

## Computer-Assisted Cognitive Rehabilitation in Stroke and Alzheimer's disease

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### Abstract

**Background:** The aim of study was to compare the effects of computer-assisted cognitive rehabilitation (CR) in mild cognitive impairment after stroke and in patients with Alzheimer disease.

**Methods:** The study included 21 patients after ischemic stroke (12 males, 9 females, age median 60.5 age range 38–81 years) and 15 patients with AD (8 males and 7 females 71.5,50–86 years). We administered WAIS-III, MMSE, and ACE-R to evaluate MCI. NEURO-4 software was employed for CR. Rehabilitation was carried out for two periods of 1.5 h each week for 3 months.

**Results:** In the stroke group we recorded significantly higher scores for the following parameters after CR: IQc (median 84 before vs 88 after  $p = 0.001$ ), IQv (83 vs 92,  $p = 0.029$ ), IQp (78 vs 86,  $p = 0.001$ ), VC (91 vs 97,  $p = 0.017$ ), PO (82 vs 94,  $p = 0.001$ ), SOP (71 vs 8,  $p = 0.0003$ ), ACE-R (79 vs 84,  $p = 0.01$ ) In the AD group only the ACE-R was increased (75 vs 83,  $p = 0.008$ ).

**Conclusions:** Our study demonstrates that the beneficial effects of computer-assisted CR in patients with MCI are more significant in stroke patients than in AD patients.

**Keywords:** Cognitive rehabilitation; Alzheimer disease; Stroke; Cognitive impairment

### Abbreviations:

AD: Alzheimer disease; ACE-R: Addenbrooke's Cognitive Examination, revised; CR: Cognitive rehabilitation; HADS: Hospital Anxiety and Depression Scale; IQc: IQ score global; IQp: IQ score performance; IQv: IQ score verbal; MMSE: Mini-Mental State Examination; WM: Working memory; PO: Perceptual organization; SOP: Speed of processing; VC: Verbal comprehension; WAIS-III Wechsler Adult Intelligence Scale, third revision

### Background

Cognitive functions are impaired in brain disorders including neurodegenerative diseases, stroke, and brain trauma. Treatment is typically pharmacological [1,2] and, in some cases, neurosurgical. However, non-pharmacological intervention, especially cognitive rehabilitation, was often neglected in the past but now there have been increasing efforts to develop cognitive interventions to ameliorate cognitive problems experienced by older adults, especially AD, stroke and brain trauma patients [3,4].

Computer-based programs specifically targeted to dementia or mild cognitive impairment have been developed as a support in rehabilitation of cognitive areas and daily living functions [5]. Computer-assisted CR is a cost-effective method for providing

individualized treatment, based on each patient's neuropsychological patterns, in which impaired cognitive areas are repeatedly stimulated [6]. Computer interventions are rapidly becoming popular and cognitive exercise has been successfully implemented because older adults are often the fastest growing group of computer technology users [7].

CR provides a structured practice of complex mental activity designed to enhance cognitive function [3,8]. Neural plasticity is a prerequisite for improvement of cognitive impairment following CR [9,10]. Several studies have been carried out on the effect of cognitive training and rehabilitation in different diseases associated with cognitive impairment. Most studies have reported mild beneficial effects of CR in patients with neurodegenerative disease such as AD [5,9,11-13]. However, studies on CR in stroke patients have been more promising [10,14-17]. Data comparing the effects of CR in patients with acute brain lesions versus chronic progressive disease, notably neurodegenerative conditions such as AD, are needed.

The aim of this pilot study was therefore to compare the effects of computer-assisted CR in patients with mild cognitive impairment following stroke versus patients with mild cognitive impairment attributed to probable AD.

### Methods

**Cognitive rehabilitation:** For computer-assisted rehabilitation we used the software NEURO-4. This program provides multimodal and

multiple-domain training of cognitive function. In order to brain memory and concentration function, we used non-verbal tasks such as assembling shapes or figures, getting through a labyrinth, memorizing cards and shapes. We used tasks focused on planning and strategic thinking for executive functions training, e.g. London Tower, Hanoi Tower, etc.

Rehabilitation was carried out for two periods of 1.5 h each week for 3 months. Rehabilitation was supervised by a neuropsychologist. The battery of the cognitive tests was administered both before the start of computer-assisted CR and after completion of CR. The effect of CR was assessed as the difference between baseline scores and post-training scores within the each group, and also by comparison between the two groups.

**Data analysis:** All results are expressed as median and minimum-maximum values. SPSS v.15 (SPSS Inc., Chicago, USA) statistical software was used to analyze the data. The Wilcoxon signed-rank test was applied to compare the paired data, and the Mann-Whitney U test was used to compare the groups. Spearman's correlation analysis was carried out to evaluate the relationship between age, other baseline variables and differences in cognitive scores in both groups. Analysis of covariance ANCOVA was used for analysis of differences between the groups with age as a covariate. Nonparametric tests were used owing to small sample sizes.  $P < 0.05$  was taken to indicate statistical significance.

## Results

We included 21 patients in our prospective study after ischemic stroke (12 males, 9 females, age median 60.5, age range 38–81 years) and 15 patients with probable AD (8 males and 7 females, age median 71.5, age range 50–86 years). Patients in both groups were matched with respect for age and sex. Table 1 presents the results of the cognitive tests before beginning the treatment in both groups. Table 2 compares the scores on the cognitive test battery at baseline and following CR, as presents the changes in scores following CR.

	AD (n=15)	Stroke (n=21)	p
Sex			
M/F	7/8	15/6.	0.175a
Age,y	71.5 (50-86)	60.5 (38-81)	0.020b*
ACE-R	79.0 (54-97)	74.5 (28-94)	0.385b
MMSE	27.0 (24-30)	26.0 (10-30)	0.409b
HADS	14.5 (12-26)	14.0 (2-30)	0.459b
Education,y	12(5-21)	13(6-24)	0.321b

**Table 1:** Baseline characteristics of the study population; a ... Fisher's exact test, b ... Mann-Whitney U test Data in the table are presented as median (minimum – maximum). \*Spearman correlation did not prove significant relationship between age and other baseline variables in both groups.

In the stroke group, the Wilcoxon signed-rank test demonstrated statistically significant increased scores after the therapy for the majority of parameters, including WAIS-III, ACE-R, and MMSE. IQc (median 84 before vs 88 after,  $p = 0.001$ ), IQv (median 83 vs 92,  $p = 0.029$ ), IQp (median 78 vs 86,  $p = 0.001$ ), VC (median 91 vs 97,  $p =$

0.017), PO (median 82 vs 94,  $p = 0.001$ ), SOP (median 71 vs 8,  $p = 0.0003$ ), ACE-R (median 79 vs 84,  $p = 0.01$ ) Only one parameter, VM, did not change significantly in the stroke group (median 84 vs 85,  $p = 0.833$ ).

Cognitive domains	AD (n=15)			Stroke (n=21)		
	Before	After	p	Before	After	p
IQc	87 (74-110)	92 (66-112)	0,61	84 (64-112)	88 (71-121)	0,001
IQv	95 (61-119)	98 (60-119)	0,755	83 (67-127)	93 (69-126)	0,029
IQp	81 (68-105)	85 (57-114)	0,208	78 (61-99)	86 (68-111)	0,001
VC	93 (34-126)	102 (64-126)	0,835	91 (68-129)	97 (66-129)	0,017
PO	84 (30-109)	90 (60-107)	0,889	82 (72-101)	94 (62-121)	0,001
WM	90 (32-113)	94 (70-110)	0,561	84 (67-117)	85 (65-115)	0,833
SOP	81 (7-113)	86 (6-117)	0,382	71 (11-120)	81 (63-118)	0,0003
ACER	79 (54-97)	84 (58-98)	0,01	75 (28-94)	83 (49-95)	0,008
MMSE	27 (24-30)	29 (24-30)	0,094	26 (10-30)	28 (20-30)	0,395

**Table 2:** Scores on the cognitive test battery at baseline and after cognitive rehabilitation; p ... significance of Wilcoxon signed-rank test for comparing before and after therapy, score median (min-max)

Cognitive domains	AD	Stroke	p
	(n=15)	(n=21)	
IQc	-1,5 (-15 ...10)	7,0 (-3 ... 16)	0,001
IQv	-0,5 (-17 ...10)	3,0 (-56 ... 25)	0,08
IQp	-4,5 (-14 ... 9)	6,0 (-4 ... 20)	0,001
VP	0 (-12 ...75)	4,0 (-6 ... 31)	0,089
PO	1,0 (-14 ... 77)	8,0 (0 ... 28)	0,017
WM	1,0 (-24 ... 77)	0 (-12 ... 10)	0,66
SOP	2,0 (-26 ... 92)	10,0 (-2 ... 87)	0,049
ACER	4,0 (-7 ...16)	3,0 (-11 ... 15)	0,904
MMSE	1,0 (-2 ... 5)	0 (-4 ... 5)	0,6
HADS	0 (-10 ... 12)	-2,0 (-9 ... 17)	0,46

**Table 3:** Differences in cognitive scores between the stroke group and AD group; Significance of Mann-Whitney U test for comparison of AD and stroke group median of difference before and after the therapy (maximum decline and maximum elevation)

By contrast, only ACE-R scores were significantly increased following rehabilitation in the AD group (median 75 vs 83,  $p = 0.008$ );

no significant improvements were recorded in any of the other tests applied.

Table 3 presents the differences in cognitive scores between the stroke group and the AD group. The Mann-Whitney U test demonstrated a statistically significant difference between the stroke and AD groups in changes in the parameters IQc ( $p = 0.001$ ), IQv ( $p = 0.001$ ), PO ( $p = 0.017$ ), and SOP ( $p = 0.049$ ).

Table 4 shows ANCOVA analysis of differences between the groups with age as a covariate. ANCOVA proves the significant difference between the groups only in one outcome parameter IQp ( $p=0,015$ ).

Adjusted mean difference before-after	AD (n=15)	Stroke (n=21)	p
IQc	0,002	5,311	0,052
IQv	1,39	2,221	0,747
IQp	-1,294	6,757	0,015
VP	5,359	3,665	0,803
PO	5,688	9,091	0,636
PP	5,75	-1,5	0,316
RZ	9,242	10,04	0,925
ACER	4,242	3,974	0,909
MMSE	0,889	0,504	0,678
HADS	-0,046	0,601	0,904

**Table 4:** ANCOVA analysis of differences between the groups with age as a covariate.

Spearman's correlation analysis showed the significant relationship between age and differences in some cognitive scores only in the stroke group ( IQc  $\rho = 0.601$ ; IQv  $\rho = 0.565$ , PO  $\rho = 0.535$ ). In the AD group, Spearman's correlation analysis does not prove any relationship between age and any outcome variables.

We conclude that cognitive parameters were significantly improved by CR in the stroke group, whereas there was little significant change in the AD group.

## Discussion

This study demonstrates that the beneficial effects of computer-assisted CR in patients with mild cognitive impairment are much more significant in stroke patients than in patients with similar mild cognitive impairment attributable to probable Alzheimer disease.

This result is supported by other studies. Systemic review and meta-analysis by Cha and Kim [16] indicated that the overall effect size of computer-assisted CR in patients with stroke is 0.54 (95% CI; 0.33–0.74). That can be interpreted as a medium effect size. By contrast, the beneficial effects of CR in AD patients are at best 'mild', [5,13] although no direct comparison between these groups has yet been performed [18]. In addition, previous studies found no significantly different effects of CR in the patients in the acute versus chronic stroke

phases [14]. In our study we therefore enrolled stroke patients from a single period (3 months after stroke).

Our results confirm the hypothesis that computer-assisted CR is more effective in patients with acute structural brain lesions (stroke) than in neurodegenerative diffuse brain disease (AD). Because brain plasticity is probably crucial for successful CR, one might anticipate a greater effect of CR in patients with acute demarcated brain lesions (as in stroke) than in patients with a diffuse neurodegenerative disorder.

We also report some improvement of cognitive function in the AD group, but the improvement was only seen in one test (ACE-R) and the extent of improvement was limited. Generally, the beneficial effects of CR were not observed using MMSE; we surmise that MMSE is unsuitable for screening patients before CR, and ACE-R is likely to be a more appropriate screening test in this context.

Study limitations: First, heterogeneity, in our study we included patients after stroke whose lesions were located variably (11 patients with lesions in the left hemisphere, 7 patients with lesions in the both hemispheres, and 3 with lesions in the right hemisphere).

Second, owing to the small number of patients in our study it was not possible to analyze cognitive subgroups such as memory, thinking operations, executive functions, and orientation. Third, there was a significant difference in age between the groups, but we excluded the relationship between age and other baseline variables in both groups.

ANCOVA, age as a covariate, showed the significant difference between the groups only in one outcome variable (IQ score global).

Despite the limitations of our study, statistical analysis provides preliminary evidence for the differential effects of CR in patients with mild cognitive impairment following stroke versus similar impairment attributed to probable AD. The effectiveness of CR in AD is unsatisfactory and there is a question of future aiming of the computer-assisted CR in AD patients. There is also no clear long-time effect of CR after stroke, and therefore we plan to retest our patients after one year.

## Conclusion

We report that computer-assisted CR is likely to provide greater cognitive benefits in patients with mild cognitive impairment after stroke than in patients with similar impairment attributable to AD. For screening of patients before CR, ACE-R testing may be superior to MMSE. Further studies are necessary to evaluate the generalizability of our results.

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