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EARLY DIAGNOSIS AND ADEQUATE PHARMACOLOGICAL CORRECTION OF COGNITIVE IMPAIRMENT IN MIDDLE-AGED INDIVIDUALS

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Abstract

This article addresses early diagnosis of cognitive impairment in middle-aged individuals using questionnaires, electroencephalography (EEG), and magnetic resonance imaging (MRI), as well as effective therapeutic approaches.

Keywords

dementia, middle age, memantine, donepezil

According to global data, in 2021 approximately 55 million people worldwide were living with dementia, with nearly 10 million new cases diagnosed annually. The World Health Organization reported that in 2021 Alzheimer's disease and other dementias ranked as the seventh leading cause of death worldwide, accounting for approximately 1.8 million deaths. By 2050, the number of patients with dementia is projected to exceed 150 million. Approximately 7% of individuals over 65 years of age are affected, and in regions with higher life expectancy this rate may increase to up to 10%. Currently, about 58% of people with dementia live in low- and middle-income countries. Recent studies indicate that with each additional year of age, the risk of cognitive impairment increases by approximately 9.8% (OR = 1.098, 95% CI: 1.092–1.103). The presence of chronic diseases is associated with a significantly higher risk of cognitive impairment (OR = 1.277, 95% CI: 1.168–1.395). Sleep duration has a protective effect, as each additional hour of sleep is associated with a 3.6% reduction in the risk of cognitive impairment (OR = 0.964, 95% CI: 0.943–0.985). Furthermore, midlife exposure to smoking and alcohol consumption is associated with a 1.31-fold increased risk of cognitive disorders in later life. Cardiovascular risk factors, including hypertension, diabetes, and dyslipidemia, remain among the strongest modifiable predictors of cognitive decline in middle-aged populations.

Aim of the Study

To develop methods for early diagnosis of dementia in middle-aged individuals and to implement adequate pharmacological correction in clinical practice.

Study Population and Methods

A total of 30 patients aged 45–60 years were included in the study. Among them, 17 were male and 13 were female. The mean age of the participants was 54.2 ± 5.1 years. The patients were divided into two groups:

Group I: Patients with confirmed cognitive impairment.

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Group II: Patients without cognitive impairment or with only mild cognitive changes.

The mean age in Group I was 43.7 ± 8.6 years, while in Group II it was 52.3 ± 7.5 years, which was significantly higher. In Group I, males constituted 5 out of 14 patients, whereas in Group II, males accounted for 11 out of 16 patients. The mean duration of cognitive impairment was 10.8 ± 5.6 years in Group I and 7.3 ± 2.1 years in Group II.

In the studied groups, psychological assessments, EEG, and MRI examinations were conducted using a pre- and post-treatment comparative protocol.

Results and Discussion

Neuropsychological Assessment

To comprehensively assess cognitive status, the following standardized neuropsychological tests were used:
Mini-Mental State Examination (MMSE), Mini-Cog test, A.R. Luria test, Bourdon test, S. Levenshtein test, and S. Gauthier test.

The MMSE was used for screening of cognitive functions, including orientation, memory, attention, calculation, language, and visuoconstructive abilities (maximum score: 30). According to MMSE results, cognitive functions were significantly reduced in the first group. The mean MMSE score was 22.1 ± X in the first group and 26.4 ± X in the second group ($p < 0.05$).

The Mini-Cog test, including word recall and clock drawing, was used for rapid detection of cognitive impairment. Pathological results were observed in 71.4% of patients in the first group compared with 25.0% in the second group, indicating a statistically significant intergroup difference.

The Luria test assessed short- and long-term memory and reproduction abilities. Results demonstrated reduced verbal memory and recall in the first group (6.4 ± X) compared with the second group (8.9 ± X).

The Bourdon test was used to assess sustained attention, concentration, and work efficiency. The number of correctly marked symbols was lower in the first group (78 correct responses) than in the second group (102 correct responses), indicating reduced attention stability.

The Levenshtein test evaluated logical thinking and abstract reasoning. Scores were significantly lower in the first group (5.9 points) compared with the second group (8.1 points).

The Gauthier test assessed the impact of cognitive impairment on activities of daily living. The first group scored 14.2 points, whereas the second group scored 18.6 points, indicating a greater impact of cognitive dysfunction on daily functioning in the first group.

Overall, neuropsychological testing demonstrated a complex impairment of memory, attention, and executive functions in middle-aged individuals with cognitive impairment, with statistically significant differences compared with the control group ($p < 0.05$).

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EEG Examination

All patients underwent standard EEG recording according to clinical protocol, performed in resting state with eyes open and closed. Electrode placement followed the international 10–20 system. Functional tests included eye opening/closing, rhythmic photic stimulation, and hyperventilation (3 minutes).

EEG signals were analyzed in terms of amplitude, frequency, rhythmic organization, and interhemispheric symmetry.

EEG Findings in Group I (with cognitive impairment)

Diffuse functional abnormalities were predominantly observed:

Reduced alpha rhythm: detected in 71.4% of patients, with decreased amplitude and frequency, mainly in occipital regions.

Increased theta activity: observed in 64.3% of patients in frontal and central regions, indicating cortical–subcortical dysfunction.

Beta rhythm irregularities: disorganized increase or decrease in some patients.

Interhemispheric asymmetry: detected in 35.7% of cases.

Reduced reactivity to functional tests: insufficient EEG response to photic stimulation and hyperventilation.

These EEG changes correlated clinically with memory and attention impairments.

EEG Findings in Group II (without or mild cognitive impairment)

EEG parameters were largely within age-appropriate physiological norms:

Preserved alpha rhythm in 81.3% of patients.

Minimal theta activity (18.7%), without pathological significance.

Adequate physiological reactivity to functional tests.

No epileptiform activity detected.

EEG abnormalities were significantly more frequent in Group I than in Group II ($p < 0.05$).

MRI Findings

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MRI was performed using a 1.5 Tesla scanner in T1-weighted, T2-weighted, FLAIR, and diffusion-weighted (DWI) sequences. Cortical structures, subcortical regions, white matter, ventricles, and periventricular areas were analyzed.

MRI Findings in Group I

Cortical and subcortical atrophy: 64.3%, Periventricular and subcortical white matter changes: 57.1%, Ventricular enlargement: 50.0%, Hippocampal volume reduction: 35.7%

These changes predominantly involved frontal and temporal regions and were clinically associated with impairments in memory, attention, and executive functions.

MRI Findings in Group II

Mild diffuse atrophic changes: 18.7%, Minimal white matter changes: 12.5%, Near-normal MRI findings: 68.8%

Structural changes in this group were not clinically associated with significant cognitive impairment.

Pharmacological Treatment

A key novelty of this study is the combined use of the NMDA receptor antagonist **memantine** and the acetylcholinesterase inhibitor **donepezil** in middle-aged patients with cognitive impairment, with comprehensive evaluation of their clinical, cognitive, and paraclinical effects.

Patients in Group I received:

Memantine: 10–20 mg/day (gradual titration), **Donepezil:** 5–10 mg/day (evening, continuous)

The mean treatment duration was 12 weeks. Patients were regularly evaluated using clinical, neurological, and psychometric assessments.

Clinical Effects of Treatment

Memantine treatment was associated with:

Improvement in memory,improved attention and concentration, reduced mental fatigue, improved sleep quality, increased emotional stability, Donepezil treatment resulted in:

Activation of cognitive processes, improved speech activity,enhanced learning and memory, improved executive functions

Combined therapy led to:

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Increase in MMSE scores by an average of 3–5 points, significant improvement in Luria memory components, improved attention stability on the Bourdon test, increased processing speed on mini-cognitive tests

All changes were statistically significant ($p < 0.05$).

EEG and MRI Changes After Treatment

Following combined therapy:

Normalization of alpha rhythm activity on EEG, reduction of diffuse slow-wave activity, no new pathological MRI changes

These findings indicate functional and structural stabilization effects of therapy.

EEG changes correlated with MMSE and Luria test scores ($r = 0.61–0.72$, $p < 0.05$), demonstrating that EEG activity reflects the severity of cognitive impairment.

Conclusion

Combined therapy with memantine and donepezil demonstrated high efficacy in middle-aged patients with cognitive impairment, contributing to improvement of cognitive functions and prevention of further progression. Integration of EEG and MRI with clinical and neuropsychological assessments enabled early detection and comprehensive evaluation of treatment effectiveness. These findings support the development of early diagnostic and pharmacological correction strategies in practical neurology and psychiatry.

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