doi: 10.14735/amcsnn2018314

Effect of a combined approach to cognitive rehabilitation in post-stroke patients

Efekt kombinované kognitivní rehabilitace u pacientů po cévní mozkové příhodě

Abstract

Aim: This study aims to investigate the effects of a combined therapy comprising a combination of computer-based cognitive rehabilitation with traditional rehabilitation techniques on cognitive functions in post-stroke patients suffering from a mild-to-moderate degree of cognitive impairment and to compare the results with a group of patients not receiving such therapy. *Methods:* 33 post-stroke patients fulfilling exclusion/inclusion criteria were allocated according to travel distance from the treatment centre to either the treatment (N = 19) or control group (N = 14). Cognitive rehabilitation was performed in 60-min-long sessions held twice a week for 12 weeks. Mini-Mental State Examination (MMSE) and Addenbrook Cognitive Examination – Revised (ACE-R) tests were performed at the beginning of the treatment, retests were performed approximately 16 weeks later and the results, including ACE-R subscores as secondary endpoints, were analysed. *Results:* In the treatment group, statistically significant improvement ($p < 0.05$) was detected in MMSE, ACE-R, and in ACE-R subtests Memory, Verbal fluency and Language, while only the Memory subtest recorded statistically significant improvement in the control group. However, due to the small number of patients, we only present the results as trends indicating that a study on a larger cohort is needed. Hence, a sample size for a future study required for proper assessment of the effects of combined approach cognitive rehabilitation was calculated, the resulting group size is 334 patients. *Conclusions:* A combination of computer-based rehabilitation and traditional rehabilitation techniques in patients suffering from mild-to-moderate cognitive impairment as a result of stroke led to a statistically significant improvement in MMSE and ACE-R tests and in ACE-R Memory, Verbal fluency and Language subtests. However, due to a small number of patients, we only present these results as trends.

Souhrn

Cíl: Tato studie si dává za cíl posoudit efekty kombinované kognitivní rehabilitace u pacientů s ischemickou cévní mozkovou příhodou s lehkým až středním stupněm kognitivního postižení v porovnání s pacienty bez této léčby. Užitá terapie kombinuje počítačovou kognitivní rehabilitaci s tradičními technikami rehabilitace kognitivních funkcí. *Metody:* 33 pacientů po cévní mozkové příhodě splňující kritéria zahrnutí bylo zařazeno a rozděleno podle kritéria dojezdové vzdálenosti do skupiny s terapií (n = 19) a do skupiny kontrolní (n = 14). Kognitivní rehabilitace byla prováděna v 60min sezeních 2× týdně po dobu 12 týdnů. Pacienti byly vyšetřeni pomocí testů Mini-Mental State Examination (MMSE) a Addenbrook Cognitive Examination – Revised (ACE-R) na začátku terapie, retesty byly provedeny přibližně o 16 týdnů později a výsledky, vč. subskórů ACE-R jako sekundárních výsledků, byly analyzovány. *Výsledky:* Ve skupině léčených bylo zaznamenáno statisticky významné zlepšení ($p < 0,05$) v testech MMSE, ACE-R a v ACE-R subtestu Paměť, Verbální fluence, Jazyk, přičemž v kontrolní skupině bylo zachyceno statisticky významné zlepšení pouze v subtestu Paměť. Vzhledem k malému množství pacientů ve studii zjištěné výsledky prezentujeme jen jako trendy, které ukazují, že je nutná studie na větším množství pacientů. Byla proto vypočtena velikost vzorku pacientů pro budoucí studii potřebná pro dostatečnou analýzu výsledků efektu kombinované kognitivní rehabilitace a výsledný potřebný počet je 334 pacientů. *Závěr:* Kombinovaná počítačová kognitivní rehabilitace a tradiční kognitivní rehabilitace u pacientů s cévní mozkovou příhodou s lehkým až středně těžkým kognitivním deficitem vedla ke statisticky signifikantnímu zlepšení v testech MMSE a ACE-R a subtestech ACE-R Paměť, Verbální fluence a Jazyk. Vzhledem k malému množství zařazených pacientů jsou prezentovány tyto výsledky jako trendy.

The authors declare they have no potential conflicts of interest concerning drugs, products, or services used in the study.
Autoři deklarují, že v souvislosti s předmětem studie nemají žádné komerční zájmy.
The Editorial Board declares that the manuscript met the ICMJE "uniform requirements" for biomedical papers.
Redakční rada potvrzuje, že rukopis práce splnil ICMJE kritéria pro publikace zasílané do biomedicínských časopisů.

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Accepted for review: 13. 9. 2017
Accepted for print: 28. 3. 2018

Key words

computer-based cognitive rehabilitation – cognitive function – stroke – post-stroke patients – combined approach – ACE-R – MMSE

Klíčová slova

počítačová kognitivní rehabilitace – kognitivní funkce – cévní mozková příhoda – pacienti po cévní mozkové příhodě – kombinovaný přístup – ACE-R – MMSE

Introduction

Cognitive impairments (such as memory impairment, visuospatial impairment, neglect, reduced processing speed, impaired attention, impairment of verbal fluency or executive dysfunction) are relatively frequent consequences of stroke, often causing dementia [1]. Development of these dysfunctions greatly affects the quality of a patient's life and self-sufficiency, making returning to everyday life difficult [2]. As a consequence, a therapeutic approach involving cognitive rehabilitation is vital for successful rehabilitation training, and using an integrated approach is therefore essential [3]. Although guidelines for neurorehabilitation are predominantly focused on compensational strategy training, restitution training focused on restoring brain functions based on the premise of residual plasticity of the adult brain should also be pursued [4].

Interventional methods for cognitive rehabilitation are generally divided into two categories – computer-based cognitive rehabilitation (CBCR) and non-computerized, therapist-assisted cognitive rehabilitation techniques (such as conventional interventions for attention or memory training, social communication skills, or executive functions) [4]. CBCR systems are still developing and although their effect on the improvement of cognitive functions after stroke has been proved in some studies [4], other studies did not show the same conclusions [5]. Some studies using a combined approach to cognitive rehabilitation, i.e., using CBCR as a part of a battery of methods, have been published [6], more studies and analyses of both CBCR and CBCR in combination with other methods are still needed [4]. In our study, we evaluated effectiveness of a combined approach to rehabilitation of cognitive functions, integrating CBCR with other methods for improving memory, attention and fine motor activity. According to the literature, it is obvious that the effectiveness of cognitive rehabilitation is significantly better in patients with a milder degree of cognitive impairments [1], which led us to focus on patients with a chronic mild degree of cognitive impairment resulting from stroke.

So far, there are no clear recommendations in place for cognitive rehabilitation following stroke. According to the American Heart Association/American Stroke Association, it is recommended to perform a screening of cognitive functions in each stroke patient prior to discharge, and where screening reveals cognitive deficits a more detailed neuropsychological evaluation to identify areas of cognitive strength and weaknesses may be beneficial. However, the recommendations for cognitive rehabilitation are quite vague and range within B–C level of evidence with no unified method of treatment [7].

According to the European Stroke Organisation Guidelines for the Management of Ischaemic Stroke and Transient Ischaemic Attack 2008, cognitive deficits are common following stroke as well as an impact on the quality of life. At present, there is no sufficient evidence for the efficacy of either specific memory rehabilitation or cognitive training for attention deficit resulting in meaningful clinical improvement in activities of daily living (ADL). Training for spatial neglect has been shown to reduce impairment, however, again, no effect on ADL performance has been demonstrated. A few studies have assessed rehabilitation training strategies in visual inattention and apraxia, however, no specific conclusions could be drawn [8].

The aim of our study was to evaluate the effect of cognitive rehabilitation on cognitive functions in post-stroke patients, measured using Addenbrook Cognitive Examination – Revised (ACE-R) a Mini-Mental State Examination (MMSE).

Subjects and methods

Ethics

The study complies with the ethical standards of the Declaration of Helsinki (1975, revised 1983). The study was approved by the Ethics Committee of University Hospital Ostrava (No. 439/2012), comprehensive information was provided to all participants and written informed consent was obtained from each subject prior to inclusion in the study. Patients were fully anonymized.

Patients

The study focused on patients with mild-to-moderate cognitive impairment resulting from stroke. Patients were recruited for the study during a period of 36 months (2012–2015) based on the inclusion and exclusion criteria set out below.

Inclusion criteria: ACE-R ≤ 79/100, MMSE ≥ 18/30, age ≥ 40 years, 4–7 months after stroke. The cut-off score for MMSE was set according to the national version of MMSE, where the score of 18 is the cut-off score for mild dementia [9]. The upper ACE-R cut-off score was set according to the ACE-R Czech language version national normative study for patients without impairment [10]. These scores were set to avoid inclusion of patients who did not suffer from consequences of stroke at the mental level (ACE-R upper cut-off) and, on the other hand, to exclude patients who would be unable to train effectively due to their impairment (e. g., due to their inability to properly understand the instructions).

Exclusion criteria: recurrent stroke (including stroke in personal history and old ischemic lesions on the brain CT), severe complications (infections, metabolic and other disorders potentially affecting cognitive impairment), aphasia (all patients underwent speech examination prior to inclusion in the study), reading or writing disorders, visual impairments potentially interfering with reading, writing or PC work, depression (Beck Depression Inventory – II; BDI-II ≥ 14 at either entry or final examination in accordance with the BDI-II cut-off score for depression, and absence of a partner or carer able and willing to supervise the home training [11]. Patients with diagnosed Alzheimer's disease or with other dementia such as diffuse Lewy bodies disease, Parkinson's disease, frototemporal dementia or other neurodegenerative diseases with dementia were also excluded.

Patients in the control group were asked prior to the tests whether or not they participated in any cognitive training and if so, whether they were excluded from the study.

The patients were allocated to the treatment and control group in a way that ensured the minimization of external factors such as different motivation for therapy. In our experience, the most significant obstacle for participating in cognitive therapy in our patients are commuting problems, i.e., lack of availability of means of regular transportation to and from the place of therapy. For this reason, we performed the allocation according to the distance to the place of residence from our hospital. Patients living within 30 km from the hospital were allocated to the treatment group while patients living a greater distance to the control group.

Cognitive rehabilitation

Cognitive rehabilitation was performed using a combination of CBCR and non-computerized methods. The sessions were

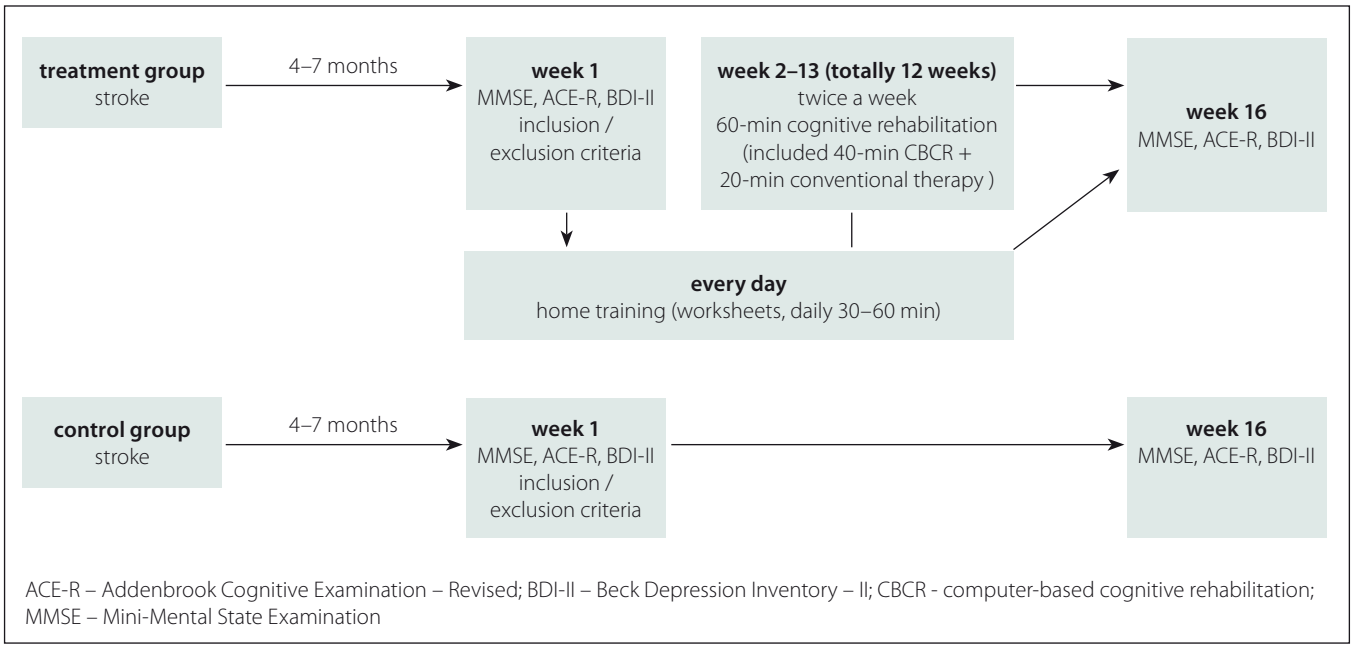

Fig. 1. Study setup – timeline of the study.
Obr. 1. Nastavení studie – časová osa.

held twice a week for 12 weeks, each session was 60 min long. Each session included a 40-min CBCR using commercially available software focused on attention, memory, visuospatial skills, and executive functions (sudoku, number search, world search, assembling words, reaction time training, word puzzles, jigsaws, pairs, Tower of London, Tower of Hanoi, tic-tac-toe, etc.). The remaining 20 min of each session were dedicated to conventional therapist-assisted group therapy, which was focused on memory and attention training using mnemonic strategies such as memorizing a growing list (e.g. shopping list) or training of visuospatial and fine motor skills (assembling blocks according to a model, tangrams). The group therapy was also used to practice interpersonal communication and to support motivation by interaction and feedback within the group. During the sessions, patients were also instructed on completing worksheets handed out for home training, recommended for 30–60 min a day. These tasks included word search puzzles, copying simple shapes and pictures, labyrinth solving, etc. Worksheets for this part of the therapy can be viewed using the link in the reference [12]. The instructions were also relayed to a family member or carer who supervised the home training. Patients in the control group received no cognitive rehabilitation.

Cognitive tests

Well-established tests validated for the Czech language, namely MMSE [13] and ACE-R [14] were used for evaluation of cognitive skills. Both MMSE and ACE-R tests were performed at the beginning of the therapy, the retest was performed approx. 16 weeks later. The same inclusion and exclusion criteria were applied for the control group, MMSE and ACE-R retests were performed after the same period. Results of MMSE and ACE-R were analysed and ACE-R subscores (Attention and Concentration, Memory, Verbal fluency, Language, Visuospatial abilities) were subsequently evaluated as secondary endpoints.

Statistical analysis

Statistical package IBM SPSS Statistics version 22 (IBM Corp., Chicago, IL, USA) was used for data analysis. The results of the tests and retests were checked for normality using the Shapiro-Wilk test. As the distribution was non-normal, non-parametric tests were used for further evaluation. Namely, Wilcoxon paired test was used to evaluate progress in both the control and treatment groups. The tested hypothesis for each of the scores was that there is no difference between results of individual patients in the initial and final test. The value of $p < 0.05$ was considered statistically significant.

The timeline of the study is shown in Fig. 1.

Results

Patients

Altogether, 154 post-stroke patients were examined for inclusion in the study. After application of the exclusion and inclusion criteria, only 33 patients were found eligible for inclusion in the study. Overall 19 of those, according to the travel distance, formed the treatment group and the remaining 14 formed the control group.

National Institutes of Health Stroke Scale (NIHSS) scores on the day of stroke for the treatment group were 5–19 (median 9) and for the control group 7–21 (median 11); on the day of enrolment, it was 3–11 (median 7) for the treatment group and 4–10 (median 7) for the control group. On the day of the final test, NIHSS scores were 1–10 (median 5) in the treatment group and 1–10 (median 6) in the control group.

Results of the treatment

Statistical tests revealed no significant difference in demographic parameters (age, gender representation, risk factors, stroke side) between the treatment and control groups (Tab. 1). The comparison of MMSE, ACE-R and ACE-R subscores results at the beginning and at the end of the study period in the treatment and control groups are summarized in Tab. 2. On the level of significance of $p < 0.05$ evaluated using Mann-Whitney U test, the initial test results did not

Tab. 1. Demographic and descriptive parameters of the treatment and control groups.

		Treatment group	Control group	p
Number of patients		19	14	
Gender	males	14 (74%)	8 (57%)	0.29
	females	5 (26%)	6 (43%)	
Age	mean ± SD	64,9 ± 11,0	68,9 ± 10,2	0.55
	median (min.–max.)	69 (47–81)	72 (45–81)	
Risk factors	hyperlipidemia	10 (52.6%)	12 (85.7%)	0.07
	coronary artery disease	8 (42.1%)	10 (71.4%)	0.06
	atrial fibrillation	2 (10.5%)	2 (14.3%)	1.00
	arterial hypertension	17 (89.5%)	11 (78.6%)	0.63
	diabetes	5 (26.3%)	4 (28.6%)	1.00
Stroke side	right	7 (36.8%)	6 (42.9%)	1.00
	left	12 (63.2%)	8 (57.1%)	

SD – standard deviation

differ between the control and treatment groups for either ACE-R (p = 0.48) or MMSE (p = 0.96).

Statistically significant improvement was revealed in MMSE, ACE-R and in ACE-R subtests of Memory, Verbal fluency and Language in the treatment group while in the control group, only the Memory subtest showed significant (p < 0.05) improvement.

Discussion

Patients

An MMSE score of 18 was set as the lowest score for inclusion as MMSE denotes the 18–25 range as mild cognitive impairment [9,13]. However, ACE-R was shown to be more sensitive in detecting mild cognitive impairments than MMSE [9,13–15]. Therefore, to be able to capture the patients with a mild degree of cognitive impairment sensitively, an ACE-R score of 79 was used as the upper

Tab. 2. Results of MMSE, ACE–R and ACE–R subscores at the beginning and at the end of the study period in the treatment and control groups.

		Treatment group				Control group			
		median	min.	max.	p	median	min.	max.	p
MMSE 30	initial test	25	20	30	0.012*	24	19	29	0.115
	retest	27	20	30		25	20	30	
	progress	2	–4	9		1	–5	8	
ACE-R 100	initial test	69	46	79	0.003*	71	44	79	0.052
	retest	77	49	100		71	54	90	
	progress	9	–11	50		8	–18	20	
Attention and Concentration	initial test	15	11	18	0.147	15	12	18	0.962
	retest	17	11	18		15	11	18	
	progress	1	–5	5		0	–4	6	
Memory	initial test	11	6	22	0.001*	12	5	18	0.042*
	retest	14	4	26		18	7	23	
	progress	3	–2	15		–3	–13	6	
Verbal fluency	initial test	3	0	12	0.009*	6	0	9	0.079
	retest	5	1	14		7	1	10	
	progress	1	14	–2		2	–7	5	
Language	initial test	24	11	26	0.022*	25	14	26	0.629
	retest	25	18	26		25	14	26	
	progress	1	–2	15		0	–2	8	
Visuospatial abilities	initial test	13	9	16	0.127	14	0	23	0.653
	retest	14	9	16		14	0	16	
	progress	0	–2	6		1	–10	5	

ACE–R – Addenbrook Cognitive Examination – Revised; MMSE – Mini–Mental State Examination; p – statistical significance according to Wilcoxon paired test

* statistically significant at the level p < 0.05

limit (ACE-R score 79 is the cut-off value for the Czech population set by a normative study in the Czech population) [10]. As the acute stage following a stroke episode can be associated with a spontaneous improvement of cognitive impairment, only patients 4–7 months after the stroke episode were included [16]. The age criterion (age ≥ 40) was introduced to adjust for the fact that younger people do not lack motivation in participating in cognitive rehabilitation and, consequently, none or only few of those could have been recruited for the control group, which would in turn lead to biased age distribution between the groups.

Results of the treatment

Despite the fact that the treatment group showed a significant improvement when compared to the entry test in MMSE, ACE-R and its Memory, Verbal fluency and Language subtests while in the control group, only Memory subtest revealed a significant improvement, we can only judge these results as trends. Verbal fluency and ACE-R results in the control group could also be considered as borderline and although the p values are notably lower in the treatment group than in the control group, drawing any firm conclusion based on a strict cut-off value of 0.05 would be misleading. The small numbers of patients, usually less than 20 in individual groups, is a common problem observed in cognitive rehabilitation studies [1,17] with our study being no exception. We are well aware of the limitation of the study due to the small number of subjects. The principal problem lies in the selection of patients in a way ensuring that both the control and treatment group are comparable and the study can be considered unbiased. To properly explain the reasons for such a small number of subjects in the groups, we have described the selection and reasoning above; from the description, it is obvious that the disproportion between the number of post-stroke patients examined for suitability for cognitive rehabilitation (154) and those eligible for inclusion in the study (33) is striking. Unfortunately, such a strict set of exclusion and inclusion criteria is necessary for creating a relatively uniform study group, which is in turn essential for obtaining valid results.

Van de Ven et al [1] stated in their review that a median of total therapy duration throughout the referred studies was 15.6 h. In our study, with 40-min CBCR along with 20 min of group therapy twice a week for 12 weeks, the net time amounts to 24 h, not including patients' homework. Despite this more intense therapy, our results cannot be interpreted as having a major effect when compared to the control group and we can only consider the results as trends. Some studies report a significant impact of rehabilitation in stroke patients [2,18] while others are more reserved [5]. According to the meta-analysis of cognitive rehabilitation (CR) in post-stroke patients performed by van de Ven et al [1], the principal problems include methodological differences (such as various therapy durations and methods used, different times elapsed from the stroke incident, etc.) and small numbers of subjects in the study groups.

Required group size

As the problem with the small number of patients in CR studies seems to persist throughout most if not all published papers, the question of the group size required for obtaining valid and meaningful results was raised. Based on our findings, the size of the group necessary for obtaining valid and reliable outcomes was estimated using the method described by Bland [19]. The tests power was set to 0.9. The group size estimates for all parameters ranged from 154 (Verbal fluency) to 290 (ACE-R) with the only exception being the Memory subtest (1,064). The result for the Memory subtest (a high number lying outside the range of all other results) probably indicates that there is indeed no significant difference between the treatment and control group in this parameter. Results of the Memory subtest indicated a significant improvement in both groups, which in turn signifies a spontaneous improvement rather than a major effect of CR [16,20]. As the sample size estimation was performed with the assumption of normal distribution and as it is likely that a non-normal distribution might be acquired during the future study of CR, the estimates were further increased by 15% as recommended by Lehmann [21]. The recommended group size increased by 15% for the ACE-R results (which required the greatest study population from the numbers within the range) which would then amount to 335 patients in each control and treatment group. Such a high number, along with the fact that only approximately a fifth of the patients considered for participation in the study passed the inclusion and exclusion criteria, underlines the need for undertaking similar research studies as multicentre studies. Besides the actual recruitment of a sufficient number of patients, such an approach would also be beneficial in that using the same methods at several centres at the same time would help to better validate these methods.

Apart from increasing the group sizes, an alternative approach could lie in selecting a different test battery that would cover the domains of attention, psychomotor speed, memory, executive functions, visuospatial abilities, speech and symbolic functions in a better way than ACE-R does.

Despite our data having only limited value with respect to therapy effectiveness, we strived to describe in as much detail as possible the methodological approach, as well as problems and limitations encountered during the study because both meta-analyses and individual studies mention the problem of insufficient therapy description [1,22]. By detailed description of the process of recruiting patients for the study, we have shown how an apparently large group of patients can shrink when applying inclusion and exclusion criteria ensuring conformity of the treatment and control groups. We also suggested sizes of groups necessary for performing a valid study and proved that unless a more sensitive test battery for evaluation of CBCR effect is applied, similar studies cannot practically be accomplished at a single facility but have to be performed as a multicentre studies.

Study limitations

The study limitations are: 1. small number of patients, which was due to a necessity of application of strict inclusion and exclusion criteria to acquire a uniform study population; 2. use of simple ACE-R and MMSE tests instead of more complex tools for testing, which was due to the fact that patients after stroke often do not tolerate higher load well, which could further reduce the number of patients in the study; 3. the way of allocation of the patients in the treatment and control groups due to the travelling distance, which could be possibly burdened with an uneven distribution of patients between the groups (however, no such statistically significant difference in any of the recorded parameters was detected). This was done due to the fact that patients

lived a greater distance away are typically reluctant to regularly commute for training and if using random allocation, this would probably significantly reduce the number of patients in the study.

This work was supported by an institutional grant from the Ministry of Health of the Czech Republic (No. 1 RVO--FNOs/2012).

References

1. van de Ven RM, Murre JM, Veltman DJ et al. Computer--based cognitive training for executive functions after stroke: a systematic review. Front Hum Neurosci 2016; 10: 150. doi: 10.3389/fnhum.2016.00150.

2. Park JH, Park JH. The effects of a Korean computer--based cognitive rehabilitation program on cognitive function and visual perception ability of patients with acute stroke. J Phys Ther Sci 2015; 27(8): 2577–2579. doi: 10.1589/jpts.27.2577.

3. Cho HY, Kim KT, Jung JH. Effects of computer assisted cognitive rehabilitation on brain wave, memory and attention of stroke patients: a randomized control trial. J Phys Ther Sci 2015; 27(4): 1029–1032. doi: 10.1589/jpts.27.1029.

4. Cicerone KD, Langenbahn DM, Braden C et al. Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. Arch Phys Med Rehabil 2011; 92(4): 519–530. doi: 10.1016/j.apmr.2010.11.015.

5. Wentink MM, Berger MA, de Kloet AJ et al. The effects of an 8-week computer-based brain training programme on cognitive functioning, QoL and self-efficacy after stroke. Neuropsychol Rehabil 2016; 26(5–6): 847–865. doi: 10.1080/09602011.2016.1162175.

6. Aparicio-Lopez C, Garcia-Molina A, Garcia-Fernandez J et al. Combination treatment in the rehabilitation of visuo-spatial neglect. Psicothema 2016; 28(2): 143–149. doi: 10.7334/psicothema2015.93.

7. Winstein CJ, Stein J, Arena R et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2016; 47(6): e98–e169. doi: 10.1161/STR.0000000000000098.

8. European Stroke Organisation (ESO) Executive Committee, ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovasc Dis 2008; 25(5): 457–507. doi: 10.1159/000131083.

9. Štěpánková H, Nikolai T, Lukavský J et al. Mini Mental State Examination – Czech normative study. Cesk Slov Neurol N 2015; 78/111(1): 57–63.

10. Beránková D, Krulová P, Mračková M et al. Addenbrooke's cognitive examination – approximate normal values for the Czech population. Cesk Slov Neurol N 2015; 78/111(3): 300–305.

11. Smarr KL, Keefer AL. Measures of depression and depressive symptoms: Beck Depression Inventory--II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). Arthritis Care Res (Hoboken) 2011; 63 (Suppl 11): S454–S466. doi: 10.1002/acr.20556.

12. Nilius P, Krulová P. Tematické listy pro skupinovou rehabilitaci a kognitivní trénink mozku. FNO 2013. [online]. Dostupné z URL: http://nela.fno.cz/doc/tematicke-listy.pdf.

13. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. J Am Geriatr Soc 1992; 40(9): 922–935.

14. Tsoi KK, Chan JY, Hirai HW et al. Cognitive tests to detect dementia: a systematic review and meta-analysis. JAMA Intern Med 2015; 175(9): 1450–1458. doi: 10.1001/jamainternmed.2015.2152.

15. Larner AJ, Mitchell AJ. A meta-analysis of the accuracy of the Addenbrooke's Cognitive Examination (ACE) and the Addenbrooke's Cognitive Examination-Revised (ACE-R) in the detection of dementia. Int Psychogeriatr 2014; 26(4): 555–563. doi: 10.1017/S1041610213002329.

16. Školoudík D, Fadrná T, Sedláková M et al. Changes in cognitive functions in patients with acute cerebrovascular event. Who tested by Mini-Mental State Examination and the Clock Drawing Test. Cesk Slov Neurol N 2007; 70/103(4): 382–387.

17. Corbett A, Owen A, Hampshire A et al. The effect of an online cognitive training package in healthy older adults: an online randomized controlled trial. J Am Med Dir Assoc 2015; 16(11): 990–997. doi: 10.1016/j.jamda.2015.06.014.

18. Yoo C, Yong MH, Chung J et al. Effect of computerized cognitive rehabilitation program on cognitive function and activities of living in stroke patients. J Phys Ther Sci 2015; 27(8): 2487–2489. doi: 10.1589/jpts.27.2487.

19. Bland M. An introduction to medical statistics. 3rd ed. Oxford: Oxford University Press 2000.

20. van de Ven RM, Schmand B, Groet E et al. The effect of computer-based cognitive flexibility training on recovery of executive function after stroke: rationale, design and methods of the TAPASS study. BMC Neurol 2015; 15: 144. doi: 10.1186/s12883-015-0397-y.

21. Lehmann EL. Nonparametrics: statistical methods based on ranks. New Jersey: Prentice Hall 1998.

22. Shigaki CL, Frey SH, Barrett AM. Rehabilitation of poststroke cognition. Semin Neurol 2014; 34(5): 496–503. doi: 10.1055/s-0034-1396003.