Improving Cognitive Function in Patients with Stroke: Can Computerized Training Be the Future?

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Background: Cognitive impairment after stroke is common and can cause disability with a high impact on quality of life and independence. Cognitive rehabilitation is a therapeutic approach designed to improve cognitive functioning after central nervous system's injuries. Computerized cognitive rehabilitation (CCR) uses multimedia and informatics resources to optimize cognitive compromised performances. The aim of this study is to evaluate the effects of pc cognitive training with Erica software in patients with stroke. *Methods:* We studied 35 subjects (randomly divided into 2 groups), affected by either ischemic or hemorrhagic stroke, having attended from January 2013 to May 2015 the Laboratory of Robotic and Cognitive Rehabilitation of Istituto di Ricerca e Cura a Carattere Scientifico Neurolesi in Messina. Cognitive dysfunctions were investigated through a complete neuropsychological battery, administered before (T0) and after (T1) each different training. *Results:* At T0, all the patients showed language and cognitive deficits, especially in attention process and memory abilities, with mood alterations. After the rehabilitation program (T1), we noted a global cognitive improvement in both groups, but a more significant increase in the scores of the different clinical scales we administered was found after CCR. *Conclusions:* Our data suggest that cognitive pc training by using the Erica software may be a useful methodology to increase the post-stroke cognitive recovery. **Key Words:** Cognitive rehabilitation—computerized training—neuropsychology—functional recovery.

Background

Stroke is one of the main causes of mortality in industrialized countries,[1] and the leading cause of adult long-term disability, often with significant gait and upper limb impairment.[2]

The prevalence of poststroke cognitive dysfunction varies from 23% to 55% within 3 months from stroke onset, and declines between 11% and 31% after 1 year.[3-5]

Most stroke patients may live with specific cognitive deficits, including attention and concentration,[6] memory,[7] spatial awareness,[8] perception,[9] praxis,[10] and executive functioning[11] alterations with a significant reduction in daily life autonomy and quality of life.

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The typical clinical strategy of recovery in patients affected by stroke is to minimize the initial damage and thereby to improve the amount of functional recovery. Following stroke, it is possible that recovery could spontaneously occur, and improvement in neuropsychological functioning is generally observed for at least 2 years after brain injury. Indeed, Robertson and Murre indicated that there are 3 groups of recovery likelihood: spontaneous recovery, assisted recovery, and no recovery.[12]

Rehabilitative treatment, through integrative approaches, should allow a shifting from the simple remediation/compensation dichotomy to a more valid skills transfer and generalization.

Cognitive rehabilitation (CR) is becoming a standard component of neurorehabilitation after stroke, given that there is important clinical and research evidence of efficacy in improving cognitive and psychosocial functioning in patients with brain injury.[13,14]

CR refers to 2 major categories of techniques, that is, traditional and computer-assisted, computer-assisted cognitive rehabilitation (CCR).

In both cases, the cognitive training implements the residual neuropsychological abilities through specific strategies based on cognitive models. In particular, CCR uses multimedia and informatics resources with specific hardware system and software, to implement the cognitive training[15,16] for memory,[17] attention,[18] problem solving, and job simulation,[19] language,[20] praxis,[21] and processing speed.[22] Some clinical trials for stroke patients with neuropsychological deficits showed that the experimental group (performing computerized training) had a greater improvement than the control group (performing only conventional treatment, i.e., pen-and-paper exercises) in different cognitive domains, such as attention, memory, visual, and auditory learning.[23]

The aim of this study is to evaluate the effect of CCR, by using the software Erica, on cognitive and daily life performance, in stroke patients with cognitive impairment.

Material and Methods

Study Population

Thirty-five patients (mean ± SD age: 43.15 ± 16.85 years; 48.57% female) were enrolled in this study and randomized into either the control (CG: n = 15) or the experimental (EG: n = 20) groups. A more detailed description of the 2 groups is in Table 1.

The patients were randomly assigned to 1 of 2 groups (experimental or standard treatment) in order of recruiting.

This clinical, single-blind, randomized trial involved 35 stroke participants. All the patients needed CR based on medical and neuropsychological team's diagnosis. The sample was enrolled from January 2013 to May 2015 at the Laboratory of Robotic and Cognitive Rehabilitation of Istituto di Ricerca e Cura a Carattere Scientifico Neurolesi of Messina. The study was approved by the Local Ethical Committee. No participant was excluded from the study. Either the patient or the legal representative were adequately informed about the study and offered their collaboration and written consent.

The patients enrolled were in a chronic phase (i.e., 3-6 months from the acute neurological event). The EG consisted of 20 participants (11 men and 9 women, with a mean age of 43.9 years ± 16.6), whereas the CG consisted of 15 participants (7 men and 8 women, with a mean age of 42.1 ± 17.7). As shown in Table 1 the 2 groups

Table 1. *Demographical description of the sample at the beginning of the study*

	Experimental	Control	All
Participants (N)	20	15	35
Age (y)	43.9 ± 16.6	42.1 ± 17.7	43.1 ± 16.8
Gender			
Male	11 (55.0%)	7 (46.7%)	18 (51.4%)
Female	9 (45.0%)	8 (53.3%)	17 (48.6%)
Interval from stroke			
Mean in months	3 ± 1	4 ± 1	3.5 ± 2
Etiology			
Ischemic	15	9	24
Hemorrhagic	5	6	11
Brain lesion site/side			
Cortical right	7	4	11
Subcortical right	5	5	10
Cortical left	5	3	8
Subcortical left	3	3	6
Education y)	1.3 ± 4.1	11.2 ± 4.4	11.3 ± 4.1

Continuous variables were expressed as mean ± standard deviation, whereas categorical variables as frequencies and percentages.

were matched for age, sex, and educational level. Inclusion criteria were (1) diagnosis of vascular brain injury of either hemorrhagic or ischemic etiology (the latter involving the middle cerebral artery); (2) presence of moderate cognitive impairment, that is, Mini-Mental State Examination (MMSE) score ranging from 12 to 20; (3) absence of severe spasticity with an Ashworth Scale less than 3; (4) absence of disabling sensory alterations (i.e., hearing and visual loss), and of severe medical and psychiatric illness according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) and International Classification of Diseases-10.

Procedures

Each patient was submitted to a complete neuropsychological evaluation before and after the rehabilitative treatment (T0 and T1, respectively). Neuropsychological assessment consisted of a screening test, that is, the MMSE, and specific test for different cognitive domains, including the Category Verbal Fluency (CVF), Letter Verbal Fluency, the Reversal Motor Learning (RML), the Attentive Matrices (AM), and the Rey Auditory Verbal Learning Test (RAVLI immediate and late RAVLR recall). The functional scales, which were filled with the help of the caregivers, included Basic Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL), Levels of Cognitive Functioning (LCF), and Barthel Index (BI). Depression and anxiety scales (i.e., Hamilton Rating Scale for Anxiety, HRS-A, and for Depression, HRS-D) were also administered.

All the study participants underwent the same traditional CR, 6 times a week for 8 weeks (i.e., 48 sessions of 45 minutes each). In addition, the EG was submitted to the pc-based Erica training, consisting of 24 sessions of 45 minutes each, 3 times a week for 8 weeks, whereas the CG performed only CR (24 sessions, 3 times a week for 8 weeks).

To summarize, the 2 groups were submitted to the same amount of neurorehabilitation, but only the EG performed CCR.

Pc-cognitive training was realized by means of an Italian computerized cognitive tool, Erica (with a user license of 3 years; www.erica.giunti.it), which consists of a number of personalized pc exercises, articulated in 5 specific cognitive domains: attention process, memory abilities, spatial cognition, verbal and nonverbal executive functions. This platform of neuropsychological rehabilitation is characterized by modularity, flexibility, and uniformity in the type of task and in the administered program. A trained cognitive therapist provided exercises with a growing hierarchy of complexity through the Erica rehabilitative platform: the exercises' difficulty was flexible to the progressive changes of the patient's performance, and consistently ensured effective and pleasant rehabilitation sessions.

CR consisted in a face-to-face approach between the patient and the therapist that was administered in individual sessions. Training was customized for the needs of each patient. Indeed, tasks were presented using a paper-and-pencil modality, and these were specifically built to stimulate specific cognitive skills (16).

Statistical Analysis

Data were analyzed using the R version 3.4.0, considering a $P < .05$ as statistically significant. Normal distribution of a sample was investigated through the Shapiro test, whereas the Fisher test was used for comparing the variances of 2 samples from normal population.

Using the car package of R, for any outcome measure, we performed a repeated measure within-subject analysis of variance for unbalanced design. We included into the model the 2-level variable "group" (1 = experimental; 0 = control), as between factor, and the 2-level variable "evaluation time" (T0, T1), as within factor. We also included an interaction term for group and evaluation time.

The Student's t test for unpaired sample and the Fisher exact test were used to compare 2 groups (intergroup analysis), where appropriate. The Student's t test for paired sample was used to compare each group between the baseline and the end of the study (intragroup analysis). Finally, in order to investigate whether the improvement was more significant in the experimental group rather than in the control group, we compared the test score variations from baseline to follow-up (i.e., for each clinical test we computed the difference between the 2 evaluation times as |score at T1 to score at T0|) by the one-tailed Student's t test.

Results

At baseline, no significant differences between the EG and the CG were found.

There were no significant differences between the 2 groups on score variation from T0 to T1, but rather an effect due to the time for most of the scales/tests: MMSE ($F = 17.84$; $P < .001$), Letter Verbal Fluency ($F = 4.87$; $P = .034$), Digit Span ($F = 12.20$; $P = .001$), Token Test ($F = 8.26$; $P = .007$), Ideomotor Apraxia ($F = 5.25$; $P = .028$), Constructive Apraxia ($F = 13.52$; $P < .001$), RAV ($F = 11.37$; $P = .002$), and Boston Naming Test ($F = 15.37$; $P < .001$). However, the interaction "group × evaluation time" was significant statistically for MMSE ($F = 12.40$; $P = .001$), CVF ($F = 5.38$; $P = .027$), and AM ($F = 10.65$; $P = .002$) models.

Although no significant differences between the EG and the CG at T1 were found, the intragroup comparisons showed some improvements in many clinical scales, especially for the EG (see Table 2). Finally, comparing the test score variations from baseline to follow-up (Fig 1), we found that the improvement in MMSE ($t = 3.34$; $P = .001$), CVF ($t = 2.55$; $P = .008$), AM ($t = 1.18$; $P < .001$), as well as BNT ($t = 1.72$; $P = .047$), HRS-A ($t = 1.96$; $P = .030$),

Table 2. *Statistical comparisons of clinical scores between baseline (T0) and follow-up (T1)*

	EG T0	EG T1	*t* Value	*P* value	CG T0	CG T1	*t* Value	*P* value
MMSE	22.7 ± 2.5	27.0 ± 2.5	12.41	<.001	23.8 ± 3.5	25.9 ± 3.0	3.53	<.01
SVF	18.5 ± 12.7	25.2 ± 10.8	3.95	<.001	20.5 ± 11.8	22.3 ± 11.9	2.05	.06
PVF	13.1 ± 10.7	19.1 ± 10.0	4.14	<.001	15.5 ± 10.2	19.0 ± 10.8	2.36	.03
AM	29.6 ± 15.1	43.1 ± 10.6	5.16	<.001	35.3 ± 14.0	37.7 ± 12.0	1.32	.21
RAVLI	27.2 ± 13.6	29.7 ± 10.0	1.49	.15	30.1 ± 12.9	30.0 ± 11.9	.03	.98
RAVLR	3.9 ± 4.3	4.5 ± 3.0	.81	.42	4.5 ± 4.9	4.9 ± 3.6	.48	.64
DS	3.4 ± 1.6	3.9 ± 1.6	3.25	<.01	3.7 ± 1.2	4.3 ± .9	3.67	<.01
TT	26.8 ± 5.2	31.7 ± 4.0	4.60	<.001	28.4 ± 4.9	31.7 ± 4.3	3.05	<.01
IA	17.7 ± 2.9	19.7 ± .6	3.34	<.01	18.0 ± 3.2	19.6 ± 1.1	2.17	.05
CA	9.5 ± 2.8	12.4 ± 2.5	4.84	<.001	9.8 ± 2.9	13.5 ± 5.0	4.37	<.001
RAV	19.6 ± 9.2	24.3 ± 7.8	3.77	<.01	21.7 ± 8.5	25.8 ± 7.5	4.66	<.001
BNT	31.1 ± 9.7	38.0 ± 7.6	6.68	<.001	33.0 ± 10.4	37.4 ± 9.4	4.32	<.001
HRS-A	12.3 ± 8.9	8.1 ± 4.7	3.15	<.01	8.5 ± 4.0	7.1 ± 3.6	2.23	.04
HRS-D	12.1 ± 6.5	8.6 ± 4.6	4.81	<.001	10.8 ± 5.2	9.2 ± 4.5	2.23	.04

Abbreviations: AM, attentive matrices; BNT, Boston Naming Test; CA, constructive apraxia; CG, control group; DS, digital span; EG, experimental group; HRS-A, Hamilton Rating Scale for Anxiety; HRS-D, Hamilton Rating Scale for Depression; IA, ideomotor apraxia; MMSE, Mini-Mental State Examination; PVF, Phonemic Verbal Fluency; RAV, Raven's Coloured Progressive Matrices; RAVLI, Rey Auditory Verbal Learning Test Immediate; RAVLR, Rey Auditory Verbal Learning Test Late; SVF, Semantic Verbal Fluency; TT, Token Test.

Scores are in mean ± standard deviation.

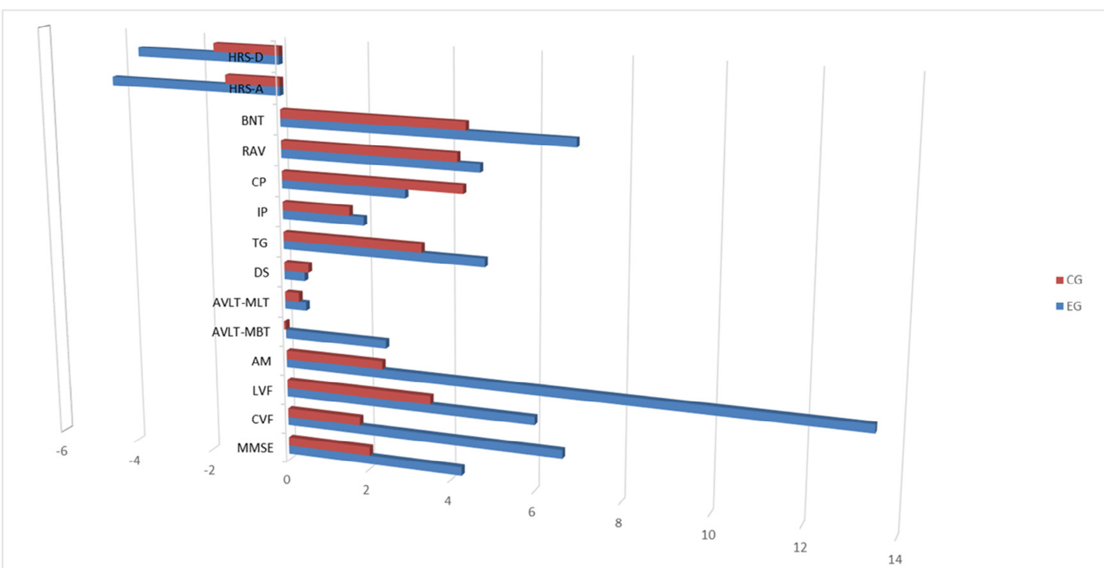

Figure 1. *Graphical representation by histograms of the average test score variations from baseline to follow-up in experimental and control groups. Abbreviations: ADL, Basic Activities of Daily Living; AM, Attentive Matrices; BI, Barthel Index; CVF, Category Verbal Fluency; HRS-A, Hamilton Rating Scale for Anxiety; HRS-D, Hamilton Rating Scale for Depression; IADL, Instrumental Activities of Daily Living; LCF, Levels of Cognitive Functioning; LVF, Letter Verbal Fluency; MMSE, Mini-Mental State Examination; RAVLI immediate and RAVLR recall, Rey Auditory Verbal Learning Test; RML, Reversal Motor Learning.*

and HRS-D ($t = 1.86$; $P = .036$) was more evident in the EG than in the CG.

Discussion

Emerging cognitive interventions, including CCR, virtual reality, and telemedicine system may be useful to optimize the quality and efficacy of rehabilitation in individuals with neurological disorders, such as stroke.[24] In particular, the use of pc-cognitive retraining has multiple potential benefits within the rehabilitative setting following brain injury: the repeatability of cognitive tasks, the rapid presentation of stimuli with multisensory stimulation, so as to boost neural plasticity and thus functional recovery. The rehabilitation carried out by pc-based trainings allows strengthening of the residual cognitive abilities as demonstrated by Fernandez et al, who considered the effect of the computer-based cognitive training on 50 patients affected by brain injury, observing an increase in the attention and memory processes.[25] Our results suggest that cognitive pc training, in addition to standard neurorehabilitation, may be a promising tool to optimize the global neuropsychological and functional recovery in poststroke patients. Indeed, the concomitant use of pc training may allow a significant increase in overall functioning and a positive influence in the optimization of specific cognitive and functional domains. Despite these results, there are only few evidences, concerning the CCR efficacy on the cognitive impairment in the patients affected by brain injury, including stroke. Among these, a very interesting study by Chen et al demonstrated a significant improvement in the global cognitive function in the individuals with traumatic brain injury who were submitted to CCR.[26] Another study by Lundqvist et al showed an improvement in the memory processes in 21 patients with acquired brain injury undergoing computerized memory training.[27] These results, confirmed by our work, demonstrated that neuropsychological computerized rehabilitation could have a relevant impact in the rehabilitative outcomes of poststroke patients. Moreover, recent studies have highlighted the potentiality of the CCR supporting the global efficacy of such approach for the recovery of patients affected by different neurological disorders.[28,29]

The novelty of this work is that it was the first time Erica, a specific software for the cognitive impairment treatment, was used in patients with stroke. Indeed, a recent review has demonstrated that CCR may be considered a good tool to optimize rehabilitation outcomes following brain injury.[28] Moreover, different neurophysiological strategies, with regard to transcranial magnetic stimulation and transcranial direct current stimulation, are demonstrating a positive effect in promoting neuroplasticity of the injured brain area, and thus better functional and cognitive recovery.[30,31]

The main limitation of the study is that the sample is small and probably it is not sufficient to prove the real efficacy of CCR in the stroke population. Moreover, we have investigated patients affected by either ischemic or hemorrhagic stroke, which may have different kinds of functional recovery. Thus, it could be interesting to evaluate a more homogeneous sample of ischemic patients, presenting possible more homogeneous side lesions. In spite of this, the study also shows some strength, as the presence of a control group and a careful assessment of the cognitive functions.

In conclusion, our data suggest that the PC-cognitive training can be an additional approach for cognitive rehabilitation after stroke, to improve the cognitive recovery and the patients' global functioning, especially concerning the semantic/verbal fluidity and the short-term memory. In the near future, further larger sample studies should be carried out, to confirm these promising results and evaluate the long-term effects.

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