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# Comprehensive Treatment of Cognitive Impairments in Chronic Cerebral Ischemia

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**Abstract** **Introduction:** Numerous scientific studies have been conducted in our country on chronic cerebral ischemia. However, there are currently conflicting opinions regarding the effect of hyperhomocysteinemia on cognitive impairments. At the same time, determining the role of homocysteine in cognitive disorders that have not progressed to dementia is a pressing issue. **Results:** Chronic cerebral ischemia (CCI) is a progressive disease of the central nervous system that affects cognitive functions. In such conditions, dynamic assessment of cognitive impairments is crucial, as it enables the detection of changes in patients' cognitive status, enhances treatment efficacy, and improves quality of life. **Conclusion:** These findings demonstrate the effectiveness of the treatment strategies and confirm their potential to improve the quality of life in patients. The statistical analyses ($\chi^2$) and McNemar's test (P-values) confirm the reliability of these changes, providing valuable insights for future therapeutic approaches.

**Keywords** Chronic cerebral ischemia, Cognitive function, Neuropsychological activity, Homocysteine

## 1. Introduction

The decline in cognitive functions often leads to patients failing to take their medications on time, highlighting the importance of early detection and correction of such impairments. In Uzbekistan, insufficient attention is being paid to these specific aspects of chronic cerebral ischemia. Due to the lack of focus on the nature of the disease progression, diagnosis, and rehabilitation measures, patients are experiencing cognitive difficulties, ultimately resulting in a decline in their quality of life. Therefore, a modern approach to the early diagnosis and treatment of cognitive impairments in chronic cerebral ischemia, as well as the improvement of diagnostic and therapeutic strategies, is a current necessity. Chronic cerebral ischemia belongs to the group of cerebrovascular diseases and affects 700 per 100,000 people worldwide. Over the past decade, the incidence of this disease has doubled globally. Cognitive impairments in chronic cerebral ischemia are observed at a high rate, and their early detection makes it possible to prevent disability. Cognitive impairments in chronic cerebral ischemia can lead to severe cerebrovascular conditions such as stroke and vascular dementia, which are major causes of disability. Therefore, early diagnosis and treatment are urgent tasks for modern medicine.

In the development of cognitive impairments in chronic cerebral ischemia, the role of metabolic changes is being extensively studied, one of which is the sulfur-containing amino acid homocysteine. Homocysteine is a byproduct of methionine metabolism, and it is known to contribute to the development or worsening of pathological conditions. In recent years, the impact of homocysteine on cognitive impairments in chronic cerebral ischemia has been investigated. Researchers have noted that homocysteine plays a role in the development of dementia (Ya-Ru Zhang, 2022). Other studies have shown that a decrease in serum homocysteine and vitamin B12 levels can lead to mild cognitive impairment and dementia (Sun, Yan, 2022). Research conducted in Cuba demonstrated elevated homocysteine levels in the blood of patients with dementia (Lanyau-Dominges I., 2020). Researchers have indicated that homocysteine increases not only the risk of cerebrovascular diseases but also the risk of degenerative dementia (Luzzi S., 2022). Experts believe that the role of homocysteine in the development of cognitive impairments should be further explored in large-scale studies, and that medications aimed at reducing its levels should be developed.

## 2. Materials and Methods

The research was conducted at the Bukhara Regional Multidisciplinary Medical Center. During the study, the diagnosis of chronic cerebral ischemia (CCI) was established based on comprehensive examinations. These included complete neurological and clinical evaluations, brain MRI or MSCT scans, Doppler ultrasonography of the brachiocephalic arteries, and EEG studies. Patients aged between 18 and 69 years suffering from CCI were included in the study. Only

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patients who agreed to participate were enrolled.

Inclusion criteria:

1. Patients aged 18–69 years suffering from CCI (based on WHO age classification).
2. Patient's informed consent.
3. A well-substantiated diagnosis of chronic cerebral ischemia.

The following procedures were carried out during the study:

- Collection and analysis of somatic and neurological status using a questionnaire-survey method (adapted quantitative neurological scale by A. I. Fedin, 2005). This scale allows the evaluation of the severity of focal neurological symptoms in the sections: "general cerebral symptoms", "cranial nerve pathology", "motor system", "sensory analyzer", and "autonomic system".
- Neuropsychological assessment: evaluation of neurological deficits (Clinical Dementia Rating Scale, Mini-Cog Test, MoCA Test, Global Deterioration Scale [Reisberg V., 1982]). Taylor's Anxiety Scale was used to assess patients' emotional status – a questionnaire consisting of 50 statements.
- Laboratory tests: lipid profile, homocysteine level determination.
- Instrumental investigations: MRI/CT scans, EEG.
- Statistical analysis.

The study involved two groups:

1. The main group consisted of 107 patients with CCI who had cognitive impairment and hyperhomocysteinemia.
2. The comparison group (Group 2) included 32 patients with CCI and cognitive impairment, but with normal homocysteine levels.

A total of 139 patients were included in the study. Within the study, patients in both groups were distributed by sex, and statistical analysis was performed for each group. The gender distribution in the main group was as follows:

- The number of male participants was 60, which constituted 56.07±4.8% (M±m) of the total.
- The number of female participants was 47, which constituted 43.93±4.8% (M±m) of the total.
- Statistical analysis using Pearson's Chi-square test yielded a value of 11.540 with $p = 0.001$, indicating a statistically significant difference between the genders.

In the second group, a total of 32 patients participated, and their gender distribution was as follows:

The number of male participants was 7, which accounted for 21.88±7.31% (M±m) of the total.

The number of female participants was 25, accounting for 78.13±7.31% (M±m) of the total.

Statistical analysis using Pearson's Chi-square test yielded a value of 10.125 with $p = 0.001$, indicating a statistically significant difference between genders.

Analysis of gender differences between the groups:

The overall gender distribution of patients in groups 1 and 2 was analyzed. Pearson's Chi-square value was 1.579 with $p = 0.209$, indicating that the difference in gender distribution between the groups was not statistically significant.

We divided the patients into two groups:

Group 1: Patients in this group received a complex of vitamins B1, B6, and B12 (Milgamma) administered intramuscularly once daily for 10 days, followed by oral administration of 1 tablet twice a day for 2 months. Folic acid was given orally in tablet form at a dose of 1 tablet three times a day for 1 month. As an antioxidant and antihypoxant, ethylmethylhydroxypyridine succinate was administered for 10 days in combination with 10 ml diluted in 100 ml of 0.9% sodium chloride solution, followed by oral administration of 125 mg (1 tablet) three times a day for 3 months. Additional standard nootropic therapy was also provided.

Group 2: Patients received the same main medications as Group 1 — a complex of vitamins B1, B6, and B12 (Milgamma) administered intramuscularly once daily for 10 days, followed by oral administration of 1 tablet twice a day for 2 months, and folic acid in tablet form at a dose of 1 tablet three times a day for 1 month. Additionally, standard nootropic therapy was provided.

## 3. Results and Discussion

Chronic cerebral ischemia (CCI) is a progressive disease of the central nervous system that affects cognitive functions. In such conditions, dynamic assessment of cognitive impairments is crucial, as it enables the detection of changes in patients' cognitive status, enhances treatment efficacy, and improves quality of life.

Firstly, dynamic evaluation of cognitive impairments allows for monitoring the progression of the disease. It helps identify whether cognitive functions are deteriorating or improving and provides a foundation for developing preventive or disease-slowing strategies.

Secondly, regular cognitive assessments help determine the effectiveness of treatment regimens. If a particular treatment shows positive effects, its dosage can be maintained or increased; otherwise, the treatment strategy should be revised.

Thirdly, such assessments provide vital information to improve patients' quality of daily life. The decline in cognitive functions may limit a patient's ability to live independently. Therefore, early identification and management of these impairments can significantly enhance their overall condition. In conclusion, dynamic evaluation of cognitive impairments associated with chronic cerebral ischemia is essential for monitoring disease progression, evaluating treatment efficacy, and improving patients' overall quality of life. This approach helps optimize health outcomes and contributes to enhancing patients' well-being.

In our study, patients were divided into groups based on their treatment protocols. Group 1 consisted of patients with elevated homocysteine levels and was randomly divided into

two subgroups:

- Group 1-A: 57 patients received a combination therapy including B-complex vitamins, nootropics, antioxidants, and an antihypoxic agent (ethylmethylhydroxypyridine succinate).
- Group 1-B: 50 patients received B-complex vitamins and nootropics only.
- Group 2: 32 patients with CCI and normal homocysteine levels who received standard nootropic therapy.

The patients' complaints before and after treatment were observed, including headache, dizziness, memory impairment, fatigue, and tinnitus. These symptoms were statistically analyzed using McNemar's test.

In Group 1-A:

- Headache was observed in all 57 patients (100%) before treatment and in 9 patients (15.79%) after treatment ($P < 0.000$).
- Dizziness occurred in 100% of patients before treatment, and in 14 patients (24.56%) after treatment ($P < 0.000$).
- Memory impairment was noted in 54 patients (94.74%) before treatment and in 11 patients (19.3%) afterward ($P < 0.000$).
- Fatigue was present in 56 patients (98.25%) before treatment and in 14 patients (24.56%) after treatment ($P < 0.000$).
- Tinnitus was reported in 43 patients (75.44%) before treatment and in 10 patients (17.54%) afterward ($P < 0.000$).

Groups 1-B and 2 also showed a reduction in these symptoms, although the most significant improvements were seen in Group 1-A. These findings demonstrate the effectiveness of the treatment strategies and confirm their potential to improve the quality of life in patients. The statistical analyses ($\chi^2$) and McNemar's test (P-values) confirm the reliability of these changes, providing valuable insights for future therapeutic approaches. If you'd like this text adapted for inclusion in a scientific article or dissertation chapter (e.g., in Results or Discussion), I can help refine it further for publication standards. When analyzing the results of the study, the dynamics of emotional functions according to the J. Taylor scale showed statistically significant differences in all three groups. Before treatment, the scores were 31.05±1.31 for Group 1-A, 30.8±1.4 for Group 1-B, and 31.25±1.0 for Group 2, with no statistically significant differences observed between the three groups. After the treatment period, J. Taylor scale scores significantly decreased: to 15.35±0.26 in Group 1-A, 15.68±0.29 in Group 1-B, and 15.28±0.4 in Group 2. Compared to the pre-treatment values, the differences were statistically significant for all three groups at $P<0.001$, indicating high statistical relevance.

## 4. Conclusions

Furthermore, comparative analysis between groups revealed no statistically significant difference between Groups 1-A and 1-B, suggesting that the treatment effectiveness in these two groups was nearly identical. The difference between their outcomes was $P>0.05$, meaning it lacked statistical significance. In conclusion, the treatment strategies used in the study led to a clear and reliable improvement in emotional functions. These findings provide an important basis for enhancing emotional function monitoring and developing strategies to manage the progression of the disease. The results of the J. Taylor scale play a crucial role in assessing the impact of treatment on patients' emotional states. According to the study, emotional status significantly improved after treatment in both groups, emphasizing the importance of psychological rehabilitation and its positive influence on the treatment process. Cognitive function changes were assessed using the Mini-Cog test. This test was employed to determine how patients' cognitive states changed before and after treatment. Pre-treatment scores were approximately the same across the three groups: 3.26±0.08 for Group 1-A, 3.28±0.09 for Group 1-B, and 3.34±0.12 for Group 2. Post-treatment results showed marked differences: Mini-Cog scores rose to 4.54±0.07 in Group 1-A, 4.11±0.05 in Group 1-B, and 3.44±0.1 in Group 2. These data indicate that Group 1-A achieved statistically the most significant improvement in cognitive function. The increase in Group 1-A was statistically more meaningful than in Group 1-B ($P<0.001$), demonstrating that this treatment modality was particularly effective for cognitive enhancement. Moreover, the results of Group 2 were inferior to Group 1-A, highlighting the comparatively lower efficacy of its treatment strategy. These indicators are vital for identifying the role of specific treatment methods and their components in cognitive improvement. In summary, the study results show that the treatment strategy used in Group 1-A was the most effective in optimizing cognitive functions. These findings lay the groundwork for improving and expanding this treatment strategy in the future.

EEG parameter changes in patients across the study groups before and after treatment were analyzed using the McNemar's test, allowing assessment of neurophysiological reactions and treatment responses.

The key EEG parameters examined included increased delta and theta wave activity, decreased alpha and beta waves, presence of pathological waves, interhemispheric asymmetry, impaired reactivity to external stimuli, and focal changes.

Regarding the increase in delta and theta waves, in Group 1-A, 41 patients (71.93±5.95%) showed this pattern before treatment, which decreased to 19 patients (33.33±6.24%) after treatment ($P=0.001$). However, in Group 1-B and Group 2, changes in this parameter were not statistically significant ($P=0.186$ and $P=0.815$, respectively).

In the reduction of alpha and beta waves, Group 1-A initially showed this issue in 33 patients (57.89±6.54%), which dropped to just 3 patients (5.26±2.96%) post-treatment ($P=0.000$). Group 1-B also showed similar significant improvements ($P=0.000$), while Group 2 did not exhibit a marked reduction ($P=0.000$). In terms of pathological waves,

a clear therapeutic effect was seen in both Group 1-A and Group 1-B, with noticeable decreases post-treatment (P=0.000 in both groups). Group 2 did not show statistically significant changes (P=0.063). For interhemispheric asymmetry and impaired reactivity to external stimuli, significant post-treatment reductions were observed in all three groups. The P-values for interhemispheric asymmetry were 0.000 (Groups 1-A and 1-B) and 0.002 (Group 2). For impaired reactivity to stimuli, Group 1-A had P=0.000, Group 1-B P=0.000, and Group 2 P=0.031. Focal changes also significantly decreased after treatment in Groups 1-A and 1-B (P=0.000 and P=0.012, respectively), with Group 2 also showing a statistically significant reduction (P=0.004). In conclusion, these analyses, conducted using McNemar's test, provide clear and reliable data on treatment effectiveness. The EEG parameter changes—ranging from delta and theta wave intensification to alpha and beta wave reductions—cover a broad spectrum of neurophysiological phenomena. Some of these changes, particularly the reduction in alpha and beta waves, reflect significant treatment effects (P=0.000). Additionally, the marked post-treatment decreases in pathological waves and interhemispheric asymmetry (P=0.000 and P=0.002, respectively) indicates neurophysiological adaptation to therapy. These findings are foundational for understanding the neurophysiological effects of treatment and developing effective strategies for patient management. The results further reinforce the role of EEG in the diagnosis and monitoring of neuropsychiatric and neurodegenerative disorders and outline key directions for future research.

Summary Dynamic assessment of cognitive impairments in chronic cerebral ischemia plays a crucial role in improving treatment efficacy and enhancing patients' quality of life. According to the main findings of the study, the complex therapy administered to patients in Group 1-A (including B-group vitamins, nootropics, and antioxidants) demonstrated the highest level of improvement in cognitive functions (P<0.001). The most notable positive changes were observed in complaints such as memory impairment, headaches, and rapid fatigue. For example, memory impairment decreased from 94.74% to 19.3% (P<0.001), while headache prevalence dropped from 100% to 15.79% (P<0.001). These results confirm the effectiveness of this treatment combination. Neurophysiological changes: According to EEG analysis, a significant reduction in delta and theta wave intensification was observed in Group 1-A (from 71.93% to 33.33%, P=0.001). Moreover, the decrease in alpha and beta wave suppression dropped from 57.89% to 5.26% (P<0.001). Statistically significant reductions were also noted in pathological waveforms and interhemispheric asymmetry (P<0.001). These findings indicate the neurophysiological efficacy of the treatment and confirm its positive influence on cerebral electrical activity.

Based on the conclusions drawn from the dissertation, diagnostic and treatment algorithms were developed. These algorithms serve as a foundation for assessing cognitive and neurophysiological conditions in patients with chronic cerebral ischemia and ensuring effective treatment.

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## Declaration of Competing Interests

All the authors declare no conflict of interest.

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## Ethics Approval and Consent to Participate

Not applicable.

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