ORIGINAL PAPER

EFFECT OF THE COGNITIVE REHABILITATION IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT AND IDENTIFIED BRAIN ATROPHY

Petr Nilius¹, Petra Krulová², Dagmar Beránková², Pavel Ressler², Olga Zapletalová², Jana Minarčíková², Jan Pouchlý²¹Department of Psychology, Philosophical Faculty of Palacký University Olomouc, Czech Republic²Department of Neurology, Centre for Cognitive Disorders, Ostrava University Hospital, Czech Republic

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Abstract

Aim: The main objective of this study was to analyse the development of cognitive functions and effect of cognitive rehabilitation on patients diagnosed with mild cognitive impairment (MCI), as a result of brain atrophy. **Design:** A quantitative non-randomized intervention study on a control sample of patients. **Methods:** The effect was observed in a group of patients ranging 59–91 years of age (N = 36). Only patients fulfilling the diagnostic criteria of mild cognitive disorder diagnosed by tomography (CT) that had undergone 22 sessions, were involved in the clinical sample (n = 21). The control sample (n = 15) consisted of patients without any neurological diagnosis and who did not undergo cognitive sessions. **Results:** The effect of cognitive rehabilitation was measured by Addenbrooke's cognitive test, revised in 2010 (ACE-R); affective changes were measured by Beck's scale of depression BDI-2 and by a scale used to detect anxiety and depression: the Hospital Anxiety and Depression Scale (HADS). Subjective change and improvement were observed using the Clinical Global Impression (CGI) psychiatric scale. Changes in the functional state of patients were measured by means of the activities of daily living scale (ADL), including the instrumental version (IADL). The effect was examined in the form of entry and output tests, which were verified by statistical analysis, a significant level being $p > 0.05$. **Conclusions:** Significant differences in verbal tests and ACE-R were observed in the clinical sample of patients. Some significant changes were observed in the field of affective symptoms, according to the HADS and BDI-2. The clinical sample showed a significant improvement in subjective clinical state (CGI). The ADL and IADL questionnaires seem to have been inadequate for purpose due to their low sensitivity. The effect of cognitive rehabilitation in patients diagnosed with mild cognitive disorder can be seen and verified in comparison with the control sample, which did not suffer from any neurological disorder and did not undergo cognitive sessions. Cognitive rehabilitation may serve as a useful tool for improving cognitive activation in patients diagnosed with brain atrophy. Results are in line with the current state of knowledge and have an overlap in nursing care.

Keywords: cognitive rehabilitation, cortical atrophy, MCI, ACE-R, depression anxiety, CGI.

Introduction

The intermediate stage between the cognitive changes of old age and dementia is often classified as mild cognitive impairment (MCI) (Sheardová, 2010). According to MKN X, MCI corresponds to the diagnostic criteria for mild cognitive disorder and is accompanied by changes in the size and structure of the brain. Based on findings on a CT scan, all observed patients showed signs of cortical atrophy. According to radiologists, cortical atrophy is characterized by the deepening of the subarachnoid spaces on the convexity of inter-hemispheric areas of

the basal cisterns and posterior fossa and may induce the emergence of cognitive deficits, affective changes, behavioural disorders and an overall change in adaptive function in seniors. In 10–15% of patients, mild cognitive disorder may bridge to a more progressive form of neurodegenerative disease and dementia (Flicker et al., 1991). Treatment of the resultant deficits is usually pharmacological and symptomatic. An additional method which may be considered is cognitive rehabilitation and activation of the central nervous system (CNS) (Holmerová et al., 2005). The effect of cognitive rehabilitation on cognitive functions has been demonstrated in patients with acute types of cognitive deficit and traumatic brain damage, namely in cognitive areas, emotional areas, and areas tracking the quality of life of patients (Karr et al., 2014). The effect of cognitive

Corresponding author: Petr Nilius, Ambulance klinické psychologie s.r.o., Spojů 835/2, Ostrava – Poruba, Czech Republic, email: petr.nilius@gmail.com

rehabilitation in patients with MCI is evident in improvements in function related to daily activities and in the framework of general mobilization of patients, rather than in the area of cognitive benefits. However, this area is constantly being explored and has become the subject of discussion that has led to improvements in medical and nursing practice (Huckans et al., 2013).

A crucial assumption for the function of cognitive rehabilitation is the principle of brain plasticity (neuroplasticity). Neuroplasticity can be defined as the natural ability of the body to overcome the limitations of genes and adapt to a rapidly changing environment. Neuroplasticity is an intrinsic property of brain function, despite the different mechanisms related to aging throughout the life cycle of a human (Pascual-Leone, 2011). This adaptability is based on the principles of the use of brain and cognitive reserve, which the organism builds throughout development. The effect of cognitive rehabilitation, whether in the form of the activation of patients' subjectively perceived positive change or the improvement of affective and cognitive function is proof of the concept of the adaptability of brain activity in the elderly. The confirmation of the function of neuroplasticity in patients with cortical brain atrophy is an important finding, especially for rehabilitation, psychological and nursing care in terms of the need to ensure continuous activation care in the areas of sub-acute, post acute and social health forms of care.

Aim

The aim of this paper is to describe the rate of change in cognitive functions and the effect of cognitive rehabilitation on patients who have incurred cortical atrophy and have been identified as having cognitive deficit at the level of mild cognitive disorder with predicted progression of the condition, after the application of cognitive rehabilitation, compared with a group of patients without neurological diagnosis.

Methods

Design

The paper has the character of a quantitative non-randomized intervention study with a control sample of patients. The monitored clinical sample consisted of 21 patients diagnosed with mild cognitive disorder on the basis of atrophic cortical brain lesion, which was confirmed by imaging (Computer tomography).

Sample

The effect of cognitive rehabilitation was studied in a group of 36 patients (Table 2). The monitored clinical

sample consisted of 21 patients diagnosed with mild cognitive disorder on the basis of atrophic cortical brain lesion, which was confirmed by imaging. The clinical sample patients underwent a cognitive rehabilitation program at the Centre for Cognitive Disorders at the University Hospital, Ostrava. The control sample included 15 elderly people without confirmed neurological and psychiatric diagnosis, living in a nursing home. The patients included in the clinical reference group met the criteria for the diagnosis on the basis of ICD-X criteria and description of computed tomography imaging (CT) and had established medication (including psychiatric) before the beginning of the rehabilitation program. Inclusion in the groups studied was determined by an independent, attested neurologist without knowledge of the outcome of the psychological examination and without prior diagnostic – clinical contact.

The exclusion criteria was the absence of atrophic lesion, MMSE < 25 points, sensory disturbance that would impede the process of cognitive rehabilitation, and long-term, pharmacoresistant psychiatric comorbidity.

Data collection

The change was determined by comparing statistical evaluation of applied psychological methods. The methods used for monitoring changes were as follows: cognitive change was observed by the Addenbrooke cognitive test (ACE-R), including MMSE score; changes in symptoms of anxiety and depression were studied using the Hospital Anxiety and Depression Scale (HADS) and the Beck depression scale (BDI-2); changes in clinical condition personally experienced by patients were monitored using the Clinical Global Index (CGI); and changes in functional status of patients were monitored using the range of activities of daily living (ADLs) and instrumental daily activities (IADL) tools.

Addenbrooke's Cognitive Examination-Revised (ACE-R, a revised version from 2010) is a comprehensive neuropsychological screening method including the Mini-Mental State Examination (MMSE) and items that are sensitive enough to capture moderate disturbances of cognition. The test is composed of a series of subtests: Attention and orientation, Memory, Fluency, Language and Visual-Spatial Components. It is used to determine a more detailed cognitive profile for the early detection of cognitive disorders and a more accurate differential diagnosis of cognitive disorders and dementia (Bartoš et al., 2011). ACE-R provides a series of reliable and valid data on the state of cognitive function

(Crawford, 2010). Using orientational standards for the Czech population, its results are calculated in gross scores (Beránková et al., 2015). Administration of the test does not necessarily require special professional competence. It is used in medical and nursing practice. Clinical Global Impression (CGI) is a psychiatric scale for measuring the observed severity of a disease. It is a seven-point scale on which the patient marks the number to identify the level of subjectively experienced change in their health condition. There are thus two estimates available – the patient's and that of the caregiver, thereby providing a clinical impression of change in health condition at a certain point, usually after from the start of the treatment (Busner, 2007). Currently the Czech revision of CGI is unavailable and is used more for experimental purposes.

The Beck depression scale (BDI-2) is a widely-used self-rating instrument to detect depression and anxiety. The currently used inventory is the Czech revision of 1996. The scale includes 21 items rated from 0 to 63 points and has been compiled to measure the depth of disease and can therefore be used over a period of time (Beck et al., 1999).

The Hospital Anxiety and Depression Scale (HADS) is a scale used for the detection of anxiety and depression. It is composed of fourteen statements which the patient assesses in connection with the appearance of anxious and depressive symptomatology and is associated with quality of life (Snaith, 2003).

Course of cognitive rehabilitation

Cognitive rehabilitation was carried out at the workplace of the Centre for Cognitive Disorders of the Neurological clinic of the University Hospital, Ostrava, at regular twice-weekly group meetings, the group being composed of up to nine people. Cognitive function rehabilitation followed the NEUROP 3 program, which includes a battery of 57 programs, the majority of which contain several options and levels of exercise. NEUROP 3 is based on the clinical experience of its authors and is especially designed for patients with organic brain impairment. An additional tool for cognitive rehabilitation were worksheets (Nilius, Krulová, et al., 2013) designed for group work with patients with mild cognitive disorders and dementia. The course of cognitive rehabilitation was provided by a nurse in collaboration with a neuropsychologist. The duration of cognitive training generally depended on the period between Test and Retest, with intervals ranging from 91 days to 646 days, with a median of 206 days / 23 sessions (Table 1). In the reporting period no systematic cognitive or non-

pharmacological activation intervention was applied to the reference control sample. The group included patients who completed at least 15 sessions in a period of 3 months and showed regularity in attendance at the sessions.

Table 1 Characteristics of cognitive rehabilitation

	Length of rehabilitation (Days, Min-Max)	Number of sessions (Hours, Min-Max)
Clinical sample (n = 21)	210 (98–646)	23 (15–58)

Data analysis

The results of the research were evaluated by statistical analysis and validated by a non-parametric Wilcoxon test for paired values at the level of significant change ($p > 0.05$) and verified by the Mann-Whitney U test using correction. The calculation was performed with the statistical software *STATISTICA Standart CZ*.

Results

The group investigated included a total of 36 patients between the ages of 59 to 91. Based on statistical comparison, it can be stated that they were of similar age and with a similar average (median) level of education. The interval between the Test and Retest was significantly longer in patients enrolled in the clinical group. However, the MMSE score input value was comparable between the monitored groups and, according to the corresponding cut-off score, the results reflected the situation in the general population. The ACE-R value (see Table 2) corresponded to a mild impairment of cognitive function (Nikolai et al., 2013), with a significantly better outcome in patients from the clinical group. All patients included in the clinical group lived either with a partner or with close family during the course of the study. Those included in the reference control sample lived in a nursing home.

To test the hypothesis regarding the significance of changes in cognitive function measured by ACE-R score, we used the non-parametric Wilcoxon rank test for paired values. It confirmed significant changes in ACE-R and word production parameters at a significance level of $p > 0.05$.

These values can be interpreted as an overall improvement in 'general rate of' cognitive function, particularly in the area of cognitive flexibility and process of thought. In other monitored areas no effect at the specified level of significance was observed.

Table 2 Basic output characteristic of the monitored groups

(n = 36)	Male/ Female	Age (Min- Max)	Education (Min- Max)	Test-ReTest (Days; Min-Max)	MMSE (Min- Max)	ACER (Min-Max)	Living (Family/Nursing house)
Clinical sample (n = 21)	10/11	71 (59–84)	13 (8–18)	206 (91–646)	28 (26–29)	83 (71–89)	21/0
Control sample (n = 15)	7/8	78 (65–91)	11 (8–18)	120 (90–150)	29 (28–30)	77 (74–83)	0/15

To verify the significance of changes we used the Mann-Whitney U-test for two independent samples. The test confirmed a significant difference between the two groups in the ACE-R parameter and language skills ($p > 0.05$).

Given the low number of patients in the observed group BDI-2 we cannot reliably interpret the result. Analysis suggests that there was a moderately progressive state of subjectively perceived anxiety and depression in the monitored control sample (see Table 3, 4, 5 in items ANX, and DEP).

In other monitored parameters, after statistical analysis, we did not find any statistically significant effect that could be interpreted to any degree of satisfaction.

Based on analysis with the Wilcoxon test, we confirmed significant changes in the language skills parameter at a significance level of $p > 0.05$. Negative values indicate a deterioration in the retest compared to the original test.

Table 3 Effective size of Cognitive Rehabilitation in clinical group (Wilcoxon signed rank test)

The Clinical sample	Test		R-test		n	Effective Size	W (criterion)	p-value $p = 0.05$
	Median	Q1–Q3	Median	Q1–Q3				
MMSE	28	26–29	29	28–29	21	13	22.5 (17)	0.11
ACE-R	83	71–89	90	85–92	21	19	28.5 (46)	0.007*
Attention and Orientation	18	16–18	18	17–18	21	12	25 (14)	0.275
Memory	18	14–22	20	17–22	21	20	74 (52)	0.247
Fluency	8	7–10	10	8–12	21	15	16 (25)	0.012*
Language	25	24–26	25	25–26	21	10	27.5 (8)	1
Visuospatial	16	15–16	15	15–16	21	12	18 (14)	0.099
ANX	6	3.5–8.5	7	5–9.5	19	14	32.5 (21)	0.209
DEP	6	5–7	6	4.5–8.5	19	14	22.5 (21)	0.232
BDI-2	9	7–13	10	7–13	9	9	18 (6)	0.593

ACE-R – Addenbrooke's Cognitive Examination-Revised; ADL – Activity of Daily Life; MMSE – Mini mental State Examination; MCI – mild cognitive impairment; ANX – Hospital Anxiety Depression Scale – Anxiety score; DEP – Hospital Anxiety Depression Scale – Depression score; BDI-2 – Beck Depression Inventory – 2nd revision; *indicates significant change at significance level of $p > 0.05$.

Table 4 Effective size of change in control sample (Wilcoxon signed rank test)

Control sample	Test		Re-test		n	Effective Size	W (criterion)	p-values $p = 0.05$
	Median	Q1–Q3	Median	Q1–Q3				
MMSE	29	28–30	29	28–29	15	8	9 (4)	0.207
ACE-R	77	74–83	80	74–82	15	14	42 (21)	0.509
Attention and Orientation	18	18–18	18	17–18	15	6	5.5 (0)	0.294
Memory	17	13–19	17	15.5–19	15	8	9.5 (4)	0.233
Fluency	7	6–8.5	7	7–9.5	15	9	20.5 (6)	0.813
Language	25	23.5–26	24	23–24.5	15	10	7 (8)	0.036*
Visuospatial	14	11.5–15	13	11–15	15	11	30.5 (11)	0.824
ANX	4	3–4.5	5	3–5.5	15	9	8 (6)	0.085
DEP	6	3.5–7	6	4.5–7	15	6	6 (0)	0.345
BDI-2	7	5.5–8	7	5.5–8.5	15	9	20.5 (6)	0.812

On the basis of the reference index of subjectively perceived changes (CGI) there was a significant perception of improvement in patients in the monitored clinical sample in comparison with the control sample who reported minimal or no change in the context of monitoring (Table 6).

Discussion

The effects of CR in terms of improvement in the ACE-R Verbal fluency subtest correspond to the current state of knowledge, in that the application of cognitive rehabilitation results in a slight improvement in the cognitive functioning of patients

with mild cognitive disorder and also to a significant subjectively perceived improvement in health status and total activation of patients (Rodawski, 2015). Improvement in the subjective experience of patients was established by significant difference in CGI. Similar conclusions are described in the works of Hofmann et al. (1996) and Cipriani et al. (2006) which deal with the CR effect in patients diagnosed with Alzheimer's type dementia.

The changes in word production ascertained in patients in the clinical sample (Table 3) suggest increased flexibility and organization of thought

rather than an improved use of speech components and capacity for recollection from long-term components of memory, also monitored by this subtest (Preiss, 2012). The ability to use memory components in the sense of the capacity for imprinting and recollection of new material was not significantly affected by cognitive rehabilitation (Table 3). A similar conclusion in terms of improvements in verbal fluency was found in patients with traumatic brain damage who underwent cognitive rehabilitation (Gaber, 2008).

Table 5 Change comparisons between clinical sample and control sample

	Clinical sample improvement (re-test) n = 21		Control sample improvement (re-test) n = 15		U	p-values (U = 96)
	Median	Q1–Q3	Median	Q1–Q3		p = 0.05
MMSE	0	0 to +1	0	-1 to 0	99	0.06
ACE-R	4	0 to +8	-1	-3 to +1.5	84	0.018*
Attention and Orientation	0	0 to +1	0	-1 to 0	116	0.183
Memory	2	-1 to +3	0	0 to +1.5	134	0.451
Fluency	1	0 to +3	0	-1 to +0.5	98,5	0.058
Language	0	0 to 0	-1	-2 to 0	94,5	0.043*
Visuospatial	0	0 to +1	0	-1 to +1.5	151	0.834
		n = 9		n = 15	(U = 34)	
BDI-2	2	-2 to +3	0	-1 to +0.5	87	0.245
		n = 19		n = 15	(U = 85)	
ANX	0	-1 to +1.5	0	0 to +1.5	161	0.52
DEP	1	0 to +2	0	0 to +0.5	115	0.34

The effect in the form of improvements in linguistic skills and capacities and aggregate ACE-R values in patients in the clinical sample compared to the control sample (Table 5) can be interpreted in the context of an improvement in cognitive flexibility and enhanced ability to organize thought and recollection from long-term semantic components of memory also included in the Verbal fluency subtext. Thus, the result itself can be interpreted as an improvement in the operation of verbal executive functions. Executive functions are a set of cognitive functions associated with the process of thought and decision-making and their function is significantly influenced by cognitive rehabilitation.

Significant factors influencing the effect of CR include age, sociodemographic status and level of education (Gehring et al., 2011). Other factors positively influencing the effect of cognitive rehabilitation can include amount of regular physical exercise, personalization, rehabilitation, education and extrinsic motivation of patients, which was also reflected in the internal motivational setting of patients, as well as the supportive family environment in which the patients in the monitored clinical sample lived (Table 1). The monitored

groups proved to be significantly different in these variables in particular, to the benefit of the clinical group. These factors were not evaluated as part of the study conducted, in so far as monitoring the impact of family environment on the development of cognitive function. From the perspective of future follow-up studies monitoring the effects of CR, it is worth considering incorporating precisely these elements and modifying the methodology of monitoring changes in activities of daily living. The changes in functional status of patients who were monitored using the scale of activities of daily living (ADLs) and instrumental daily activities (IADL) were not evaluated due to poorly chosen measurement tools, which appear to be insufficiently sensitive for measuring the focus and severity of mild cognitive disorder (MCI).

Table 6 A comparison of Clinical Global Improvement change between clinical and control sample

CGI	Median	Min	Max
Clinical (n = 21)	2	1	5
Control (n = 15)	0	0	0

The tool used for the monitoring of changes in cognitive status (ACE-R) may give false positives or be insufficiently sensitive to monitor cognitive changes in the monitored groups compared to the more detailed neuropsychological tests, especially in the context of monitoring change over short periods (Larner, 2013). This false positivity may be the price paid for retesting patients in such a short period of time. The test results revealed statistically significant changes, which were not apparent in the control sample. The ACE-R uses Czech orientational standards, and its validity and specificity have been verified. It is used as a functional diagnostic tool for monitoring changes in cognitive status in patients with mild cognitive disorders and its results may be considered valid.

Data analysis shows fluctuating results in all parameters monitored, particularly in affective changes over time in the control sample. While the clinical sample showed a slight improvement, the result of applied statistical analysis confirmed a significant change only in the ACE-R score. This result may also be influenced by the inconsistent length of testing in favour of the clinical sample (Table 3). We assume that the result of the control sample, in the case of there being a comparable distance between testing and retesting, will be significantly in favour of the group that underwent CR. This observed phenomenon can be considered a non-cognitive effect of cognitive rehabilitation (reduction in experiences of anxiety and depression, activation of the organism, reduced alexythymia, etc. (Viola et al., 2011). The deepening of anxiety and depression in patients from the control sample may also be affected by statistical randomness.

Within the context of ongoing therapy in a clinical setting, it was not possible to fully create controlled conditions in the monitoring of the effects of cognitive rehabilitation due to the overall high degree of individualization of the rehabilitation process.

Limitation of study

The study may be affected by the generally low number of patients involved and the need to use non-parametric tests. The size of the monitored group and the total number of patients non-compliant with the monitored criteria who were not enrolled or were eliminated during rehabilitation corresponds with the current state of knowledge and similar completed trials.

Recommendations for nursing practice

Based on the findings, previous studies, and meta-analyses of the effect of cognitive rehabilitation, it appears that the greatest effect on the actual cognitive

function of patients with mild cognitive disorder is produced by a combination of cognitive rehabilitation, whether in the form of computer rehabilitation using cognitive exercises in the form of logical tasks, memory exercises and attention exercises in "pencil and paper" form, or by supplementing care with physiotherapy and supporting self-sufficiency and training in everyday tasks. This combination of non-pharmacological treatment is often lacking in sub-acute and post-acute forms of treatment and social care. The absence of this care fosters stagnation in health and cognitive condition and may promote the development of behavioural and emotional disorders (Heyn et al., 2004).

Conclusion

The main objective of the study was to analyse cognitive function and the effect of cognitive rehabilitation in patients with diagnosed mild cognitive disorder based on brain cortical atrophy. On the basis of the applied methodology – involving tracking cognitive changes, affective symptoms, and patients' overall subjective perception, applied non-pharmacological intervention in the form of cognitive rehabilitation, and subsequent statistical data analysis – it was found that application of cognitive rehabilitation resulted in an overall improvement in cognitive function in the observed clinical group, made up of patients diagnosed with brain atrophy (according to the parameter of ACE-R score). There was no significant material impact on the perception and processing of experiences of anxiety and depression. In the monitored clinical sample there was a significant impact on subjective experience and an overall improvement in health status. It can be concluded that cognitive rehabilitation is an effective tool for improving cognitive activation of patients with onset cerebral atrophy. The overall results correspond to the current state of knowledge.

Ethical aspects and conflicts of interests

The study was approved by the Ethics committee of Ostrava University Hospital.

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Author contributions

Concept and design (PN), data collection (PK, JM, DB), indication of patients in the groups under study (PR, OZ), analysis and interpretation of data (PN, JP), drafting of the manuscript (PN), critical review

of the manuscript (PR, PK, DB, OZ), final completion of the article (PN).

References

- Bartoš A, Raisová M, Kopeček M. Novelizace české verze Addenbrookskeho kognitivního testu (ACE-CZ). *Česká a slovenská neurologie a neurochirurgie*. 2011;74/107(6):681–684. (in Czech)
- Beránková D, Krulová P, Mračková M, Eliášová I, Košťálová M, Janoušová E, Stehnová I, Bar M, Rössner P, Nilius P, Tomagová M, Rektorová I. Addenbrookský kognitivní test – orientační normy pro českou populaci. *Česká a slovenská neurologie a neurochirurgie*. 2015;78/111(3):300–305. (in Czech)
- Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont)*. 2007;4(7):28–37.
- Cipriani G, Bianchetti A, Trabucchi M. Outcomes of a computer-based cognitive rehabilitation program on Alzheimer's disease patients compared with those on patients affected by mild cognitive impairment. *Archives of Gerontology and Geriatrics*. 2006;43(3):327–335.
- Flicker C, Ferris SH, Reisberg B. Mild cognitive impairment in the elderly: predictors of dementia. *Neurology*. 1991;41(7):1006–1009.
- Gaber TA. Evaluation of the Addenbrooke's Cognitive Examination's validity in a brain injury rehabilitation setting. *Brain Injury*. 2008;22(7–8):589–593.
- Gehring K, Aaronson NK, Gundy CM, Taphoorn MJ, Sitskoorn MM. Predictors of neuropsychological improvement following cognitive rehabilitation in patients with gliomas. *Journal of the International Neuropsychological Society: JINS*. 2011;17(2):256–266.
- Heyn P, Abreu BC, Ottenbacher KJ. The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. *Archives of Physical Medicine and Rehabilitation*. 2004;85(10):1694–1704.
- Hofmann M, Hock C, Müller-Spahn F. Computer-based cognitive training in Alzheimer's disease patients. *Annals of the New York Academy Sciences*. 1996;777:249–254.
- Holmerová I, Janečková H, Vaňková H, Veleť P. Nefarmakologické přístupy v terapii Alzheimerovy demence a praktické aspekty péče o postižené. *Psychiatrie pro praxi*. 2005;6(4):175–178. (in Czech)
- Huckans M, Hutson L, Twamley E, Jak A, Kaye J, Storzbach D. Efficacy of cognitive rehabilitation therapies for mild cognitive impairment (MCI) in older adults: working toward a theoretical model and evidence-based interventions. *Neuropsychology Review*. 2013;23(1):63–80.
- Karr JE, Areshenkoff CN, Garcia-Barrera MA. The neuropsychological outcomes of concussion: A systematic review of meta-analyses on the cognitive sequelae of mild traumatic brain injury. *Neuropsychology*. 2014;28(3):321–336.
- Nikolai, T, Vyhnálek M, Literáková E, Marková H, Hort J. Vyšetření kognitivních funkcí v časně diagnostice Alzheimerovy nemoci. *Neurologie pro praxi*. 2013;14(6):297–301. (in Czech)
- Nilius P, Krulová P. *Tematické listy pro skupinovou rehabilitaci a kognitivní trénink mozku*. Ostrava: Fakultní nemocnice Ostrava, 2013. 74 s. [cited 2015 Nov 9]. Available from: <http://nela.fno.cz/doc/tematicke-listy.pdf> (in Czech)
- Pascual-Leone A, Freitas C, Oberman L, Horvath JC, Halko M, Eldaief M, Bashir S, Vernet M, Shafi M, Westover B, Vahabzadeh-Hagh AM, Rotenberg A. Characterizing brain cortical plasticity and network dynamics across the age-span in health and disease with TMS-EEG and TMS-fMRI. *Brain topography*. 2011;24(3–4):302–315.
- Preiss M, Vacíř K. *BDI-II. Beckova sebesposuzovací škála pro dospělé*. Brno: psychodiagnostika. 1999. (in Czech)
- Preiss M, Bartoš A, Čermáková R, Nondek M, Benešová M, Rodríguez M, Raisová M, Laing H. *Neuropsychologická baterie Psychiatrického centra Praha*. 3. vyd. Praha: Psychiatrické centrum Praha, 2012. (in Czech)
- Rodakowski J, Saghaei E, Butters MA, Skidmore ER. Non-pharmacological interventions for adults with mild cognitive impairment and early stage dementia: An updated scoping review. *Molecular Aspects of Medicine*. 2015;43–44:38–53.
- Sheardová, K. Mírná kognitivní porucha v praxi. *Psychiatrie pro praxi*. 2010;11(2):62–65. (in Czech)
- Snaith, RP. The hospital anxiety and depression scale. *Health and Quality of life outcomes*. 2003;1:29.
- Viola LF, Nunes PV, Yassuda MS, Aprahamian I, Santos FS, Santos GD, Brum PS, Borges SM, Oliveira AM, Chaves GF, Ciasca EC, Ferreira RC, Paula VJ, Takeda OH, Mirandez RM, Watari R, Falcao DV, Cachioni M, Forlenza OV. Effects of a multidisciplinary cognitive rehabilitation program for patients with mild Alzheimer's disease. *Clinics (Sao Paulo)*. 2011;66(8):1395–1400.