© Aktualn Neurol 2016, 16 (2), p. 79–84
DOI: 10.15557/AN.2016.0010

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Received: 09.12.2015
Accepted: 08.06.2016
Published: 30.06.2016

The need of neuropsychological assessment in daily care of patients without dementia

Potrzeba oceny neuropsychologicznej w codziennej opiece nad pacjentami bez zdiagnozowanej demencji

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Abstract

Aim of the study: The prevalence of cognitive impairment increases with age and features lesions observed in Alzheimer's disease, vascular dementia, Parkinson's disease and dementia with Lewy bodies. The aim of the study was to determine whether individuals without diagnosed dementia are affected by any reduction of cognitive functioning and to what extent such reduction occurs. **Material and methods:** The study enrolled 156 individuals, including 110 aged <75 years and 46 aged ≥75 years. Cambridge Neuropsychological Test Automated Battery was used in assessment of Motor Screening Task (Mean Latency and Mean Errors), Paired Associated Learning (Total Errors and Errors Shapes), Stocking of Cambridge (Mean Initial Thinking Time, Mean Subsequent Thinking Time, Problems Solved in Minimum Moves) and Graded Naming Test. Individuals who aborted tests were categorized as below the reference threshold. **Results:** Prevalence of results below the reference threshold were as follows: 8.97% in Motor Screening Task – Mean Latency, 57% in Paired Associated Learning – Total Errors, 57% in Paired Associated Learning – Errors Shapes, 30% in Stocking of Cambridge – Mean Initial Thinking Time, 28% in Stocking of Cambridge – Mean Subsequent Thinking Time, 57% in Stocking of Cambridge – Problems Solved in Minimum Moves and 32% in Graded Naming Test. The results of Motor Screening Task were above the threshold. Motor Screening Task – Mean Error was higher in the +75 group ($p < 0.001$), whereas the Motor Screening Task – Mean Latency did not differ between the groups. Also Paired Associated Learning outcomes were higher in the +75 group ($p = 0.01$). Graded Naming Test and Stocking of Cambridge – Mean Subsequent Thinking Time were lowered in the +75 group ($p = 0.01$), whereas other Stocking of Cambridge tests did not differ. The age ≥75 years was associated with 2.3 times higher risk of decreased Stocking of Cambridge – Mean Initial Thinking Time, 2.7 times higher risk of decreased Stocking of Cambridge – Mean Subsequent Thinking Time and 3.3 times higher risk of decreased Graded Naming Test. **Conclusions:** The link between cognitive functions and the age, despite the lack of diagnosis of dementia, confirms the need of neuropsychological assessment in patients without dementia.

Key words: Cambridge Neuropsychological Test Automated Battery, cognitive functions, neuropsychological assessment

Streszczenie

Cel: Rozpowszechnienie deficytów poznawczych w populacji wzrasta wraz z wiekiem. Wiąże się to ze zmianami obserwowanymi w chorobie Alzheimera, otępieniu naczyniopochodnym, chorobie Parkinsona i otępieniu z ciałami Lewy'ego. Celem badania było ustalenie, czy i w jakim stopniu osoby bez rozpoznanej demencji mają obniżone funkcjonowanie poznawcze. **Materiał i metoda:** Do badania włączono 156 osób, w tym 110 w wieku <75 lat i 46 w wieku ≥75 lat. Do oceny neuropsychologicznej wykorzystano testy metody Cambridge Neuropsychological Test Automated Battery (CANTAB): Motor Screening Task (Mean Latency i Mean Errors), Paired Associated Learning (Total Errors i Errors Shapes), Stocking of Cambridge (Mean Initial Thinking Time, Mean Subsequent Thinking Time, Problems Solved in Minimum Moves) oraz Graded Naming Test. Osoby, które przerwały testy, zostały sklasyfikowane poniżej punktu referencyjnego. **Wyniki:** Odsetki wyników poniżej punktu referencyjnego były następujące: 8,97% w Motor Screening Task – Mean Latency, 57% w Paired Associated Learning – Total Errors, 57% w Paired Associated Learning – Errors Shapes, 30% w Stocking of Cambridge – Mean Initial Thinking Time, 28% w Stocking of Cambridge – Mean Subsequent Thinking Time, 57% w Stocking of Cambridge – Problems Solved in Minimum Moves oraz 32% w Graded Naming Test.

Wyniki otrzymane w Motor Screening Task były powyżej punktu referencyjnego. Wyniki Motor Screening Task – Mean Error były wyższe w grupie osób ≥75. roku życia ($p < 0,001$), natomiast wyniki Motor Screening Task – Mean Latency nie różniły się istotnie pomiędzy grupami. Oba wyniki testu Paired Associated Learning były wyższe w grupie osób ≥75. roku życia ($p = 0,01$). Wyniki Graded Naming Test i Stocking of Cambridge – Mean Subsequent Thinking Time były obniżone w grupie osób >75. roku życia ($p = 0,01$), natomiast pozostałe wyniki Stocking of Cambridge nie różniły się między grupami. Wiek ≥75 lat był związany z 2,3 razy wyższym ryzykiem obniżonego wyniku w Stocking of Cambridge – Mean Initial Thinking Time, 2,7 razy wyższym ryzykiem obniżonego wyniku w Stocking of Cambridge – Mean Subsequent Thinking Time oraz 3,3 razy wyższym ryzykiem obniżonego wyniku w Graded Naming Test. **Wnioski:** Związek między funkcjami poznawczymi a wiekiem, mimo braku rozpoznania otępienia, potwierdza potrzebę oceny neuropsychologicznej pacjentów bez stwierdzonej demencji.

Słowa kluczowe: Cambridge Neuropsychological Test Automated Battery, funkcje poznawcze, ocena neuropsychologiczna

INTRODUCTION

The prevalence of cognitive impairment increases with age and features lesions observed in Alzheimer's disease (AD), vascular dementia, Parkinson's disease and dementia with Lewy bodies (Baptista *et al.*, 2016; Inskip *et al.*, 2016; Sun *et al.*, 2016; Xu *et al.*, 2016). However, the problem and characteristics of cognitive impairment without any overt clinical manifestation of aforementioned diseases seem to be underestimated. Many authors emphasize that healthy older persons may be affected with mild to moderate cognitive impairment in selected domains, despite presenting no symptoms of dementia examined with Mini–Mental State Examination (MMSE), which rises clinical and research implications and early identification of possible impairment (Votruba *et al.*, 2016). Therefore, a problem with simply naming such condition of the patients has occurred. Some researchers described it as "very mild dementia" (Almkvist and Bäckman, 1993; Morris *et al.*, 1991; Rubin *et al.*, 1993). Others called the condition as "predementia" or "age-associated memory impairment" (Förstl *et al.*, 1995; Jacobs *et al.*, 1995; Masur *et al.*, 1994). Names like "borderzone dementia" (Gurland, 1981) or "questionable dementia" (Forsell *et al.*, 1992; Hughes *et al.*, 1982; Morris *et al.*, 1991) were also used to diagnose impaired cognitive functions of elderly persons. It seems that the most general term – "cognitively impaired, not demented" (CIND) (Ebly *et al.*, 1995; Flicker *et al.*, 1993; Forsell *et al.*, 1992; Osterweil *et al.*, 1994) is nowadays the most commonly used. From this point, another question rises why this matter is so complex and why it is important? The answer seems to flow from its relation with neuropathogenic diseases. It is possible that if one could diagnose CIND early and appropriately, it would increase the chances of slowing down or even avoiding the risk of AD by neuropsychological intervention (Chertkow *et al.*, 2008). As a clinical symptom, AD is characterized by insidious onset and a chronic irreversible course. Many elderly patients show some degree of cognitive impairment but do not meet the criteria for dementia (Albert *et al.*, 1999). Some researchers suggest that almost 17% of elderly people can be diagnosed with CIND (Ebly *et al.*, 1995; Graham *et al.*, 1997). Approximately 50% of elderly persons is at increased risk of eventual dementia or even death (Tuokko *et al.*, 2003). In the literature, mild cognitive impairment (MCI) is the term which is the most commonly used for defining such condition and does not meet the criteria related only to the age or to neurodegenerative disease (Bartrés-Faz *et al.*, 2001; Petersen *et al.*, 1999; Ravaglia *et al.*, 2008). The prevalence of MCI in a population of elderly persons (over 65 years) is estimated at 15 to 20% (Lopez *et al.*, 2003). Individuals with MCI demonstrate deficits in instrumental activities of daily living that place them at high risk of progression to dementia (Putcha and Tremont, 2016).

The aim of the study was to determine whether active elderly individuals without diagnosed dementia are truly affected by a reduction of cognitive functioning and to what extent such reduction occurs.

METHODS

The study enrolled 156 individuals, including 110 aged <75 years and 46 aged ≥75 years. Cambridge Neuropsychological Test Automated Battery (CANTAB) was used with the following tests:

- Motor Screening Task (MOT), a tool for screening for difficulties with vision, movement and comprehension, displayed by Mean Latency (MOT ML) and Mean Errors (MOT ME);
- Paired Associated Learning (PAL), a tool for measuring declarative visual memory and new learning, displayed by Total Errors (PAL TE) and Errors Shapes (PAL ES);
- Stocking of Cambridge (SOC), a tool for measuring ability of spatial planning and motor control, displayed by Mean Initial Thinking Time (SOC MITT), Mean Subsequent Thinking Time (SOC MSTT) and Problems Solved in Minimum Moves (SOC PSMM);
- Graded Naming Test (GNT), a tool assessing object-naming ability – lexical and semantic memory.

Individuals who aborted tests were categorized as below the reference threshold. The results of the aforementioned tests were referred automatically to determined ranges of norms matched according to age and gender. The CANTAB

DOI: 10.15557/AN.2016.0010

automatically provided standard scores, in which "zero" ("0") defines the reference threshold. All patients had given their written, informed consent to the participation in the study.

Statistical analysis was performed using Statistica software version 12.0. Mann–Whitney *U* test was used to compare results between two subgroups. Logistic regression analysis was employed in order to estimate odds ratio for age 75+ as a risk factor for decreased cognitive functions defined as results below the threshold.

RESULTS

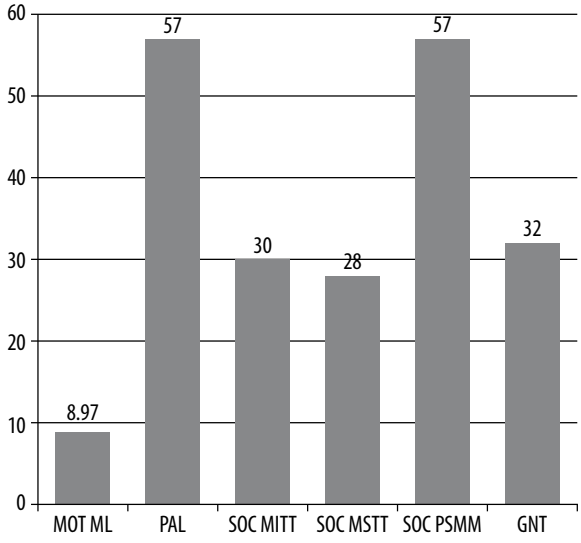
Prevalence of results below the reference threshold were as follows: 8.97% in MOT ML, 57% in PAL TE, 57% in PAL ES, 30% in SOC MITT, 28% in SOC MSTT, 57% in SOC PSMM and 32% in GNT. None of the patients presented decrease in MOT ME (Fig. 1).

In comparison of two subgroups, divided according to age: 110 individuals aged <75 years and 46 aged ≥75 years (75+), results of MOT ME were higher in the 75+ group ($p < 0.001$), whereas the MOT ML did not differ (Fig. 2).

PAL TE was higher in the 75+ group than in aged <75 ($p = 0.001$) (Fig. 3).

PAL ES was higher in the 75+ group than in aged <75 ($p = 0.01$) (Fig. 4).

SOC MSTT was lower in the 75+ group than in aged <75 ($p = 0.01$) (Figs. 5, 6).



MOT ML – Motor Screening Task – Mean Latency; **PAL** – Paired Associated Learning; **SOC MITT** – Stocking of Cambridge – Mean Initial Thinking Time; **SOC MSTT** – Stocking of Cambridge – Mean Subsequent Thinking Time; **SOC PSMM** – Stocking of Cambridge – Problems Solved in Minimum Moves; **GNT** – Graded Naming Test.

*Fig. 1. Prevalence of results below the reference threshold obtained by the entire group of patients (*n *= 156) examined with CANTAB*

Regression logistic analysis revealed that the age ≥75 years was associated with 2.3 times higher risk of decreased SOC MITT, 2.7 times higher risk of decreased SOC MSTT and 3.3 times higher risk of decreased GNT (Fig. 7).

DISCUSSION

Confirmation of a link between cognitive functions and the age, despite the lack of diagnosis of dementia in elderly individuals, would advocate the need of neuropsychological assessment in daily care of patients without diagnosed dementia and when appropriate – the implementation of cognitive training programs. The prediction of dramatic increase of people suffering from different forms of dementia

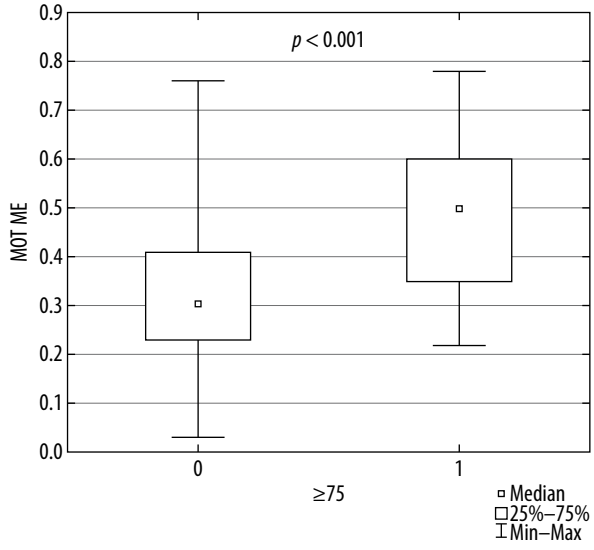


Fig. 2. Comparison of results in MOT ME obtained in two subgroups: groups aged <75 and ≥75 years

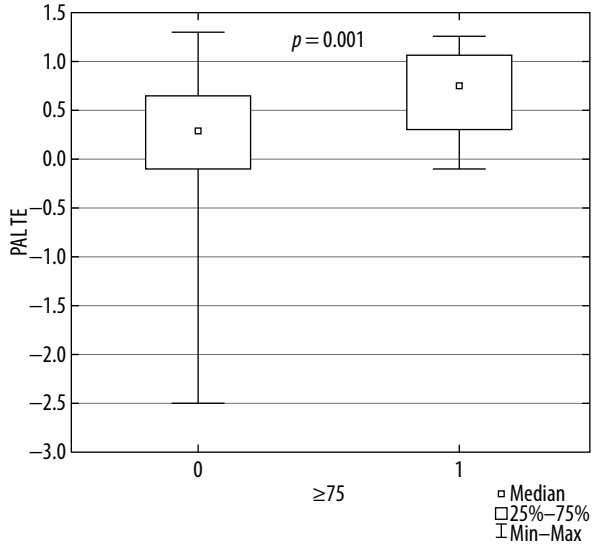


Fig. 3. Comparison of results in PAL TE obtained in two subgroups: groups aged <75 and ≥75 years

 DOI: 10.15557/AN.2016.0010

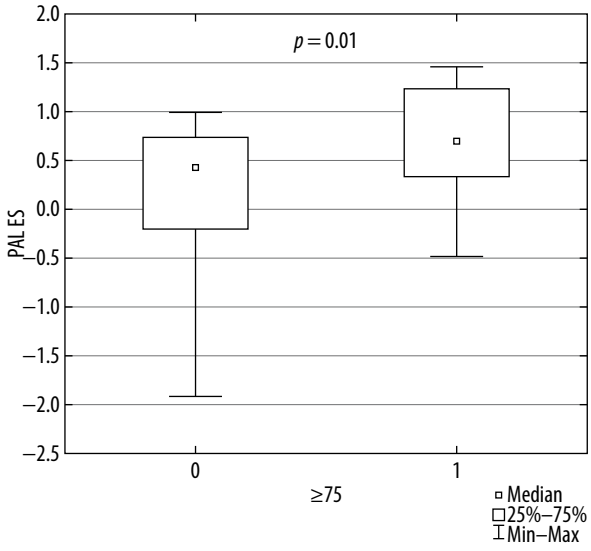


Fig. 4. Comparison of results in PAL ES obtained in two subgroups: groups aged <75 and ≥75 years

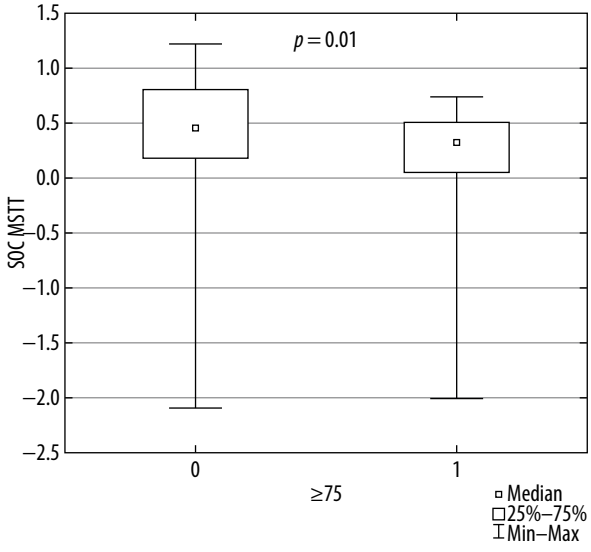


Fig. 5. Comparison of results in SOC MSTT obtained in two subgroups: groups aged <75 and ≥75 years

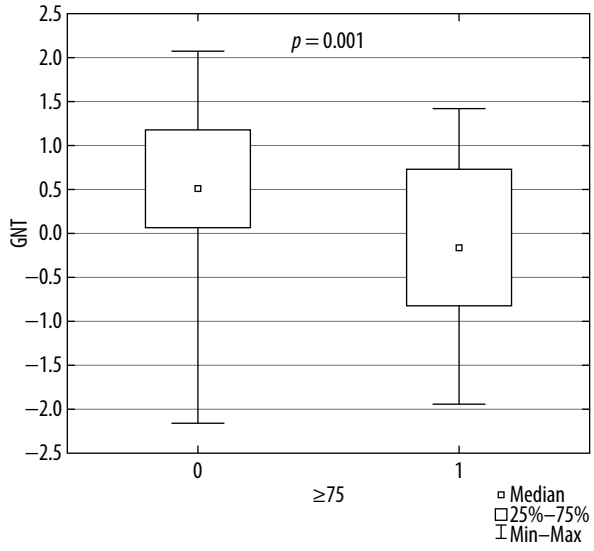


Fig. 6. Comparison of results in GNT obtained in two subgroups: groups aged <75 and ≥75 years

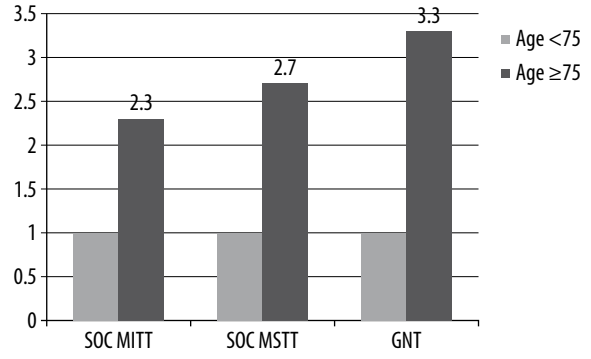


Fig. 7. Results of odds ratio obtained in the studied group in regression analysis according to age <75 and ≥75 years

represents a major public health concern to families, caretakers, doctors, elderly persons and the society, who must provide for these individuals. Coping with such a complex problem and the impact of decline of cognitive functions on the psychosocial functioning of patients depend largely on the accuracy of the diagnosis of neuropsychological assessment. In our study of individuals without diagnosis of dementia, results of selected tests of CANTAB displayed below the reference threshold, matched according to age and gender, ranged from 8 to above 50%. Votruba *et al.* (2016) investigated healthy older adults with scores above 23 in MMSE. The participants performed selected neuropsychological tests. The study group performed well on measures of naming and recall but showed mild to moderate impairment in working memory and processing speed as well as marked impairment in inhibition, sustained attention and executive functioning. Both the study by Votruba *et al.* (2016) and our research point to a decrease in at least one cognitive function in healthy elderly persons – respectively 91% and 57%. In our study, the age ≥75 years was associated with two times higher risk of decreased results of SOC tests, which is a tool for measuring ability of spatial planning and motor control. In addition, the age ≥75 years was associated with three times higher risk of decreased results of GNT, which represents object-naming ability and lexical and semantic memory. In our study, the most prevalent was decrease in results of PAL test, which is a tool for measuring declarative visual memory and new learning. Blackwell *et al.* (2004) revealed that PAL and GNT, when combined, were found to be highly accurate in detecting the cognitive dysfunction characteristic of preclinical AD. The authors found that these tests allow for performance of

DOI: 10.15557/AN.2016.0010

a highly accurate assessment of the probability of risk for an individual with mild memory impairment to develop AD (Blackwell *et al.*, 2004). In our study, spatial planning and spatial working memory, assessed by the results of SOC, were also found to be depressed. Spatial working memory represents one's ability to temporarily store and process information regarding the surrounding environment (Ang and Lee, 2008). Spatial working memory is also important in tasks which involve planning of spatial movements, such as a route through a complex building (Baddeley, 2000).

In our study, surprisingly, 75+ group performed better in MOT ME, PAL TE, and PAL ES. In contrast, SOC MSTT was lower in the 75+ group than in aged <75. It is very risky to draw specific conclusions from differences between the groups aged <75 and ≥75 years. Interestingly, the research of Binder *et al.* (2016) confirms the importance of a systematic practice of different cognitive function using computer techniques. In this study, 84 healthy older adults aged from 64 to 75 were randomly assigned to one of three single-domain training conditions (inhibition, visuomotor function, spatial navigation) or to the simultaneous training of all three cognitive functions. This multi-domain training used iPad at home. After 50 sessions, all participants showed a linear increase in training performance (Binder *et al.*, 2016). Those findings suggest that multi-domain training enhances attention control involved in handling different tasks at the same time. This aspect is a big challenge in everyday life, especially for the elderly.

As mentioned earlier, distinguishing a group of healthy elderly persons with only age-related decline of selected cognitive functions from those with mild cognitive decline encounters difficulties in clinical practice. One needs to remember that primary degenerative disorders such as AD, dementia with Lewy bodies and a vascular dementia may begin as a mild cognitive impairment. In such cases, determination of the onset of the disorders is difficult. In addition, risk factors for this group's disorders may be similar. The diagnosis of MCI requires extensive neuropsychological testing, which enables comprehensive and multi-dimensional evaluation of cognitive functions. Despite the time-consuming procedures required in diagnosing of MCI, in routine clinical practice there is a tendency to use only quick, screening tools such as MMSE, Clock Drawing Test or parts of more complex methods. On the one hand, they improve rapid assessment of the level of selected cognitive functions, but on the other, their sensitivity in diagnosing of people with MCI seems to be low. Regardless of methodological limitations of the usage of quick tests, they are of great importance because of the possibility of a diagnosis of mild cognitive impairment which is undoubtedly the most important risk factor for dementia (Bidzan, 2015). There are suggestions that determination of selected laboratory biomarkers and neuroimaging tests could be more useful in distinguishing healthy elderly people with reduced age-related cognitive functions from those with mild cognitive impairment (Mattsson *et al.*, 2009).

Despite the obvious need of better diagnosing of cognitive impairment in a routine clinical practice, there have not been many attempts of examining the impact of rehabilitation programs of cognitive functions in the elderly so far. Bossers *et al.* (2016) compared the effects of two exercise programs on proxy- and performance-based measures of activities of daily living (ADLs) and explored the potential motor and cognitive mediators underlying ADL improvements in individuals with dementia. In a group of patients with dementia, physical exercise improved activities of daily living levels but improvements were small and appeared to be independent of exercise type. Another conclusion of the study was that combined aerobic and strength exercise may be more effective than aerobic-only exercise to effectively address ADL dysfunction in individuals with dementia (Bossers *et al.*, 2016).

Jean *et al.* (2010) narrowed the study to patients with MCI only. Twenty-two individuals presenting mild cognitive impairment of the amnestic type (MCI-A) were included in cognitive training, in a 10-week randomised controlled study. Participants in the experimental group (n = 11) learned face-name associations using a paradigm combining errorless (EL) learning and spaced retrieval (SR), whereas participants in the control group (n = 11) were trained using an errorful (EF) learning paradigm. Psychoeducational sessions on memory were also provided to all participants. After neuropsychological screening and baseline evaluations, the cognitive training was conducted in 6 sessions over a 3-week period. The post-training and follow-up evaluations, in one and four weeks respectively, were performed by research assistants blind to the participant's study group. The results showed that regardless of the training condition, all participants improved their capacity to learn face-name associations (Jean *et al.*, 2010). Further researches are needed to examine the importance of the systematic cognitive rehabilitation in order to delay the onset of symptoms of dementia in people over the age of 70 years.

CONCLUSIONS

The link between cognitive functions and the age, despite the lack of diagnosis of dementia, confirms the need of neuropsychological assessment in daily care of patients without dementia and the usage of cognitive training programs when appropriate. Patients with CIND should be monitored by a specialist in order to prevent quick loss in their cognitive functioning sphere.

Conflict of interest

Authors of this publication do not report any financial or personal connections with other people or organizations which would have bad influence on the content of the publication or which would claim the rights to this publication.

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DOI: 10.15557/AN.2016.0010 AKTUALN NEUROL 2016, 16 (2), p. 79–84