defects, and possibly other organs and systems of the body. In addition, folic acid can help improve fertility potential. However, there is evidence of adverse effects of folic acid proficite on the health of older adults (hiding B12-deficient status) and the offspring of mothers taking high doses prescribed by medical specialists like a risk of infectious-inflammatory and allergic diseases of the upper respiratory tract in children, eczema, also disorders of psychomotor development and insulin resistance. In 1980, the direct excitatory effect of folic acid on synaptic transmission in the central nervous system was proven. This is due to the molecular structure, it contains L-glutamate. Therefore, the aim of the work was trying to prove the existing correlation data on probable neuropathologies, including a reduced threshold of seizures, a high risk of epilepsy in a model of offspring of Wistar rats with an increased dosage of folate throughout gestation and including at the stage of pre-gravidar preparation. In the control group, the average clonus time was 1779.6 seconds, in the experimental group with a 1 mg/kg/diet dosage of 797.3 seconds, and in the second group with a 5 mg/kg/diet 439.7 seconds ($p < 0, 01$). The results obtained of the difference in the convulsive threshold may be due to changes in synaptic density as a result of an excess of synthetic folic acid during the formation of NT and subsequently during the differentiation of nervous tissue in the central nervous system (in particular, in the 3rd trimester with a massive appearance of glutamatergic receptors), which can affect the processes of neurogenesis and the formation of neural networks.

Key words. Folic acid, surplus, seizure threshold, synaptic density, myoclonus, gestation.

Introduction.

Folic acid is an essential biologically active substance in a living organism, it provides the process of DNA replication and nucleotide synthesis. Since it is vital, it is used in metabolic processes not only by multicellular organisms, but also by microorganisms. One of the main pathways of its metabolism is methionine and homocysteine exchanges: a methylating agent, SAM(S-adenosinemethionine),isformed,whichisinvolvedinthe methylation of proteins, mediators, nucleotides, phospholipids, and hormones [1]. N 5, N 10-methylenetetrahydrofolate (MTHF) and N 10-formyltetrahydrofolate are directly involved in the biosynthesis of nucleotides de novo - in particular, the lack of these forms of folic acid can lead to severe neural tube defects as a result of the incorporation of uracil into DNA instead of thymine.

It has long been known about the positive effects of folic acid on intrauterine development of the fetus: reducing the risk of neural tube defects, as well as heart defects [2]. Embryonic cells and syncytiotrophoblast, symplastotrophoblast are extremely sensitive to folic acid deficiency, since this is a rapidly proliferating cell pool, folate deficiency leads to cell stress, since methylation processes are disrupted, incl. DNA, which can lead to the development of various kinds of anomalies of differentiation and proliferation of both embryonic axial primordia and already more differentiated tissues. Children whose mothers received folate during preconception preparation and during pregnancy (I trimester) show improvement in cognitive functions in the preschool and early school period [3].

The concentration of folic acid in maternal erythrocytes also correlates with the weight and height of newborns. In the group with a low content of folate in plasma and erythrocytes, the frequency of intrauterine growth retardation of the fetus is higher than in the normal content [4].

Lack of folate intake during pregnancy in the 1st , 2nd , and 3rd trimesters also correlates with an increased risk of autism spectrum disorders in children, as they have a reduced content of methylating agents and folic acid metabolites in their blood [5,6].

Hyperhomocysteinemia is associated with folic acid metabolism, and high blood levels of homocysteine are a proven risk factor for cardiovascular disease [7]. Homocysteine increases both with mutational changes in the genes M THFR , D HFR (the most common 677C-> T), and with a lack of folic acid intake, for example, in countries where there are no mandatory fortification programs. However, the risk of arterial hypertension (AH) during pregnancy was not associated with mandatory folate support for mothers, but the risk of developing preeclampsia (PE) was higher in the group of pregnant women without folate support [8]. The polymorphism of the MTHFR gene associated with high levels of homocysteine also proved to be the cause of menstrual dysfunction. This was shown in the BioCycle Study, a prospective long-term study (2005-2007), which included 259 women with normal menstrual cycles. An increase in the concentration of homocysteine in the control group increased the risk of an anovulatory cycle (sporadic anovulation) by 33%. These indicators were associated with the lack of adequate folate support.

Thus, folates are not only an essential micronutrient, but also a drug for the prevention of a fairly wide range of diseases.

There are two mechanisms of folate absorption, saturable and non-saturable. The former is distributed in the upper small intestine and is sensitive to reduced forms of folate and especially to MTHF. When the critical level for this mechanism, 200 μg of folates, is exceeded, the activity of the carrier apparently

Table 1. *Attack onset time.*

Control group	Experienced group 1	Experienced group 2
1680 sec	730 sec	480 sec
1685 sec	858 sec	450 sec
1920 sec	911 sec	602 sec
1260 sec	510 sec	598 sec
1800 sec	830 sec	1020 sec
1823 sec	791 sec	420 sec
1903 sec	1200 sec	30 sec
1718 sec	401 sec	840 sec
2115 sec	285 sec	330 sec
2317 sec	396 sec	300 sec
1620 sec	333 sec	285 sec
1565 sec	720 sec	275 sec
1638 sec	1205 sec	210 sec
1735 sec	1360 sec	305 sec
1915 sec	1435 sec	450 sec
∑= 1779.6 sec	∑= 797.26 sec	∑= 439.67 sec

decreases due to a decrease in the expression of folate receptor genes [9,10].

The second mechanism is non-saturable, is realized in the ileum, it is non-specific and is able to transfer both reduced and non-reduced folates in unlimited quantities. This mechanism may be the main cause of a significant increase in the level of folic acid in the body and associated folate-dependent pathological conditions. [eleven]. Therefore, since the late 1990s, disputes have arisen in the scientific and medical practice environment about the advisability of prescribing high doses of synthetic folic acid, as well as adjusting the dose in accordance with preventive measures and certain nosology.

Some cohorts of patients are prescribed an increased dosage of folates up to 5 mg per day, although in the EU and the USA, as well as the Federal Service for Supervision of Consumer Rights Protection and Human Welfare of the Russian Federation, the idea of TOV (tolerable upper intake level) (800-1000 mcg) has already been formed. In particular, pregnant women with an increased body mass index may be prescribed 1-2 tablets of 1 mg of folic acid per day due to overdiagnosis in terms of preventing B9 deficiency, hypertension, and PE. The high risk of neural tube defects and other folate-dependent developmental anomalies is a recommendation to take up to 4000 micrograms of folate per day at least 3 months before conception and up to 12 weeks of pregnancy. At the same time, 800 μg should come from multivitamin complexes, and the rest in the form of synthetic folic acid [12]. Additional intake of folic acid is also recommended with a rational and sufficient diet in micronutrient content [13].

However, it is known that an excess of folic acid in the postnatal period can increase the risk of manifestation and recurrence of malignant neoplasms.

In a cohort study of 619 patients, increased folic acid intake was shown to increase the risk of recurrence of non-invasive bladder cancer and multifocal tumors at diagnosis. Researchers on this basis suggested that an excess intake of synthetic folic acid is unsafe for such patients [14].

In a Southern California RCT, among 643 men randomly assigned to placebo or folic acid supplements, the estimated probability of being diagnosed with prostate cancer over a 10-year period was 9.7% in the folic acid group and 3.3 % in the placebo group. These results highlight the potential complex role of folic acid in prostate cancer [15].

A 2012 meta-analysis of ten RCTs showed a borderline significant increase in total cancer in the folic acid group compared with controls [16].

However, other studies have shown that folic acid supplementation has no significant effect on overall cancer incidence, colorectal cancer, prostate cancer, lung cancer, breast cancer, or hematologic malignancies, but reduces the risk of melanoma [17,18]. But, unfortunately, the criteria for statistical significance were not significant in these meta-analyses ($p = 0.10$; $p = 0.23$).

In older adults with low vitamin B12 levels, high serum folic acid levels have been associated with anemia and cognitive impairment. However, when vitamin B12 levels were normal, high serum folic acid levels were associated with protection against cognitive impairment [19,20].

High consumption of synthetic folates by women during pregnancy is one of the risk factors for infectious and inflammatory and allergic diseases of the upper respiratory tract in children, eczema, as well as impaired psychomotor development and insulin resistance. In addition, there is evidence of an increased risk of multiple pregnancy with the use of high doses of folic acid [21].

An Indian study confirms higher insulin resistance in children born to mothers with high gestational folic acid levels. It also showed that this association persists from childhood to adolescence. It also suggests that disruption of the maternal one-carbon pathway is associated with impaired fetal growth and cardiometabolic risks later in life [22].

Folic acid and its related compounds are based on dihydropteroic acid conjugated to L-glutamate, the latter being the major excitatory neurotransmitter in the brain, and the CNS excitatory nature of folic acid itself has been previously reported in vitro .

Synthetic folic acid in an unmetabolized inactive form can also enter the systemic circulation and be taken up by cells. As a result of activation of the non-saturable pathway, it accumulates in the blood. An excess of synthetic folic acid during the formation of NT and subsequently during differentiation of the nervous tissue in the CNS (in particular, in the 3rd trimester with the massive appearance of glutamatergic receptors) can affect the processes of neurogenesis and the formation of neural networks [24].

But still, there is evidence that the intake of physiological folic acid after the closure of the NT (after the first trimester) has a positive prospective effect on the cognitive functions of the offspring. At 7 years of age, children of mothers treated with folic acid had significantly higher scores than the placebo group in verbal reasoning based on the BSITD-III and WPPSI-III test systems [23].

The aim of the work was an attempt to prove the existing data on probable neuropathologies, incl. reduced seizure threshold, high risk of epilepsy in the offspring model of Wistar rats with an increased dosage of folate throughout the gestation period and incl. at the stage of pregravid preparation.

Materials and methods.

The experimental design was projected onto laboratory animals. We used Wistar rats for them. Kyoto . This breed is normotensive, with the absence of genetic polymorphism of the MTHFR , DHFR and other genes associated with the metabolism of folic acid in the body, which allowed us to exclude the risks of complicated gestation and the development of increased neurological symptoms or the development of other adverse conditions in the offspring. Experiments on rats were carried out in accordance with the "Principles for the Care of Laboratory Animals" (1996). Female and male Wistar rats (n=30) were housed individually in polypropylene cages. The females were divided into 3 groups: control, experimental group 1, and experimental group 2. The control group received a standard diet. At the stage of pre-gravid preparation and gestation, premium varieties of feed with a complete micronutrient composition, in particular, with a physiological dosage of vitamin B 12, were used in order to exclude B 12-deficient conditions that could affect the result due to the similarity of biochemical mechanisms in the macroorganism of folic acid and B 12 The dosage of folic acid was 0.4 mg/kg per diet, the 1st experimental group received a diet with a dosage of 1 mg/kg per diet, the 2nd experimental group 5 mg/kg per diet. Folic acid was administered orally in 1 ml of 10% sucrose solution. Female rats received folic acid at the stage of pregravid preparation (one week before mating) to form a pool in erythrocytes. Subsequently, females were mated with control males (1 female per 1 male) and the day the vaginal plug was detected was defined as fetal day. Pregnant females were deposited in individual polypropylene cages. Throughout the gestation, the animals were on a given diet. Only after giving birth, the females were deprived of folate support, and folates were not fed to the offspring. The offspring were kept on a standard diet for a month until maturity. A month later, the ability for the first convulsive act was determined on the offspring by administering 20% caffeine-sodium benzoate at the rate of 100 mg/kg of body weight intraperitoneally, the rat pups were preliminarily weighed. This ability was expressed in the time of onset of the attack - i.e., from the moment of drug administration to the appearance of signs of myoclonus of the extremities, loss of stability (signs of ataxia). The rat pups were subsequently humanely euthanized by overdose of the muscle relaxant atracurium, since the dosage of caffeine-sodium benzoate was highly toxic (sub-LD50) (the rat pups were severely sedated before the seizure). Results that strongly deviated from the average value of the emerging specific picture for the group were rejected. In each group n = 15. Statistical analysis of the data was carried out using the Student t-criterion.

Results.

At the stage of pregravid preparation and gestation, we noticed some features. The rats of the experimental groups, which received 1 mg/kg and 5 mg/kg per diet, showed increased behavioral activity, they performed more locomotor actions, more actively contacted each other, more readily drank, in contrast to the control group, while convulsive activity in the experimental groups of rats was not noticed. These behavioral features were of interest to us, so they are included in the results. However, they are not the focus of this study.

After determining the ability to the first convulsive act by introducing 20% sodium caffeine benzoate solution, a table was compiled and the average value for each group was calculated.

There are statistically significant differences between the experimental groups and the control group ($p < 0.01$), between the experimental groups the differences were also statistically significant ($p < 0.01$).

Discussion.

Our data may indicate a change in synaptic density as a result of an excess of synthetic folic acid during the formation of NT and subsequently during the differentiation of nervous tissue into the CNS. This may be due to the fact that folic acid, being a conjugate in structure dihydropteroic to-you and L -glutamate, is able to increase the activity of neurons as a result of increased glutamatergic transmission, acting through AMPA - R and NMDA - R. With the development of the neural tube and the differentiation of the fetal nervous tissue, it is precisely the enhancement of such transmission that can provoke a qualitative and quantitative acceleration of the development of neural connections. In physiological concentrations, this has a positive effect, eliminating severe neurodegenerative malformations, as well as possible autism spectrum disorders. However, in excess, there may be excess neural and synaptic activity.

Folic acid is also involved in methylation processes - the formation of S -adenosylmethionine, which is also involved in the methylation of cytosine in the DNA structure. In excess of methylating agents, the control of epigenetic events may be impaired, leading to excessive DNA methylation and possible neurological symptoms. In addition, folic acid is directly involved in the biosynthesis of nucleotides de novo, they can be synthesized in excess (of course, with sufficient plastic and energy supply) - which can also be the cause of a decrease in the convulsive threshold.

Conclusion.

Thus, this study shows a correlation between a surplus of folic acid in the mother's diet and a decrease in the convulsive threshold in the offspring subsequently.

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