Diagnostic value of neuropsychological tests in mild cognitive impairment comorbid with Parkinson's disease

Ilona Laskowska[1], Andrzej Koczorowski[1], Dariusz Koziorowski[2], Ludwika Gawryś[3]

[1]Department of Cognitive Psychology, University of Finance and Management in Warsaw
Head of the Department: dr hab. Simone Dalla Bella

[2]Department of Neurology, Faculty of Health Science, Medical University of Warsaw
Head of the Department: prof. dr hab. n. med. Andrzej Friedman

[3]Institute of Psychiatry and Neurology, 2nd Department of Psychiatry
Head of the Department: prof. dr hab. n. med. Tadeusz Parnowski

Summary

Mild cognitive impairment (MCI) is present in on average one-fourth of Parkinson's disease (PD) patients with no dementia diagnosis. Only recently has PD-MCI been treated as a new diagnostic entity. In 2012, unified criteria were adopted which allow both diagnosing MCI in Parkinson's disease (PD-MCI) and further classification taking into account the profile of cognitive dysfunctions and the probability of evolution towards dementia. The diagnostic criteria were presented in the form of stipulations and guidelines assuming that diagnostic process is based on the neuropsychological assessment of the patient. The notion of MCI had been borrowed and for a couple of years had been relying on definitions developed in relation to Alzheimer's disease. For the first time, in the proposed criteria memory dysfunction is not the basis of classification. Only two categories of dysfunctions have been retained, singledomain and multiple-domain. Whether the adopted criteria will contribute to an accurate diagnosis of cognitive dysfunctions and PD-specific dementing processes remains an open question. In spite of some limitations, the presented criteria can certainly improve the efficacy of monitoring the patient's state at the same time allowing the hope for an appropriate therapy and a higher quality of life. Moreover, the unification of diagnostic criteria will be crucial in assessing usefulness of neuropsychological test instruments as a basic method of investigating neurodegenerative processes not only in PD.

Key words: Parkinson's disease, mild cognitive impairment, neuropsychological tests

Introduction

Mild cognitive impairment (MCI) concept was introduced in 1988 [1-3]. In the beginning, it was used exclusively as a name for the level of cognitive

functioning equivalent to the third stage of GDS (Global Deterioration Scale) [1]. In 1991 owing to Flicker et al's [4] paper the term MCI changed its status from a purely descriptive category to a diagnostic category. In other words, the authors demonstrated that the impairment corresponding to the third stage of GDS scale enables the prediction of dementia. In 1995 Petersen et al. [5] renounced diagnosing mild cognitive impairment based on the GDS scale and acknowledged MCI as an independent diagnostic category, 'independent' in the sense that it can be clinically defined. Thereby, a new line of study of pathological aging processes began. At first, MCI was ascribed to non-demented people with preserved activities of daily living and non-lowered score on a test of general cognitive function but with memory dysfunction. When assessing memory dysfunction, both patient's subjective memory complaints and below-norms scores on tests were taken into account [2]. Petersen et al's proposition contributed to intensifying investigation of early stages of Alzheimer's disease (AD), possibility of early diagnosis of AD and preventing its effects before it reaches its final, incurable form. Regardless of the dominant role of memory in Alzheimer's disease deficits of other cognitive areas were taken into account. It resulted in distinguishing MCI subtypes according to neuropsychological assessment. The classification proposed by Petersen [6, 7] was based on two basic criteria: 1) presence of memory dysfunction or absence thereof, and 2) impairment in only one or more functions. A preliminary proposition [6] to classify MCI using these criteria did not take into account the former criterion when more cognitive domains were impaired. This way, a classification into three groups emerged: 1) amnestic, a-MCI; 2) single non-memory domain impaired, na-MCI, 3) multiple domains slightly impaired, md-MCI. Another classification [7] employed both criteria fully which resulted in a classification into four groups: 1) amnestic MCI single domain, 2) amnestic MCI multiple domain, 3) nonamnestic MCI single domain, 4) nonamnestic MCI multiple domain. The model proposed by Petersen was undoubtedly a breakthrough in conceiving cognitive dysfunctions comorbid with aging process. A search for clinical subtypes of MCI differing in etiology and treatment has since become standard in the research into neurodegenerative processes in Alzheimer disease. At the same time, the concept of cognitive profiles in MCI proved promising enough to prompt attempts at employing Petersen's model in other types of dementia [3].

In search of criteria for mild cognitive impairment in PD

In recent years interest in the occurrence of cognitive dysfunctions in PD has grown. It has not been exclusively about dementia-type dysfunctions. Also mild dysfunctions with no direct influence on patient's daily living have been researched into intensively [8-13]. Namely, it is thought that even mild cognitive dysfunctions are an inherent part of the disease [13]. The complexity of the neurodegenerative process induces one to suppose that a thorough grasp on the mechanism of the development of cognitive dysfunctions is a prerequisite for understanding PD. The notion of mild

cognitive impairment plays a special role in this evolution of views on the cognitive aspect of PD [10-12, 14]. This term was first used in relation to PD by Fernandez et al. [15] in 2005. According to Fernandez et al., diagnosis of MCI in PD should be based equally on clinical and psychometric criteria. Secondly, the criteria for probable idiopathic PD should be allowed for. Thirdly, considering the heterogeneity of dementia in PD, three MCI subtypes should be taken into account (a-MCI, md-MCI, na-MCI). Fernandez et al. [9] proposed the first operating definition of MCI based on such criteria as to enable early diagnosis and treatment of cognitive disorders and, by consequence, improve patients' functioning.

It was known [16] that subgroups of patients with different cognitive abilities could be distinguished even in the early stages of the disease and that differences between them may correspond to differences in the underlying neuropathological processes. It was also hoped that greater accuracy of employed criteria would allow to distinguish Lewy bodies pathology from subcortical pathology in a more precise manner, predict the direction of changes in cognitive dysfunctions, determine risk factors for these dysfunctions and identify mechanism underlying those changes. Within seven years from the publication of the pioneering Fernandez et al.'s paper, satisfactory criteria for MCI in PD were finally developed which are considered to be effective [12]. This unification was a solution to disparity of criteria and inability to compare results from different studies (e.g. 18,9% to 38,2%, mean 26,7%, from Litvan et al.'s review [11]). From the clinical point of view lack of unified criteria results in misinformation, prevents accurate interpretation of data and hinders diagnosis process [10-12]. Up-to-date and assumedly unified criteria are presented in Table 1.

Table 1. Diagnostic criteria for mild cognitive impairment in Parkinson's disease according to *Movement Disorder Society Task Force Guidelines* [12]

I. Inclusion criteria:
- Diagnosis of Parkinson's disease as based on the UK PD Brain Bank Criteria [17]- 18]
- Gradual decline, in the context of established PD, in cognitive ability reported by either the patient or informant, or observed by the clinician
- Cognitive deficits on either formal neuropsychological testing or a scale of global cognitive abilities (detailed in section III)
- Cognitive deficits are not sufficient to interfere significantly with functional independence, although subtle difficulties on complex functional tasks may be present

II. Exclusion criteria:
- Diagnosis of PD dementia based on *MDS Task Force* proposed criteria[a]
- Other primary explanations for cognitive impairment (e.g., delirium, stroke, major depression, metabolic abnormalities, adverse effects of medication, or head trauma)
- Other PD-associated comorbid conditions (e.g., motor impairment or severe anxiety, depression, excessive daytime sleepiness, or psychosis) that, in the opinion of the clinician, significantly influence cognitive testing

III. Specific guidelines for PD-MCI level I and level II categories

table continued on the next page

A. Level I (abbreviated assessment)
- Impairment on a scale of global cognitive abilities validated for use in PD or
- Impairment on at least two tests, when a limited battery of neuropsychological tests is performed (i.e., the battery includes less than two tests within each of the five cognitive domains, or less than five cognitive domains are assessed)

B. Level II (comprehensive assessment)
- Neuropsychological testing that includes two tests within each of the five cognitive domains (i.e., attention and working memory, executive, language, memory, and visuospatial)
- Impairment on at least two neuropsychological tests, represented by either two impaired tests in one cognitive domain or one impaired test in two different cognitive domains
- Impairment on neuropsychological tests may be demonstrated by:
  – Performance approximately 1 to 2 SDs below appropriate norms or
  – Significant decline demonstrated on serial cognitive testing or
  – Significant decline from estimated premorbid levels

IV. Subtype classification for PD-MCI (optional, requires two tests for each of the five cognitive domains assessed and is strongly suggested for research purposes)
- PD-MCI single-domain—abnormalities on two tests within a single cognitive domain (specify the domain), with other domains unimpaired or
- PD-MCI multiple-domain—abnormalities on at least one test in two or more cognitive domains (specify the domains)

[a] Diagnostic criteria for dementia in Parkinson's disease according to MDS Task Force were published in the monography: Laskowska I. (2012) *Starość i drżenie. Specyfika wybranych zaburzeń poznawczych i afektywnych w chorobie Parkinsona w świetle badań longitudinalnych*. Bydgoszcz: Wydawnictwo Uniwersytetu Kazimierza Wielkiego.

In the diagnosis of Parkinson's disease, the bradykinesia symptom is deemed the most important and only in the next step, one of the three other core symptoms of the disease can be chosen. If it concerns neuropsychological studies, the range of 1,0-2,0 SD below norm is consistently recommended in all cases. Petersen's four subtypes classification has been downsized to two subtypes (single vs multiple-domain). Recurring to the known method of increasing reliability by doubling the psychometric sample, the authors proposed performing two tests for each of the five cognitive domains (in the comprehensive version). For practical reasons, using an abbreviated version has been permitted where test battery does not satisfy that condition (less than two tests for each of the five domains, or fewer cognitive domains are assessed).

The fact that a proposition concerning the choice of neuropsychological test instruments has been added to the guidelines is an advantage of the current criteria for MCI. For the abbreviated version, a list of general cognitive function screening tests has been presented (Montreal Cognitive Assessment, MoCA; Parkinson's Disease-Cognitive Rating Scale, PD-CRS; Scales for Outcomes of Parkinson's disease–Cognition, SCOPA-COG; Mattis Dementia Rating Scale, MDRS) along with two tests assessing

premorbid level of intelligence (National Adult Reading Test (NART), Wechsler Test of Adult Reading (WTAR) – unfortunately, both unavailable in Poland). If it concerns the comprehensive version, a specific set of neuropsychological tests have been recommended; this set is presented in Table 2.

Table 2. Neuropsychological tests recommended by Movement Disorder Society Task Force in diagnosing PD-MCI [12] (names of normalized or available Polish equivalents are written in italics)

Cognitive domains	Neuropsychological tests	Estimated time of test (min)
Working memory	WAIS-IV (or earlier version), Letter/Number sequencing	5
	Digit Symbols Coding from WAIS-R (PL)*	5
	Trail Making Test (TMT)	5 to 10
	Digit span backward or a digit ordering test: Digit span backward*	5
	Stroop color word test	5 to 10
Executive functions	WCST), or modified Nelson's version of CST: WCST*	5
	Tower of London test – version developed at the university of Drexel, or its computerized version (Stockings of Cambridge)	5 to 15
	Verbal fluency test, e.g. letter fluency (COWAT) or similar ones; category fluency (animals, supermarket, or similar), or alternating category fluency task in a standardized version. 10-point Clock Drawing Test. (The use of two tests too similar to one another, e.g. a phonologic fluency test and a category fluency test does not meet the guidelines for MCI in PD).	5
Language	WAIS-IV, Similarities or earlier version: WAIS-R (PL)*	10 to 15
	Confrontation naming tests, e.g. Boston Naming Test, or Graded Naming Test; or other tests	5 to 15
Memory	Word list learning tests with delayed recall and recognition of the verbal material, e.g. AVLT, CVLT, Hopkins Verbal Learning Test (HVLT), Selective Reminding Test: CVLT*	10
	modified story from Łucki Booklets, Logical Memory from WMS-IV adapted by prof. M. Pąchalska and dr M. Lipowska, stories from Choynowski scale	10 to 15
	Brief Visuospatial Memory Test – Revised (BVMT-R)	10 to 15

Visuospatial functions	Benton's Judgment of Line Orientation test	5 to 10
	Hooper Visual Organization Test	10
	Clock copying test (e.g. Royall's CLOX)	5

* Polish normalization

The authors of PD-MCI criteria warn against using two tests which are too similar to each other (e.g. two list learning tests or two story memorizing trials) as a way of satisfying the criterion stating that to assess an impairment, one test is not enough. Similarly, highly correlated scores from two subtests of the same test (e.g. immediate and delayed recall) should not be treated as a means to fulfill the condition that the performance must be impaired on two tests [12].

Authors' intentions taken into account, it must be noticed that in research practice, deciding about the similarity of tests may disrupt the diagnostic process. For that reason it seems that proposing pairs of tests which would differ in a significant way would be a better solution. That way, the problem of the similarity of tests and the correlation of subtests scores would not impede already complex process of diagnosing PD-MCI. Moreover, the list of sample neuropsychological tests and specific guidelines as prepared by Movement Disorders Society Task Force do not satisfy the basic condition for reliable diagnosis, which is using, in research and in clinical practice, a homogeneous, routine, precisely defined test battery [19]. Also, some criticism may arise as to the magnitude of the standard deviation range (1 to 2 SD) which may impede unification and comparing different results [20]. A more detailed, critical analysis was conducted by Marras et al. [21]. They noticed three weaknesses. Firstly, allowing for premorbid level dramatically increases the number of individuals classified as PD-MCI from 33% when this criterion is not observed to 79% when it is. Moreover, the authors consider the latter figure undervalued as the used criteria undervalue premorbid level of intelligence. Secondly, after eliminating the condition of subjective patient's complaints, the percentage of individuals with diagnosed PD-MCI increases from 33% to 41%. Thirdly and lastly, in the case of the sample examined by the authors the results obtained did not differentiate PD-MCI subtypes (93% were patients with heterogeneous MCI (md-MCI)).

Diagnostic criteria for PD-MCI – a turning point in the research into Parkinson's disease?

The establishment of unified criteria for mild cognitive impairment is undoubtedly a breakthrough and lays the foundations for future research whose aim will be to understand the course of Parkinson's disease between first symptoms of cognitive impairment and the occurrence of dementia. From the clinical point of view it represents a search for objective and basic biological aspects of MCI in Parkinson's disease (e.g. pathology, genetics, functional anatomy) which trigger the process of irreversible

changes in the brain resulting in the observed cognitive deficits [9]. Cognitive deficits in PD have frequently been attributed to neurochemical alterations in dopaminergic, cholinergic, and other neurotransmitter systems, neuropathological contributions of limbic system, cortical Lewy bodies and neurites, amyloid deposition, neurofibrillary tangles, and cerebrovascular disease which affects the cortex and the limbic system. Applying a validated Alzheimer's disease pattern of brain atrophy to the MRI scans of patients with Parkinson's disease confirms the involvement of hippocampus and parieto-temporal cortex atrophy, which predicts cognitive decline in Parkinson's disease patients [22]. The presence of MCI is associated with a higher level of cortical changes (increased atrophy of the bilateral occipital, left temporal, and frontal cortices) in the group of PD patients who underwent anatomic magnetic resonance imaging [23]. Neuropathological studies of PD-MCI are limited. The neuropathological data present typical brainstem predominant Lewy bodies inclusions, neuritic plaques, amyloid depositions and old cerebral infarcts [24]. A heterogenous neuropathology was found in PD-MCI, similar to that found in MCI without PD, although Alzheimer-like lesions are the most common pathology, infarctions and mixed pathologies also being present [11]. Influence of genetic factors has been explored in PD patients with cognitive dysfunction including typical parkinsonian genes, polymorphisms related to dopamine regulation and tau proteins. The microtubule-associated protein tau gene (MAPT) H1/H1 genotype but not polymorphisms in the catechol-O-methyl transferase gene (COMT) was found to be a risk factor for PDD in PD cohort [10]. Both point mutations and multiplications of SNCA gene are associated with cognitive impairment in PD [25]. Also GBA point mutations are associated with a higher frequency of dementia in PD patients. GBA mutation status may be an independent risk factor for cognitive impairment in patients with PD [26]. On the other hand, in PARK 2 gene mutations cognitive deficits are rare [27].

Despite the progress in the research into PD-MCI biomarkers, including them is not recommended by the authors of the guidelines [12]. They consider solid neuropsychological assessment, although it is perhaps time-consuming and requires sound knowledge, to be the most effective diagnostic method so far. In Poland, requirements specified in the detailed instructions are difficult to satisfy because neuropsychological tests with strict norms are lacking. As a consequence, precise delimitation of the standard deviation is in many cases impossible. However, the essence of the propounded procedure does not boil down to detailed calculations (the proposed range of 1,0-2,0 SDs below norm leaves the interpretation to a great extent at one's discretion anyway), but consists in coupling diagnostic experience with clinical trials results. Obviously, the assumption is that the choice of test instruments and their wide gamut will allow to assess the state of the patient adequately even though there are no Polish norms.

It is worth noting here that there are no major discrepancies between the MDS Task Force authors' proposition and the binding criteria for mild cognitive impairment in Parkinson's disease from the latest DSM-V classification [28]. The category of mild neurocognitive disorders (mild NCD), which is a counterpart of MCI, has a clinical category status 331.83 (G31.84) and encompasses over a dozen different diseases

(including Parkinson's disease) resulting in cognitive dysfunction. In DSM-V the arbitrariness of differentiating norm from mild disorders and mild disorders from major disorders (in DSM-V, dementia has been superseded by the term *major* NCD) has been emphasized. Using standardized neuropsychological tests is recommended, and when they are lacking, other quantitative clinical methods. So, in comparison with DSM-IV [29], where mild neurocognitive impairment was not covered extensively (it was classified as cognitive impairment not otherwise specified (294.9)), significant modifications have been introduced. Moreover, guidelines published in Appendix B to DSM-IV, where stricter criteria for *mild* NCD were suggested, were not upheld. It is worth remembering that research criteria required diagnosing impairment in at least two cognitive domains. Moreover, a sine qua non was visible patient's social functioning impairment. In addition, a corroboration of the observed disorders by finding pathology in laboratory diagnosis was required. We can safely say then that although it bears a different name, the PD-MCI conception suggested by DSM-V is in substance not different from the one propounded by *MDS Task Force*, but does differ much from the one proposed in DSM-IV. If it concerns the ICD-10 classification [30], the term mild cognitive disorder can be found there (F06.7), whose criteria encompass symptoms of temporary nature. Because the limits of that diagnostic category (F06.7) are quite vague, that diagnosis is used as a substitute for mild cognitive impairment.

To sum up, in the last dozen or so years significant changes in understanding cognitive disorders comorbid with neurodegenerative disorders, with Parkinson's disease in particular, have occurred. The advance is visible and allows the hope that coupling different diagnostic methods including neuropsychological diagnostics will lead to detecting cognitive deficits in early stages of disease, which will enable both the broadening of the knowledge about the mechanism of their emergence and an improvement in patients' quality of life. Whether this aim will be achieved depends to a great extent on the manner in which the newly formed guidelines will be introduced into research and clinical practice.

Case presentation

Preliminaries: Below are presented the findings of a neuropsychological assessment carried out and analyzed as based on MDS Task Force guidelines (level II). It should be emphasized that Polish normalization is available only for some of the tests recommended by MDS Task Force, so only in the case of those few tasks the definition of 1 to 2 SDs below an appropriate norm could be applied. In the remaining cases, only clinical trials available in Poland, assessing particular cognitive functions, could be used (and not tests in the psychometric sense of the term); the performance level in such trials was interpreted by comparing it to estimated premorbid levels.

If it concerns visuospatial functions assessment, in addition to the recommended Royall's CLOX and Hooper Visual Organization Test (which is not readily available in Poland), the commonly used Rey Complex Figure Test was applied. The latter may

be useless in patients with strong tremor or rigidity, however, in the case of this patient the intensity of the motor symptoms of the disease was not a significant impediment.

Interview: A 62-year-old man, with secondary technical education (13 years of education). In this patient, first PD symptoms, in the form of left hand tremor, occurred 2 years earlier. At the time of the examination, the patient was treated with levodopa (4x200 mg). Severity of the disease as assessed in the Hoehn & Yahr scale was 1,5 in on state and 2,5 in off state. The patient complained of cognitive deterioration including memory. Up to the moment of PD diagnosis the patient was not treated psychiatrically nor neurologically. During the examination no significant depression symptoms were found, which was corroborated by BDI-II scale score = 6 pts.

Neuropsychological assessment

Screening tests

MMSE (*Mini Mental State Examination*) =29 pts; MoCA (*Montreal Cognitive Assesment*)=26 pts. The scores in both scales do not indicate significant cognitive impairment, however, in the case of MoCA test, which is recommended for screening diagnosis in PD, the patient's score equals cut-off point.

Episodic memory

CVLT (*California Verbal Learning Test*): learning curve, A list: 7 (sten 6),7,8,8,11 (sten 6) Σ41 (sten 5); B list=4 (sten 4)
A list Short Delay Free Recall=7 (sten 4)
A list Short Delay Cued Recall=9 (sten 4)
A list Long Delay Free Recall =7 (sten 4)
A list Long Delay Cued Recall =10 (sten 5)
Perseverations=7 (sten 4)
Intrusions in free recall =6 (sten 4)
Intrusions in cued recall =3 (sten 4)
Correct recognition total=16 (sten 10)
Incorrect recognitions =2 (sten 5)

Test performance level is within low average scores area (the area up to -1 SD). But what draws attention is relatively decreased effectiveness of free recall after distraction and after delay: out of 11 learned words, the patient recalls 7, the significance of this difference is corroborated if we compare the sten scores (6th and 4th sten, respectively). Moreover, it is worth noting that the number of perseverations and intrusions is relatively increased (although sten scores stay in the lower range of -1 SD) and that there is no effective using of material ordering strategy (the patient did not spontaneously use the categories "fruit" and "tools" during learning). Moreover, a small effect of proactive interference is present (B list). Subtle impairment of differentiation in recognition can be observed as well.

The results obtained indicate impairment of memory processes which is probably derivative of impaired executive control and working memory deficits engaged in efficient encoding and retrieval of verbal material. It results in decreased efficiency of episodic memory processes, but with no profound acquisition deficits (learning curve remains ascending) and with preserved tenacity of mnemic trace. Impairment of episodic memory efficiency is corroborated by the scores in the task, which consists in learning and recalling a short story.

Acquisition of logical material *(a modified story from Łucki Booklets* – a trial from unpublished PhD thesis of PhD Anna Barczak [31])

Direct recall: 11 elements recalled out of 21 elements of the story, with a partial change of content. 20-minute delay recall: 8 elements recalled out of 21 elements of the story, although with filling in gaps in memory with content absent from the clinical trial. Both acquisition and recall levels are slightly below expected level.

Working memory

Digit Span (range)=5; Backward Digit Span (range)=4.
The score lies within norm, in its lower portion.
Trail Making Test Part A=52s; Trail Making Test Part B=141s; 1 mistake; B-A=89; B/A=2,71

The scores indicate psychomotor retardation, the B/A index indicates impaired efficiency of information processing in working memory.

Language functions

Similarities from WAIS-R: WS=11; WP=10; score average;
Naming Trials=17+/21 (+3 mistakes self-corrected)
Word readiness only slightly impaired, without distinct deficits.

Executive functions

Verbal fluency trials: animals=22/1 min; fruit and vegetables=18/1 min; letter P=9/1min; letter K=12/ 1 min; score below the expected in respect of formal categories, semantic categories – scores within the expected range, what indicates decrease of executive control (phonological fluency trials require production of a greater number of strategies).

WCST (*Wisconsin Card Sorting Test*): Number of Categories Scored=0 (<16th centile); Total Number of Mistakes =88 (12th centile); Number of Perseverative Answers =106 (5th centile); Number of Perseverative Mistakes=78 (5th centile); Percentage of Conceptual Answers=3,9% (1st centile).

All indices much below the expected, they corroborate profound deficits in alternating attention and changing cognitive attitude in response to feedback.

Visuospatial functions

VOT (*Hooper Visual Organization Test*): Out of 30 pictures, the patient recognized incorrectly or did not try to name 12. In two cases, recognition partly correct.

RCFT (*Rey Complex Figure Test*): Copy trial-raw score=26 pts. Numerous errors indicating visuospatial synthesis and analysis disorders e.g. the bottom cross (element 17) is at the same time the bottom side of the large rectangle (el. 2). The triangle on the side (el. 13) is not symmetrical and is shifted in relation to the large rectangle (el. 2).

Royall's CLOX test – In the trial made by the patient from memory, small difficulties in even placing digits on the clock face (not present in the copy trial) can be observed. In all three tasks, impairment of visuospatial analysis and synthesis was observed: mild in the easiest test (Clox) and more visible in more difficult ones (VOT, RCFT).

Summary

Neuropsychological assessment demonstrated executive functions deficits, impairment of working memory efficiency and visuospatial functions disorders. Additionally, impaired episodic memory, but with relatively lower intensity, could be observed, partially derivative of executive control disorders, and impaired efficiency of information processing. The depth and profile of the observed disorders enables a diagnose of multiple-domain PD-MCI.

Acknowledgments

References

1. Reisberg B, Ferris SH, de Leon MJ, Franssen ESE, Kluger A, Mir P. i wsp. Stage-specific behavioral, cognitive, and in vivo changes in community residing subjects with age-associated memory impairment (AAMI) and primary degenerative dementia of the Alzheimer type. Drug Dev. Res. 1988; 15: 101–114.

2. Golomb J, Kluger A, Ferris SH. *Mild cognitive impairment: historical development and summary of research*. Dialogues Clin Neurosci. 2004; 6(4): 351–67.

3. Petersen RC, Roberts RO, Knopman DS, Boeve BF, Geda YE, Ivnik RJ i wsp. *Mild cognitive impairment: ten years later*. Arch. Neurol. 2004; 66(12): 1447–1455.

4. Flicker C, Ferris SH, Reisberg B. *Mild cognitive impairment in the elderly: predictors of dementia*. Neurology 1991; 41: 1006–1009.

5. Petersen RC, Smith GE, Ivnik RJ, Petersen RC, Smith GE, Ivnik RJ i wsp. *Apolipoprotein Estatus as a pre-dictor of the development of Alzheimer's disease in memory-impaired individuals*. JAMA 1995; 273: 1274–1278.

6. Petersen RC, Doody R, Kurz A, Mohs RC, Morris JC, Rabins PV i wsp. *Current concepts in mild cognitive impairment*. Arch. Neurol. 2001; 58(12): 1985–1992.

7. Petersen RC. *Mild cognitive impairment as a diagnostic entity*. J. Intern. Med. 2004; 256(3): 183–194.

8. Caviness JN, Driver-Dunckley E, Connor DJ, Sabbagh MN, Hentz JG, Noble B i wsp. *Defining mild cognitive impairment in Parkinson's disease*. Mov. Disord. 2007; 22(9): 1272–7.

9. Fernandez HH, Crucian GP, Okun MS, Price CC, Bowers D. *Mild cognitive impairment in Parkinson's disease: the challenge and the promise*. Neuropsychiatr. Dis. Treat. 2005; 1(1): 37–50.

10. Goldman JG, Litvan I. *Mild cognitive impairment in Parkinson's disease*. Minerva Med. 2011; 102(6): 441–459.

11. Litvan I, Aarsland D, Adler CH, Goldman JG, Kulisevsky J, Mollenhauer B i wsp. *MDS Task Force on mild cognitive impairment in Parkinson's disease: critical review of PD-MCI*. Mov. Disord. 2011; 26(10): 1814–1824.

12. Litvan I, Goldman JG, Tröster AI, Schmand BA, Weintraub D, Petersen RC i wsp. *Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines*. Mov. Disord. 2012; 27(3): 349–356.

13. Meireles J, Massano J. *Cognitive impairment and dementia in Parkinson's disease: clinical features, diagnosis, and management*. Front. Neurol. 2012; 3: 88.

14. Dalrymple-Alford JC, Livingston L, MacAskill MR, Graham C, Melzer TR, Porter RJ i wsp. *Characterizing mild cognitive impairment in Parkinson's dis*ease. Mov. Disord. 2011; 26(4): 629–636.

15. Troster AI. *MCI in Lewy Body Disorders: Definition, Frequency, Progression and Differentiation from Other MCI*. www.alzforum.org/res/for/vir/miami/presentations/troster_miami09.ppt (access 14.03.2014)

16. Foltynie T, Brayne CE, Robbins TW, Barker RA. *The cognitive ability of an incident cohort of Parkinson's patients in the UK. The CamPaIGN study*. Brain 2004; 127(3): 550–560.

17. Gibb WRG, Lees AJ. *The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease*. J. Neurol. Neurosurg. Psychiatry 1988; 51(6): 745–752.

18. Opala G. *Różnicowanie zespołów parkinsonowskich*. Neurol. Neurochir. Pol. 2005; 39(4; supl.3): 579–583.

19. Biundo R, Weis L, Pilleri M, Facchini S, Formento-Dojot P, Vallelunga A i wsp. *Diagnostic and screening power of neuropsychological testing in detecting mild cognitive impairment in Parkinson's disease*. Neural. Transm. 2013; 120(4): 627–633.

20. Burn DJ, Barker RA. *Mild cognitive impairment in Parkinson's disease millstone or milestone?* Pract. Neurol. 2013; 13(2): 68–69.

21. Marras C, Armstrong MJ, Meaney CA, Fox S, Rothberg B, Reginold W i wsp. *Measuring mild cognitive impairment in patients with Parkinson's disease*. Mov. Disord. 2013; 28(5): 626–633.

22. Weintraub D, Dietz N, Duda JE, Wolk DA, Doshi J, Xie SX i wsp. *Alzheimer's disease pattern of brain atrophy predicts cognitive decline in Parkinson's disease*. Brain 2012; 135:170–180.

23. Hanganu A, Bedetti C, Jubault T, Gagnon JF, Mejia-Constain B, Degroot C i wsp. *Mild cognitive impairment in patients with Parkinson's disease is associated with increased cortical degeneration*. Mov. Disord. 2013; 28(10): 1360–1369.

24. Jellinger KA. *Mild cognitive impairment in Parkinson disease: heterogenous mechanisms*. J. Neural. Transm. 2013; 120(1):157–167.

25. Hoffman-Zacharska D, Koziorowski D, Ross OA, Milewski M, Poznański J, Jurek M i wsp. *Novel A18T and pA29S substitutions in α-synuclein may be associated with sporadic Parkinson's disease*. Parkinsonism Relat. Disord. 2013; 19(11): 1057–1060.

26. Alcalay RN, Caccappolo E, Mejia-Santana H, Tang M, Rosado L, Orbe Reilly M i wsp. *Cognitive performance of GBA mutation carriers with early-onset PD: the CORE-PD study*. Neurology 2012; 78(18): 1434–1440.

27. Koziorowski D, Hoffman-Zacharska D, Sławek J, Szirkowiec W, Janik P, Bal J, Friedman A. *Low frequency of the PARK2 gene mutations in Polish patients with the early-onset form of Parkinson disease*. Parkinsonism Relat. Disord. 2010; 16(2): 136–138.

28. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. Arlington, VA: American Psychiatric Association; 2013.

29. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Test Revision*. Washington, DC: APA; 2000.

30. *Międzynarodowa Statystyczna Klasyfikacja chorób i problemów zdrowotnych (rewizja dziesiąta). Klasyfikacja zaburzeń psychicznych i zaburzeń zachowania w ICD-10. Opisy kliniczne i wskazówki diagnostyczne*. Kraków–Warszawa: Uniwersyteckie Wydawnictwo Medyczne „Vesalius", Instytut Psychiatrii i Neurologii; 1997.

31. Barczak AK. *Zastosowanie badań neuropsychologicznych i spektroskopii rezonansu magnetycznego do oceny przebiegu funkcji planowania i ich zaburzeń*. Niepublikowana praca doktorska. Warszawa: Instytut Medycyny Doświadczalnej i Klinicznej PAN; 2011.