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## ABSTRACT

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## FEATURES OF NEUROCOGNITIVE IMPAIRMENTS IN PATIENTS WITH MILD COGNITIVE DISORDER OF DIFFERENT ETIOLOGY

**Introduction.** Mild cognitive disorder (MCD) is a heterogeneous syndrome that involves problems with memory, speech, and thinking that are inconspicuous and do not affect the patient's independence and daily life. The article considers similarities and differences in the neurocognitive profiles of patients with mild cognitive disorders of various etiologies.

**Materials and methods.** We examined 60 people: 30 subjects aged 50 to 83 years with a mild cognitive disorder of various etiologies and 30 relatively healthy individuals as the control group. All patients underwent a magnetic resonance imaging (MRI) examination of the brain. We used the psychometric method and the following scales: the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment Scale (MoCA), the Frontal Assessment Battery (FAB), the Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-cog), the Clinical Dementia Rating (CDR); the results were analyzed using the method of statistical processing.

**Results.** According to the results of neurocognitive testing, no significant differences were found in the total scores ( $p = 0.6209$ ), in particular, using the MMSE scale in patients with non-anamnestic (nMCD) and amnestic (aMCD) mild cognitive disorder and mild cognitive disorder (aMCD). However, patients with nMCD showed significantly lower results with subtests: "attention and calculation" ( $p = 0.0443$ ). According to the MoCA scale, patients with nMCD had a higher score vs. patients with aMCD ( $p = 0.0457$ ), namely in the "delayed recall" subtests ( $p = 0.0102$ ). Patients with nMCD had significantly lower results with the "attention and calculation" subtest ( $p = 0.0468$ ). No significant differences were found between the groups of patients with MCD according to the results of testing with the FAB scale ( $p = 0.4778$ ). According to some subtests of the ADAS-cog scale, patients with aMCD showed worse results with the "word recall" test ( $p = 0.0069$ ) and "word recognition" ( $p = 0.0350$ ). In patients with nMCD, lower scores were observed for the subtests "concentration and distractibility" ( $p = 0.0468$ ), "number cancellation task" ( $p = 0.0217$ ), and "passing the labyrinth" ( $p = 0.0015$ ). Patients with aMCD showed significantly lower cognitive abilities than

patients with nMCD. Consequently, patients with aMCD may be significantly at high risk of progression to Alzheimer's disease.

**Conclusions.** After comparing the data of neurocognitive profiles, we established that in patients with anamnestic mild cognitive disorder, the clinical picture presented with a pronounced memory disorder, especially delayed recall, while the patients with non-anamnestic mild cognitive disorder were characterized by regulatory cognitive impairment (attention and calculation, reduced speed of thinking, impaired planning of activities).

The MoCA and ADAS-cog scores had better diagnostic accuracy and specificity for the detection and differential diagnosis of mild cognitive disorders than the MMSE scale.

**Keywords:** mild cognitive disorder, cognitive screening, diagnosis, neurocognitive scales.

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## РЕЗЮМЕ

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## ОСОБЛИВОСТІ НЕЙРОКОГНІТИВНИХ ПОРУШЕНЬ У ХВОРИХ З МАЛИМ КОГНІТИВНИМ РОЗЛАДОМ РІЗНОЇ ЕТІОЛОГІЇ

**Вступ.** Малий когнітивний розлад (МКР) – це гетерогенний синдром, який включає проблеми з пам'яттю, з мовою, мисленням, є малопомітним і не впливає на самостійність і повсякденне життя пацієнта. У статті розглянуто подібності та відмінності у нейрокогнітивних профілях пацієнтів з малим когнітивним розладом різної етіології.

**Матеріали та методи.** Обстежено 60 осіб, 30 – з малим когнітивним розладом різної етіології, віком від 50 до 83 років, та 30 здорових осіб, які склали групу контролю. Усім хворим було проведено магнітно-резонансну томографію мозку. Використовували психометричний метод, шкали: коротка шкала дослідження психічного статусу (MMSE), Монреальська шкала оцінки когнітивних функцій (MoCA), батарея лобової дисфункції (FAB), шкала Alzheimer disease assessment scale-cognitive (ADAS-cog), метод статистичної обробки результатів.

**Результати.** За результатами нейрокогнітивного тестування було виявлено, що, зокрема, за шкалою MMSE у хворих з малим когнітивним розладом неанамнестичного (нМКР) та анамнестичного типів (аМКР) не спостерігалось достовірних відмінностей загальної кількості балів ( $p = 0,6209$ ). Однак, хворі з нМКР показали значно нижчі результати за субтестами «увага та рахунок» ( $p = 0,0443$ ). За шкалою MoCA, хворі з аМКР мали нижчий бал, ніж пацієнти з нМКР ( $p = 0,0457$ ), а саме в субтестах на відстрочене відтворення ( $p = 0,0102$ ). У хворих з нМКР було відзначено значно нижчі показники за субтестом «увага та рахунок» ( $p = 0,0468$ ). Достовірних відмінностей між групами хворих на МКР за результатами тестування шкалою FAB не знайдено ( $p = 0,4778$ ). За окремими субтестами шкали ADAS-cog, пацієнти з аМКР продемонстрували найгірші результати у виконанні завдань «повторення слів» ( $p = 0,0069$ ) та «впізнання

слів» ( $p = 0,0350$ ). У хворих з нМКР спостерігалися нижчі бали в підтестах «концентрація та відволікання» ( $p = 0,0468$ ), «закреслення цифр» ( $p = 0,0217$ ) та «проходження лабіринту» ( $p = 0,0015$ ). Пацієнти з аМКР показали значно нижчі когнітивні функції, ніж пацієнти з нМКР. Отже, хворі з аМКР значною мірою можуть бути схильні до високого ризику переходу в хворобу Альцгеймера.

**Висновок.** Таким чином, при зіставленні даних нейрокогнітивних профілів у пацієнтів з малим когнітивним розладом амнестичного типу провідними в клінічній картині були виражені порушення пам'яті, особливо відстроченого відтворення, у хворих з неамнестичним – регуляторні когнітивні порушення (увага та рахунок, зниження швидкості процесу мислення, порушення організації діяльності). Шкали MoCA та ADAS-cog мали більш діагностичну точність та специфічність для виявлення та диференціальної діагностики малих когнітивних розладів, ніж MMSE.

**Ключові слова:** малий когнітивний розлад, когнітивний скринінг, діагностика, нейрокогнітивні шкали.

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## INTRODUCTION / ВСТУП

Mild cognitive disorder (MCD) is a heterogeneous syndrome that involves problems with memory, speech, and thinking that are inconspicuous and do not affect the patient's independence and daily life [1]. Patients with MCD have a 4–10 times greater risk of developing dementia compared to cognitively normal elderly people [2, 3]. In particular, the amnestic subtype of MCD (aMCD) is usually associated with a higher risk of developing Alzheimer's disease (AD) and is considered an early, "prodromal" phase with a conversion rate of 15–25% annually [4, 5]. Vascular dementia (VD) is the second most common form of dementia in the elderly after AD, and its subcortical form is caused by damage to small vessels in the brain, which is probably preceded by a non-amnestic type of MCD (nMCD) [6]. A prospective population-based study among the elderly showed that the incidence of dementia was highest in patients with aMCD [7, 8]. Therefore, early prediction and identification can prevent the transformation of MCD into dementia.

**The aim of the study** was to study the neurocognitive profile of patients with mild cognitive disorder of various etiologies.

**Materials and methods.** 60 patients were examined: 30 subjects with mild cognitive impairment of various etiologies (18 men (60%) and 12 women (40%)), aged from 50 to 83 years (mean age  $65.67 \pm 0.8$  years), and 30 relatively healthy individuals as the control group (10 men (33.33%) and 20 women (66.67%)), aged from 51 to 67 years (average age  $65.73 \pm 0.9$  years). The diagnosis of mild cognitive impairment was established according to the updated criteria proposed by the association of the National Institute on Aging in 2016 for the diagnosis of Alzheimer's disease [9].

The criteria for inclusion in the study were: complaints of memory impairment, a decrease in cognitive indicators in one or more domains, including memory, according to the results of neuropsychological testing (no more than 1.5 deviations from the average statistical age indicator), adjusted for education, the absence of pronounced cognitive disorders according to the result of the short scale of mental status assessment (Mini-Mental

State Examination, more than > 24 points), the clinical assessment according to the dementia rating scale (CDR) of 0.5 points, the absence of functional activity disorders in everyday life.

Exclusion criteria were: a history of traumatic brain injury, mental illness and other CNS diseases that could lead to cognitive impairment; severe behavioral and emotional disorders: delirium, anxiety, depression; systemic diseases including thyroid dysfunction, syphilis, severe anemia or HIV that may cause cognitive impairment, brain tumors; use of psychoactive substances (barbiturates, neuroleptics, benzodiazepines, antidepressants, antiepileptic drugs); hydrocephalus, severe visual or hearing impairments that did not allow for sufficient verbal contact.

All patients underwent a comprehensive neurocognitive examination using the following research methods: the Short Mental Status Assessment Scale (MMSE), the Montreal Cognitive Function Test (MoCA), the Frontal Dysfunction Battery (FAB), the Clinical Dementia Rating Scale (CDR) and the cognitive subtest of the Disease Assessment Scale Alzheimer's disease (ADAS-cog) [10, 11]. All patients underwent magnetic resonance imaging (MRI) of the brain. Based on the results of the examinations, the patients were divided into 3 groups: a group with mild cognitive impairment of the amnesic type – 9 patients (aMCD) and 21 – with a minor cognitive disorder of the non-amnesic type (nMCD) and 30 people – a control group. To determine the clinical variant of minor cognitive disorder, cognitive function impairments were assessed according to Luria's brain theory of system dynamic localization of higher mental functions. When a small cognitive impairment was detected in the structure of the II functional block, with memory disorders, in the absence of impairment in blocks I and III, patients were assigned to the group with aMCD. In the case of the presence of disorders in the structure of the functional block I or III, with a violation of attention, regulatory functions, patients were assigned to the group with nMCD [12].

In all patients with nMCD, vascular risk factors and signs of cerebrovascular pathology were determined and confirmed by neuroimaging diagnostic methods (CT, MRI). Patients of this group had a clinical diagnosis of stage I–II dyscirculatory encephalopathy. All patients provided written informed consent before being included in the study. The work was carried out in accordance with the principles of the Helsinki Declaration of the World Medical Association

"Ethical principles of medical research involving a person as a research object", Order of the Ministry of Health of Ukraine No. 690 (from 23.09.2009) and approved by the bioethical commission of Sumy State University (Protocol No. 1/04 dated 04/19/2022).

Statistical processing was carried out using Microsoft Excel 2016 software. A statistical difference was considered at  $p < 0.05$ . Average values are given in the form  $M (m)$ , where  $M$  is the arithmetic mean,  $m$  is the standard deviation. Means were compared using the Mann–Whitney method.

**Results and discussion.** All examined patients with minor cognitive disorders corresponded to 0.5 points on the CDR scale. The average indicator in patients with MCD was lower than in the control group according to the following scales: MMSE ( $p < 0.0001$ ), MoCA ( $p < 0.0001$ ), FAB ( $p = 0.0586$ ), (Table 1).

**Table 1 – Statistical indicators of cognitive scales in groups of patients with mild cognitive disorder and controls ( $M \pm m$ )**

Scale (scores)	MCD (n = 30)	Control group (n = 30)	P value
MMSE mean score	25.2 ± 0.85	29.6 ± 0.49	< 0.0001
MoCA mean score	24.2 ± 0.86	28.8 ± 0.48	< 0.0001
FAB mean score	15.3 ± 0.9	17.2 ± 0.4	0.0586

According to the results of the neurocognitive examination, significant differences were found in the groups of patients with mild cognitive impairment of amnesic and non-amnesic types (Table 2).

The total MMSE score in patients with aMCD and nMCD was lower than in the control group ( $p_2 < 0.0001$ ), ( $p_3 < 0.0001$ ). In particular, patients with aMCD had worse results in the domains "memory" ( $p_2 < 0.0001$ ), "orientation" ( $p_2 = 0.0046$ ). Patients with nMCD – according to the subtests "attention and calculation" ( $p_3 = 0.0019$ ), "memory" ( $p_3 = 0.0124$ ). However, when comparing the neurocognitive parameters on the MMSE scale of patients with nMCD and aMCD, no significant differences in the total number of points were observed ( $p = 0.6209$ ). However, patients with nMCD had significantly lower results on the subtest: "attention and calculation" ( $p = 0.0443$ ).

**Table 2 – Statistical indicators of cognitive scales in groups of patients with various variants of mild cognitive disorder and a control group (M ± m)**

Scale (scores)	aMCD (n = 9)	nMCD (n = 21)	Control group (n = 30)	P value
MMSE mean score	25.1 ± 0.3	25.5 ± 0.5	29.6 ± 0.49	p <sub>1</sub> = 0.6209 p <sub>2</sub> < 0.0001 p <sub>3</sub> < 0.0001
Orientation	8.4 ± 0.7	9.3 ± 0.5	9.9 ± 0.18	p <sub>1</sub> = 0.3215 p <sub>2</sub> = 0.0046 p <sub>3</sub> = 0.2069
Naming	2.5 ± 0.5	2.7 ± 0.4	3.0 ± 0.0	p <sub>1</sub> = 0.7756 p <sub>2</sub> = 0.0671 p <sub>3</sub> = 0.3723
Attention and calculation	4.5 ± 0.52	3.3 ± 0.3	4.87 ± 0.34	p <sub>1</sub> = 0.0443 p <sub>2</sub> = 0.5921 p <sub>3</sub> = 0.0019
Memory	1.5 ± 0.2	2.2 ± 0.37	3.0 ± 0.0	p <sub>1</sub> = 0.2529 p <sub>2</sub> < 0.0001 p <sub>3</sub> = 0.0124
Language	8.4 ± 0.7	8.19 ± 0.4	8.9 ± 0.3	p <sub>1</sub> = 0.7218 p <sub>2</sub> = 0.4579 p <sub>3</sub> = 0.0550
MoCA mean score	23.7 ± 0.4	25.4 ± 0.5	28.8 ± 0.48	p <sub>1</sub> = 0.0457 p <sub>2</sub> < 0.0001 p <sub>3</sub> < 0.0001
Visual and spatial functions	4.3 ± 0.5	4.5 ± 0.5	4.7 ± 0.4	p <sub>1</sub> = 0.8125 p <sub>2</sub> = 0.6127 p <sub>3</sub> = 0.7542
Naming	2.77 ± 0.4	2.8 ± 0.35	2.96 ± 0.18	p <sub>1</sub> = 0.9603 p <sub>2</sub> = 0.6322 p <sub>3</sub> = 0.6611
Attention and calculation	5.2 ± 0.4	4.1 ± 0.3	5.5 ± 0.5	p <sub>1</sub> = 0.0468 p <sub>2</sub> = 0.7528 p <sub>3</sub> = 0.0360
Language	2.44 ± 0.5	2.2 ± 0.4	2.86 ± 0.3	p <sub>1</sub> = 0.7324 p <sub>2</sub> = 0.4614 p <sub>3</sub> = 0.1844
Abstraction	1.88 ± 0.3	1.76 ± 0.4	2.0 ± 0.0	p <sub>1</sub> = 0.8540 p <sub>2</sub> = 0.4553 p <sub>3</sub> = 0.4748
Delayed recall	3.0 ± 0.0	4.7 ± 0.4	4.9 ± 0.3	p <sub>1</sub> = 0.0102 p <sub>2</sub> = 0.0037 p <sub>3</sub> = 0.8392
Orientation	4.2 ± 0.4	5.4 ± 0.5	5.9 ± 0.3	p <sub>1</sub> = 0.1510 p <sub>2</sub> = 0.0067 p <sub>3</sub> = 0.3680
FAB mean score	15.6 ± .5	15.1 ± 0.4	17.2 ± 0.4	p <sub>1</sub> = 0.4778 p <sub>2</sub> = 0.0483 p <sub>3</sub> = 0.0007

Table 2 Continued

Scale (scores)	aMCD (n = 9)	nMCD (n = 21)	Control group (n = 30)	P value
Conceptualization	2.66 ± 0.5	2.47 ± 0.5	2.93 ± 0.2	p <sub>1</sub> = 0.8217 p <sub>2</sub> = 0.5557 p <sub>3</sub> = 0.3432
Lexical Fluency	2.55 ± 0.5	2.47 ± 0.5	2.86 ± 0.3	p <sub>1</sub> = 0.9244 p <sub>2</sub> = 0.6161 p <sub>3</sub> = 0.4819
Motor Series ("Luria's Test")	2.55 ± 0.5	2.52 ± 0.5	2.86 ± 0.3	p <sub>1</sub> = 0.9716 p <sub>2</sub> = 0.6161 p <sub>3</sub> = 0.6006
Conflicting Instructions	2.77 ± 0.4	2.61 ± 0.4	2.9 ± 0.3	p <sub>1</sub> = 0.8125 p <sub>2</sub> = 0.8274 p <sub>3</sub> = 0.5569
Go-No Go	2.55 ± 0.5	2.57 ± 0.5	2.83 ± 0.3	p <sub>1</sub> = 0.9811 p <sub>2</sub> = 0.6506 p <sub>3</sub> = 0.6387
Prehension Behaviour (Grasp Reflex)	2.55 ± 0.5	2.52 ± 0.5	2.96 ± 0.18	p <sub>1</sub> = 0.9716 p <sub>2</sub> = 0.3405 p <sub>3</sub> = 0.3528

Notes: p<sub>1</sub> – significant difference between indicators of subgroups of patients with aMCD and nMCD; p<sub>2</sub> – significant difference between the indicators of the subgroup of patients with aMCD and the control group; p<sub>3</sub> – significant difference between the indicators of the subgroup of patients with nMCD and the control group

According to the MoCA scale, patients with aMCD and nMCD also had lower indicators compared to the control group (p<sub>2</sub> < 0.0001), (p<sub>3</sub> < 0.0001). Patients with aMCD showed a somewhat worse result than patients with nMCD (p<sub>1</sub> = 0.0457), especially on the subtest "delayed recall" (p<sub>1</sub> = 0.0102). Patients with nMCD – according to the subtest "attention and calculation" (p = 0.0468).

According to the FAB test results, patients with aMCD and nMCD had lower indicators compared to the control group (p<sub>2</sub> = 0.0483, p<sub>3</sub> = 0.0007). However, no significant differences were found between the groups of patients with MCD (p<sub>1</sub> = 0.4778). Although, the total score in patients with nMCD was slightly lower than with aMCD.

Therefore, when studying the neurocognitive profile in patients with aMCD, more pronounced memory disorders, especially delayed reproduction, prevailed, in patients with nMCD – regulatory cognitive disorders (attention and calculation, impaired planning and organization of activities). It should be noted that the MoCA scale, compared to the MMSE, had more diagnostic accuracy for the detection and differential diagnosis of minor cognitive disorders, in particular, of the anamnestic type.

When comparing the data of the conducted study according to the ADAS-cog scale, significant differences in cognitive profiles were obtained in the subgroups of patients with MCD (Table 3).

According to separate tests of the ADAS-cog scale, patients with aMCD had worse results in the tasks of "word recall" (p = 0.0069) and "word recognition" (p = 0.0350). Such disorders, as a rule, reflect a violation of semantic processes. This group of patients showed signs of "primary" (hippocampal) memory disorder (in particular, low and false recognition). Some studies show that semantic dysfunction is the main cause of false naming [13]. Duff and Broadhouse demonstrated a partially similar profile of memory impairment associated with a higher risk of transformation into dementia, especially in AD [14, 15]. Moreover, the presence of a similar type of memory disorder is accepted as one of the criteria for early diagnosis of AD in the pre-demented stage [16].

Patients with nMCD had lower scores on the tests "concentration and distractibility" (p = 0.0468), "number cancellation task" (p = 0.0217) and "passing the labyrinth" (p = 0.0015). Patients with nMCD type were characterized mainly by

frontal dysfunction, which is probably related to primary pathological changes in the frontal cortex, or the manifestation of subcortical-frontal syndrome. This type was distinguished by preserved recognition and indirect memorization

and secondary memory deterioration. Studies have reported that increased activity of the brain's glutamatergic system (glutamate and aspartate) leads to memory impairment, memorization, difficulty concentrating, and distraction [17, 18].

**Table 3 – Statistical indicators of the ADAS-cog scale in patients with mild cognitive disorder of various etiologies (scores) (M ± m)**

ADAS-cog subscales	aMCD (n = 9)	nMCD (n = 21)	P value
Word recall	3.4 ± 0.2	2.0 ± 0.3	0.0069
Naming objects and fingers	1.1 ± 0.2	0.61 ± 0.24	0.2214
Commands	0.88 ± 0.16	1.3 ± 0.21	0.2267
Constructional praxis	0.77 ± 0.37	0.47 ± 0.12	0.3263
Ideational praxis	0.77 ± 0.37	0.42 ± 0.2	0.3756
Orientation	1.5 ± 0.5	0.6 ± 0.3	0.1208
Word recognition	2.2 ± 0.44	1.0 ± 0.3	0.0350
Remembering word recognition test instructions	0.88 ± 0.16	0.47 ± 0.12	0.0627
Comprehension of spoken language	0.77 ± 0.37	0.38 ± 0.3	0.4593
Word-finding difficulty	0.88 ± 0.16	0.33 ± 0.21	0.1167
Spoken language ability	0.55 ± 0.2	0.28 ± 0.1	0.5579
Concentration and distractibility	0.66 ± 0.16	1.1 ± 0.12	0.0468
Number cancellation task	0.77 ± 0.37	1.5 ± 0.12	0.0217
Passing the labyrinth	0.55 ± 0.2	1.0 ± 0.0	0.0015
ADAS-cog total score	15.6 ± 1.1	11.4 ± 0.92	0.0130

Thus, according to the ADAS-cog subscale, in the groups of patients with mild cognitive disorder, it was found that the performance of tasks for repetition and recognition of words in patients with mild cognitive disorder of

anamnesic type and concentration and distraction, crossing out numbers and passing a maze in patients with mild cognitive impairment were worse disorder of non-amnesic type.

### CONCLUSIONS / ВИСНОВКИ

After analyzing the indicators of the neurocognitive examination of patients with cognitive disorders of various etiologies, it was possible to identify the patterns of development of this syndrome.

1. Patients with a mild cognitive disorder of the anamnestic type were characterized by significantly pronounced disorders of short-term memory (episodic) with memory impairment (reproduction, indirect memorization and recognition).

2. For patients with a minor cognitive disorder of the non-amnesic type, first of all, a violation of

concentration of attention and a decrease in the speed of the thinking process.

Therefore, patients with mild cognitive impairment of the anamnestic type may be prone to a high risk of transition to Alzheimer's disease. In this study, it was also noted that the MoCA and ADAS-cog scales had greater sensitivity and specificity in the detection and differential diagnosis of cognitive disorders than the MMSE. Neuropsychological testing is extremely useful both for making a diagnosis of mild cognitive impairment and for tracking the dynamics of cognitive symptoms over time.

### PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

Prospects for further research consist in a more detailed study of clinical and psychoneurological features in people with mild cognitive disorder of various etiologies.

**CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ**

The authors declare no conflict of interest.

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None.

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