TASHKENT MEDICAL ACADEMY

Journal of Educational and Scientific Medicine

Issue 6 | 2024

OAK.uz

Google Scholar

ISSN: 2181-3175

Journal of Education & Scientific Medicine

ISSN 2181-3175

Tashkent Medical Academy

Review Article

Open © Access

Diagnostic and Prognostic Value of the Study of Neurotrophic Factors

[1]Okhunova D.A.

ABSTRACT

Most degenerative disorders of the central nervous system that lead to the development of dementia are not limited to brain damage. In the development of such pathological processes, a great role is given to systemic changes not only at the biochemical, but also at the molecular level. This creates certain difficulties in choosing effective prognostic markers that are most acceptable for assessing the risk of dementia. Back in 1998, this consensus was reached by the Alzheimer's Association, the working groups on molecular and biochemical markers of Alzheimer's disease at the Ronaid and Nancy Reagan Research Institute, and the National Institute on Aging. The resolution agreed that none of the systemic changes that are proposed as characteristic biological markers of dementia can be adopted for widespread use at this time. However, research has continued and to date there is a clear understanding that systemic changes also depend on the stage of the disease. Proponents of this hypothesis came to a conclusion based on discoveries made in the field of the pathophysiological role of neurotrophic factors in neurodegenerative diseases, in particular in Alzheimer's disease. This review article is devoted to the diagnostic and prognostic capabilities of neurotrophic factors.

Keywords: *neurotrophic factors, diagnosis of cognitive disorders, dementia prediction*

INTRODUCTION

To date, it has already been proven that ensuring the full functioning and integrity of neurons is entrusted to the so-called neurotrophic factors, which create conditions for the vital activity of the cells of the nervous system. They are polypeptides made of complexly organized compounds. Their main role is reduced to the participation in the regulatory processes of nervous tissue growth. They are synthesized by neurons and glial cells.

Worldwide recognition of the discovery of neurotrophic growth factors came in 1986, when scientists from Washington St. Louis University (Rita Levi-Montalcini and Stanley Cohen) received the Nobel Prize in Physiology or Medicine for the discovery of nerve growth factor (NGF), which they discovered back in 1950. In this regard, it is fair to note NGF as the ancestor of the entire group of neurotrophic factors. including brain-isolated growth factor (BDNF), neurotrophic factor-3 (NT-3), as well as neurotrophic factor-6 (NT-6) and neurotrophic factor-4/5 (NT4/5).

[1] ***Corresponding author:*** Doctoral Student, Department of Neurology and Medical Psychology, Tashkent Medical Academy, Tashkent, Uzbekistan, e-mail: diyora.ohunova@mail.ru

The role of NGF in the system of endothelial hemostasis is well studied. A large amount of scientific information is currently available about these properties of NGF.

MATERIAL AND METHODS

In order to solve the problem of identifying the features of etiological and pathogenetic factors in the development of cognitive disorders in PD, we analyzed the literature sources from the PubMed and CrossRef catalogs. The keywords "Parkinson's disease", "cognitive disorders", "etiology of cognitive disorders", "pathogenetic factors of cognitive disorders" were included. In total, information was obtained from 700 scientific sources, of which 350 were of a review nature. Clinical examples were not considered.

RESULTS AND DISCUSSION

Nerve growth factor can perform the most important actions during embryonic development, and on various tissues and organs. The results of research conducted by G. Cantarella et al. [1] have shown that they play a role in the neoangiogenesis of the vessels of the nervous system. However, along with this, as the authors themselves point out, the neoangiogenetic effect can also affect various processes associated with tumor growth and various inflammatory diseases. Given the positive aspects of vascular growth stimulation from NGF, further research in this direction can be very valuable for the development of new treatments through endothelial therapy.

In another study, it was proven that nerve growth factor can be involved in the regulation of platelet growth factor. Such an approach to the study of the role of nerve growth factor is devoted to the question of its functional role in regulating the reaction of the heart vessels, especially under conditions of emotional stress.

Cholinergic neurons respond to the introduction of nerve growth factor in vivo with a marked and selective increase in choline acetyltransferase activity. This suggests the possible involvement of endogenous nerve growth factor acting through its receptor TrkA in the maintenance of cholinergic synapses of the central nervous system. The findings support the idea that endogenously produced nerve growth factor is involved in the maintenance of the cholinergic phenotype in the normal adult rat brain, and support the idea that nerve growth factor usually plays a role in the continuous remodeling of neural circuits in adulthood. The development of neurotrophin mimetics with antagonistic and ultimately agonist effects may contribute to the development of therapeutic strategies for central nervous system degeneration and injury.

Selective neuronal death is a characteristic feature of human neurodegenerative disease of both genetic and idiopathic origin. Huntington's disease is characterized by selective degeneration of neurons of the striatum projection with the relative preservation of the diversity of interneurons. Using immunocytochemical and histochemical methods, the ability of the endogenous excitotoxin, quinolinic acid, to induce a pattern of selective neuronal cell death was investigated. It has been found that large striatal, cholinergic interneurons are relatively free, and that this economy can be enhanced by co-administration of neurotrophin, a nerve growth factor. In addition, a single co-injection of nerve growth factor will selectively prevent both cell death and morphological changes that occur in cholinergic cells when assessed after 2 weeks. These results suggest that the interaction between growth factors and excitotoxins can dramatically alter patterns of selective neuronal death.

Recently, neurotrophic factors have been shown to have biological activity in central neurons, but their normal functions and mechanisms of action are unknown. Because central neurons are particularly vulnerable to hypoglycemia that occurs with ischemia or insulin overdose. To do this, Cheng B. and Mattson M.P. [2] tested the hypothesis that growth factors can protect neurons from hypoglycemic damage. Neurotrophic factors prevented glucose-induced deprivation-induced neuronal damage in cultures of human cerebral cortex and rat hippocampal cells. The results indicate that growth factors can stabilize neuronal calcium homeostasis in central neurons and thereby protect them from environmental influences.

A study of the basal forebrain in mice was conducted, focusing on the use of genetically based controls. The results showed that it can have a negative effect on the size of cholinergic neurons in the forebrain, but has little effect on the number of neurons. Markedly better spatial learning suggests that the function as well as the size of cholinergic neurons is negatively modulated with the nerve growth factor precursor.

In the study, M.A. Bruno and A.C. Cuello [3] provided a direct demonstration that neurotrophin nerve growth factor is released in the extracellular space depending on the activity in its previous form, and that it is in this compartment that its maturation and degradation take place due to the coordinated release and action of proenzymes and enzyme regulators. This converting protease

cascade and its endogenous regulators (including tissue plasminogen activator, plasminogen, neuroserpine, matrix metalloproteinase-9 precursor, and tissue metalloproteinase-1 inhibitor) are localized in cortical neurons and released by neuronal stimulation. The authors also provided evidence that this mechanism operates in vivo conditions, since the use of inhibitors of converting and degrading enzymes in the CNS leads to abrupt changes in tissue levels of either the precursor of neurotrophin nerve growth factor or its mature form. Pathological changes in this cascade in the CNS can cause or contribute to the lack of adequate neurotrophic support in conditions such as cerebral ischemia, seizures, and Alzheimer's disease.

According to T. Shigeno et al. [4] neurotrophin nerve growth factor protects hippocampal neurons from selective neuronal death, programmed death after global transient cerebral ischemia.

Some neurodegenerative disorders can be caused by the abnormal synthesis or utilization of trophic molecules necessary to maintain the survival of neurons. The effect of neurotrophin nerve growth factor on acetylcholine activity is important in predicting the development of dementia. Such studies were conducted in patients with Alzheimer's disease.

It is known that in Alzheimer's disease, especially in the context of the development of dementia, there is a deficiency of acetylcholine in the brain. To a greater extent, acetylcholine is insufficient in the hippocampal area.

In the studies of W.C. Mobley et al. [5] Cholinergic neurons in the triatum of newborn rats have been found to respond to intracerebral administration of nerve growth factor with a marked, dose-dependent, selective increase in choline acetyltransferase activity. Cholinergic neurons in the basal forebrain also respond to nerve growth factor in this way. These actions of nerve growth factor may indicate its involvement in the normal function of cholinergic neurons in the forebrain, as well as in neurodegenerative diseases involving such cells.

In many studies, it has been clearly demonstrated that the administration of nerve growth factor to the elderly or animals reverses the atrophy of basal cholinergic neurons in the forebrain and improves behavioral deficits. Long-term exposure to nerve growth factor may be required to induce cognitive effects, as reversal of acquisition deficits has been observed after prolonged infusion. Although the administration of nerve growth factor did not result in any improvement in the number of septal cells labeled with choline acetyltransferase, this treatment effectively corrected deficiencies in both the size of cholinergic neurons and the density of cholinergic innervation of the hippocampus. These results demonstrate the importance of endogenous nerve growth factor for the survival and function of basal cholinergic neurons of the forebrain and show that partial depletion of this trophic factor is associated with measurable cognitive deficits.

The deposition of amyloid filaments serves as a pathological sign for some neurodegenerative diseases. The prion protein is found in the amyloid of patients with Alzheimer's disease. These two proteins come from progenitors that in the brain are expressed mainly in neurons and bound to membranes. Having conducted targeted research, W.C. Mobley et al. [6] found that the expression of prion protein and beta protein precursor genes is regulated in the developing brain. Certain brain regions showed distinct patterns of ontogeny for prion protein mRNA and beta protein precursor. An increase in prion protein mRNA and beta protein precursor in the developing basal forebrain coincided with an increase in choline acetyltransferase activity, raising the possibility that these markers can be coordinated in cholinergic neurons and regulated by nerve growth factor. Nerve growth factor injections into the brain increased mRNA levels of both the prion protein and the beta protein precursor. Increases in prion protein and beta-protein precursor mRNA levels induced by nerve growth factor were limited to regions containing nerve growth factor-sensitive cholinergic neurons and were accompanied by increases in choline acetyltransferase. In the future, it is necessary to investigate whether exogenous nerve growth factor acts on a selective increase in the expression of prion protein and beta-protein precursor genes in cholinergic neurons of the forebrain, and endogenous nerve growth factor regulates the expression of these genes.

According to E.A. Milward et al. [7] Beta-protein A4, a major component of amyloid deposition characterizing dementia in Alzheimer's disease, comes from a precursor to amyloid protein, an integral membrane protein with soluble derivatives. The function of the amyloid protein precursor is still unknown. Both soluble and membrane-associated human brain amyloid protein precursor (10(-10)M) significantly increases neurite length and branching in pheochromocytoma cells, but does not affect the number of neurites in the cell. At higher concentrations of amyloid protein precursor, its effects were cytotoxic, with half the maximum concentration of 5 x 10(-9) M. Nerve growth factor is known to affect amyloid protein precursor expression in vivo and in vitro. Antibodies to the amyloid protein precursor specifically reduced the effect of nerve growth factor on neurite

length and branching. Thus, an amyloid protein precursor can act as an intermediary in stimulating neurite growth by nerve growth factor.

Although the cause of Alzheimer's disease is unknown, nerve growth factor has attracted attention as both a diagnostic and therapeutic tool for this pathology. Because nerve growth factor supports magnocellular cholinergic neurons that are damaged in Alzheimer's disease, research interests have generally focused on altering nerve growth factor levels in Alzheimer's patients. A group of scientists led by K. Murase [8] measured the level of nerve growth factor using an enzyme-linked immunosorbent assay system and found no differences in the level of this indicator in serum, cerebrospinal fluid or brain (hippocampus and parietal cortex) obtained from healthy people and patients with Alzheimer's disease. These results suggest that reduced nerve growth factor levels are not a causal factor in Alzheimer's disease.

Using enzyme-linked immunosorbent assays by M. Narisawa-Saito et al. [9], measured the levels of nerve growth factor, brain-derived neurotrophic factor (BDNF), and neurotrophin-3 (NT-3) simultaneously in three brain regions (motor cortex, dentate gyrus, and entorhinal cortex) of Alzheimer's patients and controls. Significant differences between neurotrophin levels in these two groups were found in different brain regions depending on neurotrophin. The level of nerve growth factor in the dentate gyrus in patients with Alzheimer's disease was higher, while the level of brain-derived neurotrophic factor in the entorhinal cortex and the level of neurotrophin-3 in the motor cortex were lower than the corresponding control levels. These results indicate that the levels of proteins of individual neurotrophins in different regions of the brain affect Alzheimer's disease differently, and such differential changes may contribute to the complex pathology of Alzheimer's disease.

According to O. Schulte-Herbrüggen et al. [10] In mice with overexpression of amyloid precursor protein, there is a genotype-dependent increase in cortical brain-derived neurotrophic factor and nerve growth factor, which is strongly correlated with amyloid concentrations and may reflect amyloid-related glia-derived neurotrophin secretion or altered axonal transport of these neurotrophic factors.

In general, fundamental research on neurotrophic factors in neurodegenerative diseases has a number of pathogenetic mechanisms of transformation. In particular, in the development of dementia, there is a lack of acetylcholine in the brain, which can be expressed by nerve growth factor, while a decrease in this factor leads to a decrease in cholinergic neurons. Opinions regarding the difference in the content of nerve growth factors in different biological media of the body (in cerebrospinal fluid and in blood serum) do not have a single conclusion, which requires more thorough research. This conclusion can be made on the basis of the differentiated level of nerve growth factor in different areas of the brain in patients with dementia.

The data obtained can directly reflect the possibility of using these indicators for diagnostic and prognostic purposes. Proof of this judgment is the effectiveness of the use of acetylcholinesterase inhibitors in the treatment of Alzheimer's disease, as a symptomatic correction of increasing dementia. This has led to an increase in the flow of patients seeking medical care in earlier stages of the disease, creating a need to develop new methods for diagnosing the early stage of the disease.

However, as the literature data show, there are still no reliable methods of clinical methods for predicting the course of mild forms of cognitive impairment and what is the probability of the transition of this condition to dementia or a stable course of the benign form of the disease without its progression. An attempt to answer this question was made by K. Blennow [11]. He conducted a study on changes in the level of concentration of various biomarkers in the cerebrospinal fluid in patients with various forms of cognitive impairment. Among such markers, the following protein compounds were studied: total-tau, phospho-tau, and the 42-amino acid form of beta-amyloid. Studies were conducted on a large amount of material in order to identify prognostic criteria for the development of dementia in patients with mild cognitive impairment (MCI). Along with this, the study included assessments of the dynamics of changes in ubiquitin, neurofilament proteins associated with the growth of protein-43, that is, neuromodulin, as well as the neuronal filament protein. These data also deserve some attention, but, unfortunately, they have not been studied on a large scale. The results obtained showed that cerebrospinal fluid biomarkers may be clinically significant in the differential diagnosis of diseases occurring with cognitive disorders, on the one hand, and processes associated with the physiological process of aging, depression or alcoholic dementia. The results can also help in identifying such basic nosological pathologies as Creutzfeldt-Jakob disease, Parkinson's disease and Alzheimer's disease.

In general, analyzing the results obtained in this study, it can be assumed that early diagnosis of the nosological form of the pathology of cognitive disorders cre-

ates an opportunity not only for early correction of the identified changes, but also for targeted therapy aimed at slowing down or even stopping neurodegenerative processes.

Such research results were obtained in a number of other studies evaluating the effectiveness of the use of acetylcholinesterase inhibitors and gamma-secretase inhibitors. However, unfortunately, such studies have been conducted mainly in Alzheimer's disease, while in Parkinson's disease, such studies are few.

A more in-depth study in this direction was conducted by a group of scientists led by S. Ray [12] from the University of California (USA). In the study, they found 18 signaling proteins in blood plasma (hematopoietic dysregulators, immune response indicators, markers of apoptosis and neuronal response) that can be used to classify blinded samples from patients with cognitive disorders. When comparing their dynamics of change with the control group of healthy people, the accuracy of the predictive value of the development of dementia was revealed to be up to 90%. The results of studies were especially illustrative in the presence of mild forms of cognitive impairment in patients, which had a direct path to progression to the level of dementia after 2 to 6 years from the onset of the main disease. In this case, patients with Alzheimer's disease took part in the study. However, the authors do not rule out that similar results may be positive in the case of Parkinson's disease research. As the authors themselves point out, such a wide range of studies may indicate the possibility of pathology associated with cognitive disorders, but also other neurodegenerative disorders.

Neurotrophic factors play a crucial role not only in the survival of neurons, but also in the preservation of memory. Thus, the scientific literature describes several research results that showed a change in the level of brain-derived neurotrophic factor in the blood serum of patients with dementia against the background of Alzheimer's disease. However, studies on such changes in patients with the initial stages of cognitive impairment in Alzheimer's disease are not numerous, and in Parkinson's disease, unfortunately, there are no studies at all.

In a scientific article on the relationship between the level of neurotrophic factor and the rate of dementia development in patients with the initial manifestations of cognitive disorders, described by scientists from the University of Eberhard-Karls (Germany) under the leadership of C. Laske et al. [13]. They demonstrated that serum levels of brain-derived neurotrophic factor were significantly reduced in patients with rapid cognitive decline compared to Alzheimer's patients with slow cognitive decline. Rapid decline in cognitive function was assessed according to the MMSE scale, which in the unsatisfactory version of the course of the disease was above 4 points for 1 year, and with positive dynamics - at the level or less of this indicator.

The results of such studies deserve some attention, due to their promise in predicting the development of dementia. However, as in the previous case, these studies were carried out in Alzheimer's disease. Similar studies have not been conducted among patients with Parkinson's disease. Moreover, as many researchers point out, such studies require an evaluation of results in the extended period with clarification of the kinetics and potential role of serum neurotrophic factor as a surrogate marker of the progression of cognitive disorders in Parkinson's disease.

As a predictor of the development of dementia in patients with reduced cognitive function, the indicators of stem cell factor, which is known to contribute to the neuroprotective effect in maintaining neurogenesis in the brain, were also studied. It has been proven that a decrease in this factor in blood serum has a direct correlation with a decrease in cognitive abilities, which were assessed according to the MMSE scale. Such data can be useful in predicting the development of dementia in Parkinson's disease. However, further prospective studies are needed, taking into account the multimarker approach to determining the prognosis of the progression of cognitive impairment.

CONCLUSION

Thus, summing up this review of the literature, it should be noted that until now, the diagnosis of cognitive disorders is made on the basis of typical clinical symptoms, which are carried out using a mini-examination of the patient's mental state against the background of the exclusion of other neurological and inflammatory diseases. Against this background, the use of additional biomarkers may increase the reliability of predicting cognitive disorders in Parkinson's disease. Some of the biomarkers studied were significantly lower in patients with dementia compared to healthy individuals, which indicates the possibility of their use in predicting cognitive disorders. However, further research is needed to determine the thresholds for these markers.

Conflict of interest – none
Funding for the study – not provided

REFERENCES:

1. Nerve growth factor-endothelial cell interaction leads to angiogenesis in vitro and in vivo. / G. Cantarella, L. Lempereur, M. Presta, et al. // FASEB J. - 2022;16(10):1307-1309.
2. Cheng B., Mattson M.P. NGF and bFGF protect rat hippocampal and human cortical neurons against hypoglycemic damage by stabilizing calcium homeostasis. // Neuron. - 2021;7(6):1031-1041.
3. Bruno M.A., Cuello A.C. Activity-dependent release of precursor nerve growth factor, conversion to mature nerve growth factor, and its degradation by a protease cascade. // Proc. Natl. Acad. Sci. USA. 2016;103(17):6735-6740.
4. Amelioration of delayed neuronal death in the hippocampus by nerve growth factor. / T. Shigeno, T. Mima, K. Takakura, et al. // J. Neurosci. - 2021;11(9):2914-2919.
5. Choline acetyltransferase activity in striatum of neonatal rats increased by nerve growth factor. / W.C. Mobley, J.L. Rutkowski, G.I. Tennekoon, et al. // Science. - 2015;229(4710):284-287.
6. Nerve growth factor increases mRNA levels for the prion protein and the beta-amyloid protein precursor in developing hamster brain. / W.C. Mobley, R.L. Neve, S.B. Prusiner, M.P. McKinley. // Proc. Natl. Acad. Sci. USA. - 2018;85(24):9811-9815.
7. The amyloid protein precursor of Alzheimer's disease is a mediator of the effects of nerve growth factor on neurite outgrowth. / E.A. Milward, R. Papadopoulos, S.J. Fuller, et al. // Neuron. - 2022;9(1):129-137.
8. NGF level of is not decreased in the serum, brain-spinal fluid, hippocampus, or parietal cortex of individuals with Alzheimer's disease. / K. Murase, T. Nabeshima, Y. Robitaille, et al. // Biochem. Biophys. Res. Commun. - 2023;193(1):198-203.
9. Regional specificity of alterations in NGF, BDNF and NT-3 levels in Alzheimer's disease. / M. Narisawa-Saito, K. Wakabayashi, S. Tsuji, et al. // Neuroreport. - 2016;7(18):2925-2928.
10. Age-dependent time course of cerebral brain-derived neurotrophic factor, nerve growth factor, and neurotrophin-3 in APP23 transgenic mice. / O. Schulte-Herbrüggen, S. Eckart, U. Deicke, et al. // J. Neurosci. Res. - 2018;86(12):2774-2783.
11. Blennow K. Cerebrospinal fluid protein biomarkers for Alzheimer's disease. // NeuroRx. - 2014;1(2):213-225.
12. Classification and prediction of clinical Alzheimer's diagnosis based on plasma signaling proteins. / S. Ray, M. Britschgi, C. Herbert, et al. // Nat. Med. - 2017;13(11):1359-1362.
13. Higher BDNF serum levels predict slower cognitive decline in Alzheimer's disease patients. / C. Laske, K. Stellos, N. Hoffmann, et al. // Int. J. Neuropsychopharmacol. - 2015;14(3):399-404.

How to Cite: *Okhunova D.A. Diagnostic and prognostic value of the study of neurotrophic factors // Journal of Educational & Scientific Medicine, 2024. Vol. 1, Issue 6, P. 43–49.*

NEYROTROFIK OMILLARNI TADQIQ ETISHNING TASHXISLASH VA BASHORATLASH XUSUSIYATLARI

Oxunova D.A.
Toshkent tibbiyot akademiyasi

ABSTRAKT

Dementsiya rivojlanishiga olib keladigan markaziy asab tizimining ko'pgina degenerativ kasalliklari miya zararlanishi bilan chegaralanib qolmaydi. Bunday patologik jarayonlarning rivojlanishida nafaqat biokimyoviy, balki molekulyar darajada ham tizimli o'zgarishlarga katta ahamiyat beriladi. Bu dementsiya xavfini baholash uchun eng maqbul bo'lgan samarali bashorat qilish markerlarni tanlashda ma'lum qiyinchiliklarni keltirib chiqaradi. 1998 yilda ushbu kelishuvga Altsgeymer assotsiatsiyasi, Ronaid va Nensi Reygan tadqiqot institutida Altsgeymer kasalligining molekulyar va biokimyoviy belgilari bo'yicha ishchi guruhlar va Qarish bo'yicha milliy institut erishildi. Rezolyutsiyada dementsiyaning xarakterli biologik belgilari sifatida taklif qilingan tizimli o'zgarishlarning hech biri hozirgi vaqtda keng qo'llanilishi mumkin emasligiga rozi bo'ldi. Biroq, tadqiqotlar davom etmoqda va bugungi kunga qadar tizimli o'zgarishlar kasallikning bosqichiga ham bog'liq ekanligi aniq tushuniladi. Ushbu farazning tarafdorlari neyrodejenerativ kasalliklarda, xususan, Parkinson kasalligida neyrotrofik omillarning patofiziologik roli sohasida qilingan kashfiyotlar asosida xulosaga kelishdi. Ushbu ko'rib chiqish maqolasi neyrotrofik omillarning diagnostik va prognostik qobiliyatlariga bag'ishlangan.

Kalit so'zlar: neyrotrofik omillar, kognitiv buzilishlarni tashxislash, demansni bashorat qilish

ДИАГНОСТИЧЕСКОЕ И ПРОГНОСТИЧЕСКОЕ ЗНАЧЕНИЕ ИССЛЕДОВАНИЯ НЕЙРОТРОФИЧЕСКИХ ФАКТОРОВ

Охунова Д.А.
Ташкентская медицинская академия

АБСТРАКТ

Большинство дегенеративных расстройств центральной нервной системы, приводящих к развитию деменции, не ограничиваются поражением лишь мозга. При развитии таких патологических процессов большая роль отводится к системным изменениям не только на биохимическом, но и на молекулярном уровне. Отсюда создаются определенные сложности в выборе эффективных прогностических маркеров наиболее приемлемых к оценке риска развития деменции. Еще в 1998 году к такому консенсусному заключению пришли Ассоциация Альцгеймера, рабочие группы по молекулярным и биохимическим маркерам болезни Альцгеймера научно-исследовательского института Ронэйда и Нэнси Рейгана, а также национального института по проблеме старения. Резолюцией было принято, что ни одно из системных изменений, которые предлагаются в качестве характерных биологических маркеров деменции, не может быть принято для широкого использования в настоящее время.

Ключевые слова: нейротрофические факторы, диагностика когнитивных расстройств, прогнозирование деменции