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THE ROLE OF HYPERHOMOCYTEINEMIA IN THE DEVELOPMENT OF COGNITIVE DISORDERS IN CHRONIC BRAIN ISCHEMIA

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Summary
Chronic ischemia of the brain (dyscirculatory encephalopathy) in terms of prevalence occupies a leading place in the structure of cerebrovascular diseases [P. Kamchatnov P. R., et al., 2008]. One of the dominant manifestations of chronic cerebral ischemia is a violation of cognitive functions, leading to social disadaptation of patients [NN Yakhno, 2006]. Currently, there are conflicting data in the literature on the relationship of hyperhomocysteinemia with cognitive impairment and on the effect of hyperhomocysteinemia on the progression of cognitive disorders [Kim J., et.al., 2007]. There is also an opinion that denies the existence of a relationship between hyperhomocysteinemia and the increase in cognitive disorders. Many articles and dissertations by international scientists were analyzed, which were based on various books, dissertations, as well as electronic journals.

Keywords: cognitive functions, dyscirculatory encephalopathy, cognitive impairment, brain damage, vascular dementia

РОЛЬ ГИПЕРГОММОЦИТЕИНЕМИИ В РАЗВИТИИ КОГНИТИВНЫХ НАРУШЕНИЙ ПРИ ХРОНИЧЕСКОЙ ИШЕМИИ МОЗГА

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Резюме
Хроническая ишемия головного мозга (дисциркуляторная энцефалопатия) по распространенности занимает ведущее место в структуре цереброваскулярных заболеваний [П.Камчатнов П. Р., и соавт., 2008]. Одним из доминирующих проявлений хронической ишемии мозга является нарушение когнитивных функций, приводящее к социальной дезадаптации больных [Н.Н.Яхно, 2006]. В настоящее время в литературе имеются противоречивые данные о связи гипергомоцистеинемии с когнитивными нарушениями и о влиянии гипергомоцистеинемии на прогрессирование когнитивных расстройств [Kim J., et.al., 2007]. Существует также мнение, отрицающее наличие взаимосвязи

гипергомоцистеинемии и нарастания когнитивных расстройств. Было проанализировано множество статьей и диссертаций международных ученых, в основе которых были различные книги, диссертации, а также электронные журналы.

Ключевые слова: когнитивные функции, дисциркуляторная энцефалопатия, когнитивные нарушения, поражение головного мозга, сосудистая деменция.

BOSH MIYANING SURUNKALI ISKEMIYASIDA KOGNITİV BUZILISHLAR RIVOJLANISHIDA GIPERGOMOTSİTEINEMİYANING ROLI

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Annotatsiya
Miyaning surunkali ishemiyasi (diskirkulyator ensefalopatiya) tarqalish darajasi bo'yicha serebrovaskulyar kasalliklar tarkibida etakchi o'rinni egallaydi [P. Kamchatnov P. R., va boshq., 2008]. Surunkali miya ishemiyasining asosiy ko'rinishlaridan biri bu kognitiv funktsiyalarning buzilishi bo'lib, bemorlarning ijtimoiy disadaptatsiyasiga olib keladi [NN Yaxno, 2006]. Hozirgi vaqtda adabiyotda giperhomosisteinemiyaning kognitiv buzilishlar bilan bog'liqligi va giperhomosisteinemiyaning kognitiv buzilishlarning rivojlanishiga ta'siri bo'yicha qarama-qarshi ma'lumotlar mavjud [Kim J., va boshq., 2007]. Giperhomosisteinemiya va kognitiv buzilishlarning kuchayishi o'rtasidagi bog'liqlik mavjudligini inkor etuvchi fikr ham mavjud. Xalqaro olimlarning ko‘plab maqola va dissertatsiyalari tahlil qilindi, ular turli kitoblar, dissertatsiyalar, shuningdek, elektron jurnallar asosida tayyorlandi.

Kalit so'zlar: kognitiv funktsiyalar, dissirkulyator ensefalopatiya, kognitiv buzilish, miya shikastlanishi, qon tomir demans

Relevance
Currently, the prevalence of cerebrovascular disease (CVD) is increasing due to the steady aging of the population. Depending on the localization of the pathological process, CVDs can manifest themselves as motor, sensory, speech, emotional, and other disorders. In economically developed countries, mortality from these diseases occupies the 2nd–3rd place in the structure of total mortality. Over the past 40 years,

the incidence of stroke has increased by 42% in high-income countries per capita, while in middle- and low-income countries it has increased by more than 100%. Cerebrovascular diseases are a serious health problem that entails significant economic losses and the burden of individual medical expenses, which necessitates early prevention and diagnosis of this pathology. With the exception of rare congenital forms of CVD, most of them can be prevented by controlling risk factors such as arterial hypertension (AH), smoking, obesity, and diabetes mellitus (DM). The incidence of CVD increases with age. In 2017, people aged 60 and over accounted for 13% of the world's population, i.e. approximately 962 million people. It is predicted that by 2030, 2050 and 2100 their number will increase to 1.4 billion, 2.1 billion and 3.1 billion people, respectively. A recently published Korean study presents the risks of developing CVD. In the general population, which included 3662 individuals aged 40 to 80 years, 52.0% were men (n = 1904). The mean age of participants at entry into the study was 50.5 ± 7.5 years for the entire population and 50.1 ± 7.3 and 50.9 ± 7.8 years for men and women, respectively. During the 12-year follow-up period, CVD developed in 128 individuals, including 69 men and 59 women. The incidence was significantly higher in men (3.5/1000 person-years) than in women (3.2/1000 person-years). The incidence of CVD increased from 2.2% in the first 3 years of follow-up to 4.3% in the next 3 years of follow-up and to 5.0% in the last 3 years of follow-up. In an earlier study by J. Marrugat et al., conducted in Spain, the cumulative incidence of CVD per 100,000 people was 218 in men and 127 in women [Pizova N.V., 2022].

Cerebrovascular diseases are one of the most important medical and social problems. One of the severe consequences of cerebrovascular diseases is the impairment of cognitive functions. Cognitive disorders (CD), along with other neurological disorders, are important manifestations of the organic pathology of the brain. Vascular CRs go through several stages in their development, and the most severe form of damage to cognitive functions is vascular dementia (DM). In DM, neuropsychological symptoms of frontal dysfunction predominate over memory impairment, as well as the presence of neurological symptoms in the initial stages of the disease. The main factors in the development of CR are: arterial hypertension, atherosclerosis, heart disease, diabetes mellitus, etc. These factors contribute to the development of lacunar infarcts and leukoaraiosis, which precede the occurrence of both moderate CR and dementia.

In patients with diabetes, depressive disorders are observed in 87% of cases. Attachment of depression to the vascular lesion of the brain leads to a deepening of the CR. The relationship between depression and vascular disease is determined by

hemodynamic factors, which manifest themselves in an increase in blood pressure and a decrease in cardiac output in response to various emotions of the subjects. Also, with depressive disorders, hypercoagulation syndrome is noted. Neuroimaging methods reveal functional changes in the brain in depression in the form of a decrease in blood flow and glucose metabolism, mainly in areas responsible for cognitive functions. [Abdurakhmanova R.F., 2014].

Chronic ischemia of the brain (dyscirculatory encephalopathy) in terms of prevalence occupies a leading place in the structure of cerebrovascular diseases [P. Kamchatnov P. R., et al., 2008]. One of the dominant manifestations of chronic cerebral ischemia is a violation of cognitive functions, leading to social disadaptation of patients [NN Yakhno, 2006].

Cognitive impairment can vary in severity from mild forms to the most severe condition - dementia. Mild and moderate cognitive impairments do not significantly impede professional and social activity, but are predominantly progressive in nature. In 55-65% of cases, within 5 years, there is a transformation of moderate cognitive impairment into clinically defined dementia, predominantly of the Alzheimer's type [A.B. Lokshina, 2008].

In addition to the most well-known pathogenic factors in the development of cognitive impairment in patients with chronic cerebral ischemia (atherosclerotic vascular lesions and arterial hypertension), the role of dysfunction of metabolic substances, one of which is the sulfur-containing amino acid homocysteine, is currently being actively studied. An increase in the level of homocysteine, which is formed as a result of the metabolism of methionine, which enters the body with food proteins, can be either an independent onset of a pathological condition or a consequence of a developed disease. Excessive accumulation of homocysteine inside the cell can lead to DNA damage, disruption of cell activity, up to its death. This amino acid is able to activate the aggregation activity of platelets, as well as block endothelial NO-synthase, which is manifested by dysregulation of vascular tone, thickening of the intima/media of the arteries, and hyperplasia of smooth muscle tissues. In addition, homocysteine has a neurotoxic effect.

Currently, there are conflicting data in the literature on the relationship of hyperhomocysteinemia with cognitive impairment and on the effect of hyperhomocysteinemia on the progression of cognitive disorders [Kim J., et.al., 2007]. There is also an opinion that denies the existence of a relationship between hyperhomocysteinemia and the increase in cognitive disorders.

At the same time, works on the study of the level of homocysteine in patients with cognitive impairments who do not reach the degree of dementia are single and fragmentary, which determined the relevance of this study.

Chronic ischemia of the brain (dyscirculatory encephalopathy) in terms of prevalence occupies a leading place in the structure of cerebrovascular diseases (Gusev E.I., Skvortsova V.I., 2001, 2005; Skvortsova V.I., 2002, 2008; Suslina Z.A., 2002, 2006; Yakhno H.H., 2002, 2004; Fedin A.I., 2004, 2009; Boyko A.N. et al., 2008; Bergener M., 1993; Petersen R. S., 1997, 2002; Collie A., Maruff P., 2002). One of the dominant manifestations of chronic cerebral ischemia is a violation of cognitive functions, leading to social exclusion of patients (Rukhmanov A.A., 1991; Damulin I.V., 1997; Yakhno H.H., 2004, 2006; Fedin A.I., 2005, 2007; Zakharov V. .V., Yakhno H.H., 2005; Bullock R., 2002; Sarra S.F., 2008).

In addition to the most well-known pathogenetic factors in the development of cognitive impairment in patients with chronic cerebral ischemia (atherosclerotic vascular lesions and arterial hypertension), the role of dysfunction of metabolic substances is currently being actively studied, one of which is the sulfur-containing amino acid homocyssin. An increase in the level of homocysteine, which is formed as a result of the metabolism of methionine, which enters the body with food proteins, can be either an independent onset of a pathological condition or a consequence of a developed disease. (Fedin A.I. et al., 2002; Kalashnikova JI.A. et al., 2004; Boot G.L., 2000; Janson J.J., 2002; Hainaut P., 2002; Ozmen V., 2006; Orzechowska-Pawilojc A. , 2007). Excessive accumulation of homocysteine inside the cell can lead to DNA damage, disruption of cell activity, up to its death. This amino acid is able to activate platelet aggregation activity, as well as block endothelial NO-synthase, which is manifested by dysregulation of vascular tone, thickening of the intima / media of arteries and hyperplasia of smooth muscle tissues (Mayer E., 1996; Lentz S., 1997; Spence J., 1997 ; Stein J., Me Bride P., 1998). In addition, homocysteine has a neurotoxic effect (Fedin A. I. et al., 2002; Bisschops R., 2004)

Currently, there are conflicting data in the literature on the relationship of hyperhomocysteinemia with cognitive impairment and on the effect of hyperhomocysteinemia on the progression of cognitive disorders (Quadri R., 2005; Ravaglia G., 2005; Dimopoulos N "2006; Kim J., 2007; Nilsson K" 2007 ; Haan M.N., 2007; Blasko I., 2008; Oulhaj A., 2009). There is also an opinion that denies the existence of a relationship between hyperhomocysteinemia and an increase in cognitive impairment (Ariogul S., 2005; Lewerin C., 2005; Tabet N 2006; Krieg E.F., 2009; Hengstermann S., 2009).

A comprehensive clinical, neurological, neuropsychological and laboratory examination of 121 patients found that dysmetabolic disorders, among which an important role is played by a violation of homocysteine metabolism, are one of the mechanisms for the development of cognitive impairment in chronic cerebral ischemia. In patients with chronic cerebral ischemia, moderate hyperhomocysteinemia with a level of more than 15 μmol/l (mean values of the indicator were 18.8±0.8 μmol/l) leads to an increase in the severity of cognitive impairment. The most informative neuropsychological tests for detecting cognitive impairment in hyperhomocysteinemia in patients with chronic cerebral ischemia are a battery of frontal dysfunction tests and a test for speech activity with the study of literal and semantic associations, which was expressed in a statistically significant average inverse correlation with the level of homocysteine in blood plasma. The same trend persisted in the clock drawing test, the MMBE test, and the five word test, but the correlation was less pronounced. An increase in the level of hyperhomocysteinemia is associated with an increase in the severity of clinical manifestations of chronic cerebral ischemia, which is confirmed by data from a study of quantitative neurological scales, and does not depend on the age of patients. Hyperhomocysteinemia can be a marker of cognitive impairment and an independent risk factor for the development of dementia, which proves the need for a mandatory study of the level of homocysteine and, if it is detected, therapeutic and preventive measures in patients with clinical signs of chronic cerebral ischemia. [A.S. Kaluga, 2010].

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