DYNAMICS OF NEUROCOGNITIVE CHANGE IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT

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Abstract

Purpose: To examine the dynamics and cognitive indicators of neuropsychological change in patients with mild cognitive impairment (MCI).

Methods: A total of 50 patients with MCI diagnosis and a control group of 33 healthy people took part in the study. A multidomain cognitive battery was administered and the volume of both regions of the hippocampus were measured using magnetic resonance imaging. Two assessments were made at a 24 month interval. According to the dynamics of global cognitive decline in two years the MCI patients were divided into stable (sMCI) and deteriorating (dMCI) groups. The three groups were comparable in terms of demographic variables and emotional state.

Results: At baseline there was no significant difference between MCI groups on the level of the General Cognitive Functioning Index (GFI); however, the dMCI patients made significantly more errors in their performance. Hippocampal volumes were also similar in the MCI groups. After two years, the dMCI patients showed significant decline in the GFI and verbal memory as compared with the remaining groups. Hippocampal volumes significantly decreased in both MCI groups. There was a moderate relationship between the change in cognitive state and the change in left hippocampal volumetry in the MCI group as a whole ($r = 0.4$). Cognitive factors of inaccurate recall and perseverations differentiated the sMCI and dMCI patients at baseline ($p = 0.04$ and $p = 0.01$, respectively).

Conclusions: Our findings suggest that neuropsychological indicators of verbal memory functions and executive aspects of memory seem to have a significant value in predicting cognitive deterioration in MCI patients.

Key words: executive functions, dementia, mild cognitive impairment, memory, hippocampal volumetry.

Streszczenie

Cel: Celem pracy było opisanie dynamiki zmian funkcji poznawczych i próba znalezienia wskaźników neuropsychologicznych pomocnych w przewidywaniu tych zmian u pacjentów z diagnozą łagodnych zaburzeń poznawczych (LZP).

Metody: W badaniu wzięło udział 50 pacjentów z diagnozą LZP i 33 osoby z grupy kontrolnej. Wykonano szczegółowe badania neuropsychologiczne i pomiary objętości obydwu hipokampów na podstawie badań rezonansu magnetycznego mózgu. Badania zostały przeprowadzone dwukrotnie, w odstępie 24 miesięcy. Na podstawie oceny zmiany ogólnego wskaźnika sprawności poznawczej między pierwszym i drugim badaniem grupa pacjentów z LZP została podzielona na „stabilną” (sLZP) i „pogarszającą się” (pLZP). Grupy nie różniły się pod względem zmiennych demograficznych i wskaźników stanu emocjonalnego.
INTRODUCTION

Mild cognitive impairment (MCI) is a transitional state between normal cognitive functioning and dementia. The concept of MCI has been evolving, and various definitions and diagnostic criteria have been developed over the past two decades [1]. The latest classification points to the possible causes of various MCI types that can lead to different neurological diseases [2]. According to Winblad et al., the principal cognitive impairment can be amnestic (“amnestic MCI”), single non-memory domain (“single non-memory MCI”), or involving multiple cognitive domains (amnestic and other domains – “multidomain amnestic MCI” or only non-amnestic domains – “multidomain non-amnestic MCI”) [3]. The range and profile of cognitive deficits can vary and include, in particular, attention, language, visual-spatial, memory and executive functions [4, 5].

The course of cognitive change in MCI patients depends on many neurobiological and social-demographic factors. The role of age, cognitive reserves and educational level, active lifestyle and the status of an individual’s general mental and physical health status are considered [6, 7]. The course of the disease in particular cases can be different. Moreover, it is still not clear which indicators are the most important in predicting the neurocognitive state of subjects with an MCI diagnosis.

The rate of progression of MCI into dementia is estimated as 10-15% per year, depending on the diagnostic criteria used [8]. A meta-analysis of population-based studies showed that almost half of MCI patients will develop dementia, and that the risk is about 5-10% per year [9]. On the other hand, there are studies showing that cognitive deficits in MCI patients remained stable or even improved over time [10]. The most important risk factors for the conversion of MCI into dementia are: older age, lower level of education, hypertension, and the presence of APOE ε4 [11]. Neurological risk factors include atrophy of the hippocampus, amygdala or entorhinal cortex, as well as olfactory loss [12, 13]. Researchers also point to the role of combined risk, based on information gained from neuroimaging, genetic, olfactory, and neuropsychological studies [14].

Neuropsychological investigations indicate that the most valuable indicators in predicting cognitive decline are the level of performance in tests assessing verbal learning, delayed recall and recognition of verbal information, and tests of executive functions [15, 16]. Tests of visual memory, semantic memory, attention and mental speed also have a predictive value [17]. The co-incidence of psychiatric, i.e. behavioral and emotional symptoms, like depression, anxiety, apathy and irritability, increases the rate of MCI conversion into dementia [18, 19].

Despite the extensive literature on the risk factors in the conversion of MCI to dementia, most authors have been focused on analyzing different sorts of data separately, e.g. structural imaging, olfactory loss, or neuropsychological findings [11-13, 15, 16]. There are only a few papers focusing on combined neurostructural and neuropsychological information, and most of them have been based on cognitive screening measures, staging-based rating scales or limited neuropsychological assessment tools [14, 20]. There have not been enough studies examining data from a detailed neuropsychological assessment combined with volumetric indicators that rely on longitudinal observation [21]. Mostly, they have concentrated on progression into dementia, and haven’t taken into account the subtle cognitive change that is still bordered by mild cognitive impairment criteria, but can be subjectively experienced by patients as a worsening of the cognitive status. There is still a need to elucidate the types of predictors that may help identify the MCI patients at risk of neurocognitive deterioration.

This paper presents the findings of research into the dynamics of the Institute of neurocognitive change in MCI patients with similar demographic characteristics, volumetric measures, general cognitive functioning and emotional status and the search for variables that can be useful in predicting the progression of neurocognitive deficits in patients with an MCI diagnosis.
METHODS

Participants

The study was a part of a longitudinal research project on MCI conducted at the Neurological Department of the Institute. The study design was accepted by the Ethics Committee. The classification of patients into clinical groups was made on the basis of the Mayo Clinic Group criteria of MCI [22]. The participants were patients of the hospital or ambulatory care as well as patients’ families and volunteers who had responded to an advertisement placed in the outpatient clinic. The participants signed an informed consent form and passed the qualification process including clinical interview, neurological examination, and neuropsychological screening testing.

The inclusion criteria were: age of minimum 50 years, memory complaints that have lasted 6 months to 10 years prior to inclusion in the study, absence of dementia according to the DSM-IV criteria, a score of 26 to 29 points in the Mini Mental State Examination, a score of 0–0.5 in the Clinical Dementia Rating [23] and a score of 1 to 3 points on the Global Deterioration Scale [24]. The exclusion criteria were: evidence of dementia, presence of major depression or another psychiatric disease, alcohol abuse (in the past or present), history of ischemic stroke (or presence of a lesion equal to or over 2 cm in the MRI study) or another neurological condition that could influence neurocognitive status. The inclusion criteria for the control group were: age minimum 50 years, lack of memory complaints, absence of dementia, an MMSE score of 28 or more, and absence of a neurological or psychiatric condition in the individual’s medical history.

The qualification of MCI status was made by a certified clinical neuropsychologist on the basis of a detailed neuropsychological examination. 46 (92%) participants were diagnosed as having multidomain amnestic MCI, 3 patients (6%) had single domain MCI – amnestic and 1 (2%) participant had single domain non-amnestic MCI. Because most patients had “multidomain amnestic” MCI, the clinical group wasn’t divided according the type of deficits.

The MCI group was divided into two subgroups (stable vs. deteriorating) according to the level of change in cognitive state after two years of observation. The change in neuropsychological functioning was calculated in the way described in the “Data preparation” section. The MCI group consisted of 34 women and 16 with ages ranging between 50 and 79 years. The stable MCI (sMCI) group included 35 patients, and the deteriorating MCI (dMCI) group 15 patients, respectively. The control group consisted of 33 healthy subjects. The sMCI, dMCI and control groups did not differ significantly regarding age and the level of education (number of years of formal education) (Table 1). At baseline, the two MCI groups and the control group didn’t differ in the level of depressive symptoms ($p = 0.64$ between MCI groups; $p = 0.3$ and $p = 0.28$ between the sMCI and dMCI and control groups, respectively).

Neuropsychological assessment

Neuropsychological assessment included:
- The Mini Mental State Examination (MMSE) [25] and the Clock Drawing Test (CDT) [26] – as screening instruments for dementia in the qualification process.
- The California Verbal Learning Test (CVLT) [27] to assess processes of memory and learning.
- The Benton Visual Retention Test (BVRT) [28] – to examine visual attention, visual perception and construction and immediate visual memory; and the naming task (NT), based on the Boston Naming Test (short 21-item version) [29] – to assess semantic memory.
- The Trail Making Test (TMT) parts A and B [30] – to evaluate visual attentional processes and executive functions [29];
- and verbal fluency tasks (VFT) [29], to examine executive functions and semantic memory (“name of animals” for semantic fluency and a “word starting with the letter K” for phonetic fluency).

Table 1. Participants – demographic data and the level of depressive symptoms at baseline

|                | sMCI                           | dMCI                           | Controls                     | Between group differences (p < 0.05) |
|----------------|--------------------------------|--------------------------------|------------------------------|-------------------------------------|
| N              | 35 (21 female, 14 male)        | 15 (13 female, 2 male)         | 33 (20 female, 13 male)      | n.s. ($p = 0.16$)                   |
| Age            |                                |                                |                              |                                     |
| M              | 65.68                          | 69.20                          | 67.66                        |                                     |
| SD             | 6.88                           | 6.68                           | 6.41                         |                                     |
| Education (years) |                               |                                |                              |                                     |
| M              | 13.88                          | 12.80                          | 13.60                        | n.s. ($p = 0.44$)                   |
| SD             | 3.49                           | 2.81                           | 3.13                         |                                     |
| GDS            |                                |                                |                              |                                     |
| M              | 3.76                           | 4.00                           | 3.13                         | n.s. ($p = 0.58$)                   |
| SD             | 1.47                           | 1.93                           | 2.07                         |                                     |

sMCI – stable MCI group, dMCI – deteriorating MCI group, M – mean, SD – standard deviation, GDS – Geriatric Depression Scale score, n.s. – no significant difference
Dynamics of neurocognitive change in patients with mild cognitive impairment

- The Ruff Figural Fluency Test (RFFT) [32] for the assessment of executive functions based on visual stimuli [29].
- The Verbal Concept Attainment Test (VCAT) [33] to examine verbal conceptual thinking.

Additionally, the Geriatric Depression Scale – 15-item version (GDS) [34] as a screening tool assessing depressive signs in older people was used to evaluate the possible influence of emotional state on cognitive functions.

Volumetric measures

The magnetic resonance imaging (MRI) measurement of the volume of brain structures was performed using FLAIR, with T2-weighted and 3-D T1 sequences in the coronal plane perpendicular to the long axis of the hippocampus. The Regions of Interest (ROIs) were the hippocampus (HIP) in both the left and right hemispheres. As described in Lojkowska et al. [35], the calculated volume was normalized for each structure (i.e. divided by the volume of the section of the posterior commissure of the brain).

The neuropsychological and MRI examination were conducted twice, at an interval of approximately two-years.

Data preparation

The construct of the dynamics of cognitive change was created in order to classify MCI patients into two groups (stable MCI and deteriorating MCI). To assess the dynamics of global cognitive changes, the General Functioning Index (GFI) score was counted for each participant. The score in each test was standardized in order to avoid a diversity of units of raw scores. Standardization was based on the scores of the control group, so that the mean score of each was 50, with an SD of 10. The GFI was made as the mean from the standardized scores of chosen indicators: the number of correct answers in the NT, the number of words given in the VFT, the time of performance of part A and part B of the TMT, the number of correct drawings and number of errors in the BVRT and from the CVLT – the sum of recalled words in five immediate recall trials, number of words recalled from list B, number of words recalled after a short and long delay (free and cued recall), total number of repetitions, total number of intrusions, number of correctly and falsely recognized words. According to the authors' assumptions, a higher rate of the GFI means a higher level of cognitive functioning.

A variable of dynamics of cognitive change (dGFI) was counted for each participant based on the difference in the General Functioning Index between the first and second examination (dGFI = GFI1 – GFI2). To find cognitive change, the criterion of one standard deviation was applied (dGFI < 1 SD in the stable MCI group and dGFI ≥ 1 SD in the deteriorating MCI group).

Statistical analyses

Statistical analyses were performed using Statistica software (version 12.0, StatSoft). On the basis of the Kolmogorov-Smirnov test scores, the hypothesis of a normal distribution of scores was rejected, so only non-parametric statistics were used: the Mann-Whitney U test to compare group means, the Wilcoxon paired difference test to compare scores of the first and second examinations, and Spearman correlation analysis to examine the relationship between the cognitive and volumetric changes.

Descriptive statistics revealed some outliers both in the level of performance of particular neuropsychological tests and in hippocampal volumetry. However, due to the longitudinal character of the study and the small groups those outliers weren’t excluded from analyses.

To reduce the number of cognitive variables, statistical factor analysis was performed. This allowed us to define

Table 2. Cognitive factors emerged in statistical factor analysis

| Name of cognitive factor/Test and analyzed variable | Factor loadings (varimax normalized) |
|---------------------------------------------------|-------------------------------------|
| Verbal memory                                     |                                     |
| California Verbal Learning Test:                  |                                     |
| • Total immediate recall                            | 0.86                                |
| • Immediate recall – list B                          | 0.66                                |
| • Short delay free recall                           | 0.73                                |
| • Long delay free recall                            | 0.66                                |
| Visual-spatial memory                              |                                     |
| Benton Visual Retention Test:                      |                                     |
| • Number of correct drawings                        | 0.71                                |
| • Number of errors                                  | -0.69                               |
| Inaccurate recall                                  |                                     |
| California Verbal Learning Test:                  |                                     |
| • Total number of intrusions                        | -0.84                               |
| • Number of false recognized words                  | -0.82                               |
| Perseverations                                     |                                     |
| Ruff Figural Fluency Test – number of repetitions | 0.83                                |
| California Verbal Learning Test – number of repetitions | 0.72                            |
| Executive functions (attention and fluency)        |                                     |
| Ruff Figural Fluency Test:                         |                                     |
| • Number of unique designs                          | 0.66                                |
| Trail Making Test:                                 |                                     |
| • Time of performance of Part A                     | -0.67                               |
| • Time of performance of Part B                     | -0.67                               |
| Verbal fluency tasks:                              |                                     |
| • Number of names of animals                        | 0.67                                |
| • number of words starting with the letter 'k'      | 0.67                                |
5 groups of variables that reflect different cognitive domains, as can be seen in Table 2: verbal memory, visual-spatial memory, inaccurate recall, perseverations and executive functions (attention and verbal fluency). The names of cognitive factors were based on neuropsychological knowledge on the assessment of cognitive functions [29].

To measure the range of changes in cognitive state and hippocampal volumetry between assessments, Stability Indicators were created for each participant. The Cognitive Stability Indicator (CSI) was calculated using the following formula: CSI = (GFI2/GFI1) × 100%. The Hippocampal Stability Indicator (HSI) was calculated for both the right and left hippocampus, according to the formula: HSI = (HIP2/HIP1) × 100% (HIP1 and HIP2 – hippocampal volume in the first and second exam, respectively, based on Lojkowska et al., 2011 [35]).

To control the possible influence of age on neurocognitive and volumetric results the variable “age” was correlated with the Cognitive Stability Indicator, the Hippocampal Stability Indicator and with the GFI and cognitive factors at baseline. None of the correlations were statistically significant, so further analysis was based on scores that were not corrected for age.

To examine the relationship of the level of depressive symptoms and the level of cognitive functions, the scores of the GDS were correlated with the GFI in all groups of participants at baseline and at the follow up. The only significant correlation was found between the level of depressive symptoms and level of cognitive functioning in the deteriorating MCI group at follow-up (r = 0.54).

RESULTS

Neuropsychological and volumetric characteristics

A comparison of cognitive factors, the General Functioning Index and scores on the Geriatric Depression Scale are presented in Table 3. At baseline both MCI groups performed worse in the verbal memory test than the control group. The dMCI group had a higher number of intrusion and perseverative errors (meaning inaccurate recall and cognitive factors in perseveration) than the stable MCI group. The GFI was lower in both the dMCI and sMCI groups than in the control group. But there was no statistically significant difference in the level of GFI between the stable and deteriorating MCI groups at baseline. At follow up, there were significant differences between the dMCI and control groups in verbal memory, inaccurate recall and perseverations and also in GFI. The MCI groups differed significantly in the verbal memory factor, inaccurate recall factor and GFI. There were no significant differences between groups in visual-spatial memory, attention or fluency factors.

### Table 3. Comparison of cognitive factors, General Functioning Index and Geriatric Depression Scale at the 1st and the 2nd examination of study groups

| Indicator                  | 1st examination | 2nd examination | Course of group differences (d) | dMCI group | dMCI > C (p = 0.00) | dMCI < C (p = 0.00) | sMCI group | sMCI > C (p = 0.00) | sMCI < C (p = 0.00) | Control group | Control group | Control group | dMCI group | dMCI > C (p = 0.00) | dMCI < C (p = 0.00) | sMCI group | sMCI > C (p = 0.00) | sMCI < C (p = 0.00) |
|----------------------------|----------------|----------------|---------------------------------|------------|---------------------|---------------------|------------|---------------------|---------------------|----------------|----------------|----------------|------------|---------------------|---------------------|------------|---------------------|---------------------|
| Verbal memory              | 43.23 (11.65)  | 45.35 (11.51)  | 0.01                            | 50.00 (8.20)| -                   | -                   | 45.35 (11.51)| 0.01                            | 50.00 (8.20)| -                   | -                   | 45.35 (11.51)| 0.01                            | 50.00 (8.20)| -                   | -                   | 45.35 (11.51)| 0.01                            | 50.00 (8.20)| -                   | -                   |
| Inaccurate recall          | 50.22 (4.08)   | 50.89 (4.12)   | -                               | 50.00 (4.40)| -                   | -                   | 50.89 (4.12)| -                               | 50.00 (4.40)| -                   | -                   | 50.89 (4.12)| -                               | 50.00 (4.40)| -                   | -                   | 50.89 (4.12)| -                               | 50.00 (4.40)| -                   | -                   |
| Executive functions (att. and fluency) | 56.07 (10.38) | 54.86 (3.49)   | 0.06                            | 50.00 (7.20)| -                   | -                   | 54.86 (3.49)| 0.06                            | 50.00 (7.20)| -                   | -                   | 54.86 (3.49)| 0.06                            | 50.00 (7.20)| -                   | -                   | 54.86 (3.49)| 0.06                            | 50.00 (7.20)| -                   | -                   |
| General Functioning Index  | 51.19 (14.12)  | 45.13 (10.86)  | 0.03                            | 50.00 (8.20)| -                   | -                   | 45.13 (10.86)| 0.03                            | 50.00 (8.20)| -                   | -                   | 45.13 (10.86)| 0.03                            | 50.00 (8.20)| -                   | -                   | 45.13 (10.86)| 0.03                            | 50.00 (8.20)| -                   | -                   |
| Geriatric Depression Scale | 3.92 (1.42)    | 3.87 (1.98)    | 0.64                            | 50.00 (7.20)| -                   | -                   | 3.87 (1.98)| 0.64                            | 50.00 (7.20)| -                   | -                   | 3.87 (1.98)| 0.64                            | 50.00 (7.20)| -                   | -                   | 3.87 (1.98)| 0.64                            | 50.00 (7.20)| -                   | -                   |
The comparison of hippocampal volumetry between the sMCI and the dMCI groups is presented in Figure I (at baseline) and Figure II (at follow-up). There were no significant differences in volumetric measures at baseline, neither in left or right hippocampal volumes, respectively ($p = 0.46$, $p = 1$). At follow-up, there were also no differences in the hippocampal volumetry between the sMCI and dMCI groups ($p = 0.95$ and $p = 0.40$).

### Dynamics of cognitive and volumetric changes

At follow-up, on the basis of clinical interview, CDR score, and screening neuropsychological assessment, dementia was diagnosed in 4 participants from the dMCI group (according to the cut-off criterion, i.e., a score of maximum 24 points in the MMSE). The comparison of cognitive tests results between the first and the second examination in the MCI groups (Table 4) showed that the sMCI group had also deteriorated regarding verbal memory and executive functions. In the dMCI group, worsening verbal memory, inaccurate recall and attention, and cognitive fluency factors were observed. The General Functioning Index was statistically lower only in the dMCI group at follow-up.

In both MCI groups, the hippocampal volume measures decreased statistically during the two years (Table 5).
A comparison of the Hippocampal Stability Indicators (HSI-L and HSI-R) showed a statistically significant difference between the dMCI and sMCI groups in the volumes of the left hippocampus after two years. The bigger change was detected in the dMCI group (Figure III).

In order to analyze the relationship between changes in the cognitive state and volumetric measures, the Cognitive Stability Indicator (CSI) was correlated with the Hippocampal Stability Indicators (HSI-L and HSI-R). This is presented in Figure IV. The only significant correlation was found between change in volume of the left hippocampus and change in the General Functioning Index in the whole group of MCI patients ($r = 0.40, p < 0.05$).

**DISCUSSION**

The aim of this study was to characterize the dynamics of cognitive change in patients with an MCI diagnosis and search for variables that can be useful in predicting neurocognitive deterioration.

At baseline, there were no significant differences between deteriorating and stable MCI patients in social-demographic characteristics, hippocampal volumes and depressive symptoms. Only in the MCI group did the severity of depressive symptoms correlate with general cognitive functioning at follow-up. In previous studies it has been observed that the co-incidence of mood disorders increases the risk of progression of cognitive decline in MCI patients [36].

The MCI patients, both in the first and second examination, presented a significantly lower level of functioning than the control group in several cognitive dimensions. In the deteriorating MCI patients, there were more cognitive domains impaired than in the stable MCI

**Table 4. Comparison of the level of cognitive factors and the General Functioning Index between the first and second examination in both MCI groups and in the control group**

| Variable                           | sMCI group | dMCI group | Control group |
|------------------------------------|------------|------------|---------------|
| Verbal memory                      | 0.03       | < 0.01     | 0.49          |
| Visual-spatial memory              | 0.58       | 0.11       | 0.76          |
| Inaccurate recall                  | 0.80       | < 0.01     | 0.81          |
| Perseverations                     | 0.51       | 0.90       | 0.75          |
| Executive functions (attention and fluency) | < 0.01 | 0.02 | < 0.01 |
| General Functioning Index          | 0.38       | < 0.01     | 0.84          |

**Table 5. Changes in volumetric measurements between the first and second examination in the MCI and the control group**

| ROIs          | MCI group $p$ | sMCI group $p$ | dMCI group $p$ | Control group $p$ |
|---------------|---------------|----------------|----------------|-------------------|
| HIPL          | 0.01*         | 0.15           | < 0.001**      | < 0.001**         |
| HIPR          | < 0.001**     | < 0.001**      | 0.19           | < 0.001**         |

ROIs – regions of interest, HIPL – left hippocampus, HIPR – right hippocampus.

*p level < 0.01, *p level < 0.05

**Figure III. Comparison of the Hippocampal Stability Indicator (HSI) of right and left hippocampus between the stable MCI (sMCI) and deteriorating MCI (dMCI) groups**
Dynamics of neurocognitive change in patients with mild cognitive impairment

Dynamika zmian funkcji poznawczych u pacjentów z diagnozą łagodnych zaburzeń poznawczych

Group: differences were found in verbal episodic memory, inaccurate recall and perseverations. In several papers, the decline in verbal episodic memory is the main, or one, of the most important predictors of MCI conversion to dementia [37-39]. It appeared that the executive aspects of the verbal memory processes, such as intrusions and perseverations while recalling of information, were impaired in the deteriorating MCI group, as was found in previous studies [40, 41]. In addition, patients with MCI, who are at higher risk of progressive cognitive decline, present more severe cognitive deficits than people with a stable cognitive state.

In 4 patients from the MCI group, based on the clinical interview, clinical presentation and DSM-IV criteria, a diagnosis of dementia was established after two years of observation. This means that 8% of the MCI group converted to dementia. The rate of progression of MCI into dementia reported by other authors varied from 6% to 25% per year [39].

Apart from the evident progression into dementia, a significant deterioration in neuropsychological test performance was also observed in the MCI groups. Statistical differences between baseline and follow-up examinations in the group of dMCI patients were found in verbal memory, in the level of inaccurate recall and in attention and fluency. This outcome shows that at follow-up more cognitive domains became impaired. A few studies examining the dynamics of cognitive functions in MCI patients prior to dementia diagnosis show the variety of the level and trajectory of cognitive decline [42-44].

Simultaneously, a significant reduction was observed in the volumes of both the left and right hippocampus in all of the participants from the MCI groups. The change in the volumes of the left hippocampus was correlated with the change in global cognitive state. In dMCI patients the loss of left hippocampus volume has been more pronounced than in the sMCI group. Such relationships between volumetric changes and progression of cognitive decline have been widely discussed [45]. The hippocampus is identified as the brain structure that is related to memory processes [29]. Hippocampal atrophy is associated with MCI and early stages of AD [46] and with MCI progression [13].

It should be noted that only two cognitive factors – inaccurate recall and perseverations – differentiated the stable and deteriorating MCI patients at baseline, so they can be set out as the measures sensitive to the progression of cognitive decline in the MCI group. The California Verbal Learning Test, i.e. the verbal memory test used in this study, allowed for the assessment of memory functions in detail, including the executive aspects of verbal mnemonic processes [29]. The cognitive factor “inaccurate recall” contains indicators of the number of falsely recognized words in the recognition trial, the sum of repetition errors in recalling information, and the sum of intrusion-type errors in recalling information. Such errors suggest impaired control of recalling processes, which can be observed as difficulties with the inhibition of incorrect responses [47]. Also the cognitive factor “perseverations” that reflects a tendency to perseverative responses, not only in the verbal memory task but in nonverbal fluency test as well, appeared to be the significant indicator of cognitive change [29]. Deficits in executive aspects of memory processes in people with MCI who are at risk of developing dementia were found in earlier studies [47, 48]. There is a close relationship between memory processes and certain aspects of executive functions, as the authors pointed out – it is impossible to understand those functions if
and when considering them separately [49]. The influence of executive functions on memory processes seems to be significant, especially in older people [50].

Using the multidomain cognitive battery allows for the detailed examination of a patient’s functioning. It gives an opportunity to find even very subtle cognitive changes that are not visible in a screening test or in observation-based scales. There is still a need to improve evidence-based neuropsychological knowledge on the specific cognitive domains that are affected in neurodegenerative disorders, so as to more accurately and convincingly predict the progression of decline in neuropsychological disorders [51]. In our study, it was found that performance in verbal memory tests can predict cognitive decline. The California Verbal Learning Test appears to be the valuable method for predicting the progression of cognitive decline in MCI patients. Our results are consistent with those of other studies, suggesting that CVLT should be the preferred test in diagnosing MCI and the prediction of the conversion of MCI into dementia [52]. They also add more to the evidence on the role of neuropsychological tools not only in diagnosis but also in estimating the possible course of cognitive decline in MCI patients.

A limitation of this study was the small number of participants. Also, the mean number of reported years of education is high and suggests an over-representation of well-educated participants. The latter may influence the distribution of cognitive deficits and also the rate of progression into dementia. Only a few cases of dementia emerged in the study participants, so that generalization of the conclusions may be limited. Another issue is that in this study most of the patients were diagnosed as having multidomain amnestic MCI. The consideration of other types of mild cognitive impairment could provide more accurate data. Thus there is a need for further investigation in this area.

Conflict of interest / Konflikt interesu
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Dynamics of neurocognitive change in patients with mild cognitive impairment

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