Beyond Cognitive Rehabilitation: Immersive but Noninvasive Treatment for Elderly

Elisa Pedroli[1(✉)], Pietro Cipresso[1,2], Silvia Serino[3], Michelle Toti[1], Karine Goulen[4], Mauro Grigioni[5], Marco Stramba-Badiale[4], Andrea Gaggioli[1,2], and Giuseppe Riva[1,2]

[1] Applied Technology for Neuro-Psychology Lab, IRCCS Istituto Auxologico Italiano, Milan, Italy
{e.pedroli,p.cipresso}@auxologico.it, michelletoti5@gmail.com

[2] Department of Psychology, Università Cattolica del Sacro Cuore, Milan, Italy
{andrea.gaggioli,giuseppe.riva}@unicatt.it

[3] MySpace Lab, Department of Clinical Neurosciences, University Hospital Lausanne (CHUV), Lausanne, Switzerland
silvia.serino@gmail.com

[4] Department of Geriatrics and Cardiovascular Medicine, IRCCS Istituto Auxologico Italiano, Milan, Italy
{goulene,stramba_badiale}@auxologico.it

[5] National Center of Innovative Technologies in Public Health, Istituto Superiore di Sanità, Rome, Italy
mauro.grigioni@iss.it

Abstract. With the rapid increase of the aging population in Italy, the number of subjects with cognitive deficits also increases. Two of the most damaged cognitive domains since the first phase of decline are Executive Functions and Spatial Memory. The general aim of this study is to evaluate the efficacy of a novel VR-based mixed training protocol for improving executive functions and spatial memory in patients with cognitive decline. To achieve this objective, the neuropsychological performance of two groups of a subjects with cognitive decline were compared before and at the end of the training period. One group underwent a classic rehabilitation protocol, the other underwent the new VR-based protocol. The results showed an improve in executive functioning in the VR group after the training period.

Keywords: Cognitive decline · Rehabilitation · Virtual reality · CAVE · Executive functions · Spatial memory

1 Introduction

1.1 Cognitive Decline

Nowadays, about 19% of the European population are 65 or more years old and probably will reach 150 million by 2080 [1]. With increasing age, health problems also increase, including cognitive impairments [2, 3]. Before developing dementia, subjects

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can go through different stages of impairments. Different definitions have been given to these initial stages of cognitive impairment; i.e. Cognitive Frailty [4] or Mild Cognitive Impairment [2]. Regardless of the definition, these problems lead to a reduction in the autonomy of the subjects and their quality of life, impacting the ability to live safely and independently [5].

It is widely accepted the need to act promptly by targeting rehabilitation programs to prevent the negative consequences of decline. Accordingly, each rehabilitation programs should be implemented in pre-clinical or early stage of the cognitive impairment. Prompt interventions could improve the ability of the elderly individuals and preserve their autonomy, thus avoiding an early hospitalization [6].

Two of the most damaged cognitive domains since the first phase of decline are executive functions [7, 8] and spatial memory [9–11]. Both executive functions and spatial memory deficits are complex phenomena that the classical assessment and rehabilitation protocols are not able to detect and manage adequately [12]. A more ecological and customized procedure could help clinicians to improve the quality of the clinical care [12]. VR is an important technology for the improvement and amelioration of the classical paper &pencil protocols used both for assessment and rehabilitation sessions. VR can make more neuropsychological practice more engaging, generalizable, and ecological thanks to its ability to measure behavior in valid, safe, and controlled environments objectively and automatically; dynamic learning also may increase patients' engagement [13, 14]. In the last decade, VR-based protocols have been developed for many neurological diseases, for both motor [15, 16] and cognitive [17, 18] impairments.

In this regard, there is a growing urgency to identify the most effective strategies to prevent cognitive decline using all the tools available. The modern pharmacological treatments are not able to reduce symptoms or slow down the unavoidable progression of the cognitive impairment [19]. Therefore, there is increased interest for computerized or virtual reality-based cognitive rehabilitation programs that is assumed to improve, or at least stabilize, performance in a given cognitive domain (i.e. near transfer effect [20]). These kinds of protocols are based on the principles of neuronal plasticity and cognitive ability restoration, but also generalized effects beyond immediate training contexts are expected (i.e. far transfer effects) [21]. Here we present an innovative VR-based training for the rehabilitation of Executive Functions and Spatial Memory and some preliminary data from a larger trial that is still taking place.

2 Materials and Methods

2.1 Sample

In this preliminary phase of the trial we recruited 14 elderly subjects from the Department of Geriatrics and Cardiovascular Medicine of the IRCCS Istituto Auxologico Italiano located in Milan (Italy). The presence of cognitive decline was assessed by Mini-Mental State Examination (MMSE) [22] and only individuals who had a score between 23 and 26 were included in the study. Participants were randomly assigned to "VR training" ("VR Group"; n = 7) or "Control Group" ("NN-VR Group"; n = 7).

Exclusion criteria for the groups were: (1) presence of visual and balance deficits which may interfere with the use of VR technology; and (2) the additional presence of psychiatric disorders or other neurological conditions, such as traumatic brain injuries or strokes.

The VR Group included six men and one woman, while the NN-VR Group included four women and three men. The demographic information are show in the Table 1 There were no significant differences between two groups in terms of age [t(12) = 0.818; p = 0. 429] or education [t(12) = −0.899; p = 0.386].

Table 1. Demographic information.

	Age		YoE		MMSE	
	Mean	SD	Mean	SD	Mean	SD
VR group	78,86	4,22	13	4,08	25,99	2,10
NN-VR group	81,29	6,63	11	4,24	24,63	1,63

Note: YoE = Years of Educations, MMSE = Mini-Mental State Examination; SD = Standard Deviation.

All participants provided written informed consent, which was approved by the Ethical Committee of IRCCS Istituto Auxologico Italiano. The study was conducted in compliance with the Helsinki Declaration of 1975, as revised in 2008.

2.2 Rehabilitation Protocol

The protocol includes an assessment (T0), 5 weeks off, a second assessment (T1), 10 training sessions and one last evaluation (T2). During the assessment, a complete neuropsychological battery was performed. The cognitive rehabilitation sessions were held twice a week for at least 30 min each one, for five weeks. Accordingly to literature, we created two different highly-ecological virtual rehabilitation protocols for Executive Functions and Spatial Memory [23]. Both protocols could be implemented using low-end and high-end virtual reality systems [24]. NN-VR Group underwent a protocol for executive functions and spatial memory designed with traditional cognitive rehabilitative activities using paper & pencil materials.

Cognitive Assessment. A complete and extensive cognitive assessment was conducted to analyze a wide range of cognitive domains. All participants underwent a detailed neuropsychological assessment conducted by an experienced neuropsychologist three time. The neuropsychological assessments analyze several cognitive domains: executive functions, selective attention, short and long-term spatial and verbal memory, and visuo-spatial abilities. the neuropsychological battery was composed of: (a) phonemic verbal fluency and categorical verbal fluency test [25], (b) Frontal Assessment Battery (FAB) [26], (c) the Digit Span Test [27], (d) the Corsi Span Block Test [27], (e) Story recall [28], (f) Corsi Supra-span Block Test [28], and (g) Clock Drowing Test [29].

All scores obtained from the neuropsychological battery were corrected for age, education level and, when necessary, gender according to Italian normative data.

Executive Functions Training. The training environment is a virtual supermarket developed with Unity according to our needs (Fig. 1). The tasks were based on a VR-based assessment for the Executive Functions "Virtual Multiple Errands Test" (VMET), developed by Riva and colleagues [13, 30]. To move around and buy products in the shop patients could use a X-Box controller connected to the system. To complete the tasks the patients must buy several products on shelves following precise rules. First, the patient and the clinician analyze the task and the rules in order to understand and plan the different steps needed to solve the task. Then, patient start the shopping session in the virtual environment and the clinician helps patient only to avoid main errors and for technical support. At the end of the task a brief discussion about the outcome of the task is done. The software automatically records every object taken from the shelves and the path taken by the patient.

For the VR-based rehabilitation protocol, 10 different tasks with increasing difficulty are developed.

Spatial Memory Training. A virtual city (Fig. 1) was developed for the memory training. Patients can move around in the city using the X-Box controller connected to the system. The tasks are divided in encoding and retrieval phases. In the first phase patients start from the center of the city and have to explore the environment in order to find one, two or three objects located in different predefined place. In the retrieval phase, patients are asked to remember and reach the place where the objects were located before. Also, patient have to respect the order in which he found the objects in the previous phase. Here, the starting point is different for each session and is one of the target points where the patient does not return. In the first five tasks the clinician shows an allocentric map of the city and shows the patient the starting point of the retrieval phase in order to simplify the use of allocentric representation. If the patient gets lost during the task the software provides a cue, a green path that connects the present position of the subject to the forgotten point. Moreover, the system automatically records the path taken by the patient, when all target points have been achieved, and if the cue has been used. This task is developed to improve individuals' ability in storing, retrieving and synchronizing different spatial information, starting from results obtained from a previous trial with patients with dementia [31–33].

Fig. 1. The virtual environments: supermarket and city.

VR System. The virtual-based training took place inside a Cave Automatic Virtual Environment (CAVE) of Istituto Auxologico Italiano, CAVE is a room-sized cube with three walls and a floor. The 3D visualization occurs thanks to the combination of four stereoscopic projectors (Full HD 3D UXGA DLP), and the screens with a projectable area of 266 cm × 200 cm. A cluster system composed of two HPZ620 Graphics Workstations, mounting Nvidia Quadro K6000 GPU with dedicated Quadro Sync cards, is responsible for the rendering of the projection surfaces, user tracking and functional logic. Also, CAVE is equipped with a Vicon motion tracking system, with four infrared cameras, which allows the tracking of specific reflective markers positioned on target objects and a correct reading of the simulated spaces and distances with a 1:1 scale ratio, thus enhancing the feeling of being immersed in the virtual scene.

2.3 Statistical Analysis

Given the limited sample size a Wilcoxon test was done to compare the delta scores of the VR and NN-VR groups separately. The first delta scores (D1) were calculated by subtracting the results of the first evaluation to those of the second one. The second delta scores (D2) were calculated by subtracting the results of the second evaluation to those of the third one. Also, a comparison between D1 and D2 of each group was done with Mann-Whitney U test. This procedure was done for each of the analyzed outcome measures. Two separate hypotheses were done; in each group we hypnotize that D1 is less than D2. When the comparison was made between the groups, we expect that the values of D2 of the control group are less than the control group. All statistical analyses were performed using JASP for Windows, version 0.9.2. A $p < 0.05$ was considered statistically significant.

3 Results

3.1 Pre-post Comparison Within Groups

For each outcome measures the delta score were calculated. for the Frontal Assessment Battery, the score of each sub-test were analyzed separately, except for the “Prehension Behavior” in which all the patients obtained the maximum score. In the Table 2 the descriptive statistics were presented.

Accordingly to the results, a significant difference emerged for the Frontal Assessment Battery. This result indicates that there is an improvement aft virtual treatment there that is not found in the NN-VR group (Table 3). The graphical representation of these data are showed in the Figs. 2 and 3. Also for the Go-No-Go task it is possible to observe an improvement in scores for patients in VR-based group, although it was not statistically significant (Table 3).

Table 2. Descriptive analysis of Delta scores.

	D1				D2			
	NN-VR group		VR-group		NN-VR group		VR-group	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
CORSI_SUPRASPAN	1,12	5,54	0,49	6,9	1,3	3,61	3,41	7,9
FAB	0,86	2,8	−1,29	2,06	−0,04	1,98	2,47	2,17
PH_FLU	1	6,22	1,43	6,27	−0,14	6,15	1,71	3,68
CAT_FLU	1,57	8,22	2,14	3,13	1,14	10,98	0,71	6,08
DIGIT_SPAN	0,57	1,51	0,29	1,38	0,29	1,41	0	1,16
CORSI_SPAN	0,17	0,98	0,17	0,75	0,14	0,76	−0,14	0,38
FAB_SIM	0	1,16	0,14	1,07	0	1,16	0,57	0,79
FAB_PVF	−0,14	0,38	−0,14	0,69	0	0,58	0,14	0,38
FAB_MS	0,86	1,46	0,14	1,57	−0,14	0,69	0,43	1,13
FAB_CI	0,14	0,9	−0,71	1,25	0	0,58	0,71	1,6
FAB_GNG	0	0,58	−0,71	1,11	0,29	1,11	0,71	1,11
CLOCK	1	1,61	1,79	4,17	−0,29	1,58	−0,97	1,72
STORY	2,39	5,6	−1,61	6,9	2,22	5,36	1,54	5,3

FAB = Frontal Assessment Battery; PH_FLU = phonemic verbal fluency, CAT_FLU = categorical verbal fluency, SIM = Similarities, PVF = Phonological Verbal Fluency, MS = Motor Series, CI = Conflicting Instructions, GNG = Go-No Go Task.

Table 3. Results of Wilcoxon test.

D1 vs D2	NN-VR-group		VR-group	
	W	p	W	p
CORSI_SUPRA_SPAN	9,00	0,422	11,00	0,344
FAB	17,50	0,751	1,00	0,016*
PH_FLU	15,00	0,594	15,50	0,633
CAT_FLU	6,00	0,200	15,00	0,600
DIGIT_SPAN	16,00	0,664	16,00	0,667
CORSI_SPAN	5,00	0,572	7,50	0,885
FAB_SIM	6,00	0,710	2,00	0,172
FAB_PVF	2,00	0,386	1,50	0,293
FAB_MS	17,00	0,932	4,50	0,500
FAB_CI	2,00	0,814	1,00	0,211
FAB_GNG	6,00	0,392	3,00	0,069
CLOCK	17,00	0,929	16,50	0,915
STORY	14,00	0,534	10,00	0,500

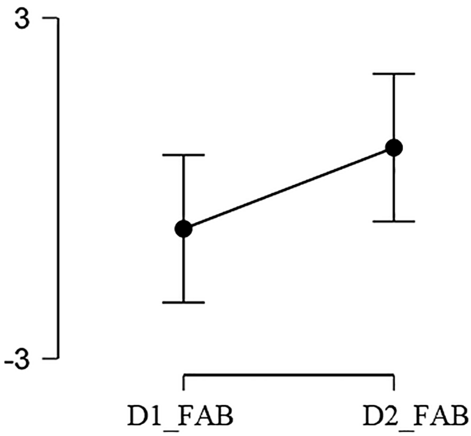

Fig. 2. Difference between D1 and D2 in the NN-VR Group.

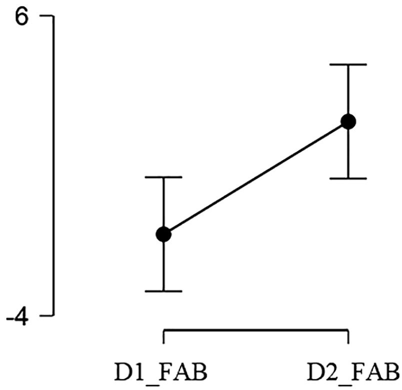

Fig. 3. Difference between D1 and D2 in the VR Group.

3.2 Between Groups Comparison

First, no significant results emerged from the analysis of D1 in the two groups for none of the outcome measures. As for the previous analysis, a significant difference emerged by analyzing FAB in D2. The results are highlighted in the Table 4 and in the Fig. 4.

Table 4. Results of Mann-Whitney U test.

VR vs NN-VR	D1		D2	
	W	p	W	p
CORSI_SUPRA_SPAN	22,00	0,582	15,00	0,223
FAB	35,50	0,933	11,00	0,047*
PH_FLU	22,00	0,398	22,00	0,398
CAT_FLU	18,50	0,239	29,00	0,740
DIGIT_SPAN	27,00	0,652	25,00	0,552
CORSI_SPAN	16,50	0,429	33,00	0,910
FAB_SIM	23,00	0,446	15,50	0,127
FAB_PVF	25,00	0,564	21,50	0,328
FAB_MS	30,50	0,807	18,00	0,196
FAB_CI	31,50	0,885	20,50	0,301
FAB_GNG	34,50	0,926	19,00	0,255
CLOCK	20,00	0,303	30,00	0,781
STORY	31	0,816	32	0,847

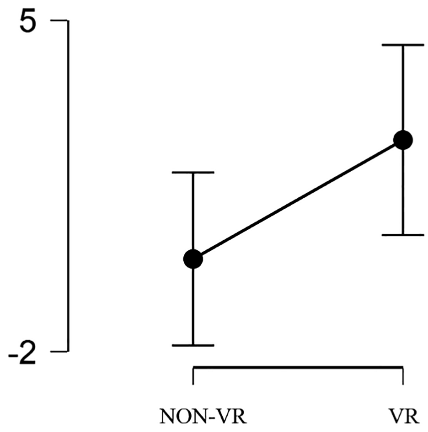

Fig. 4. Difference between NN-VR and VR in the FAB at D2.

4 Discussion

Here we presented the preliminary data of a larger project funded by the Italian government. The trial and patient's recruitment are still ongoing at the IRCCS Istituto Auxologico Italiano.

The aim of this study is to evaluate the efficacy of a novel VR-based mixed training protocol for both executive functions and spatial memory. The new training was compared with the classic rehabilitation tasks used for the stimulation of these cognitive domains. status of elderly individuals enrolled in the trails, especially as regards the targeted cognitive functions (i.e., executive functions and spatial memory).

The data are preliminary but encouraging. It was found an improvement in one of the two target cognitive domains: executive functions. The score of the Frontal Assessment Battery showed improvement in the VR group after the training period. This improvement is not highlighted in NN-VR group.

Also, the D2 scores are significantly different between the two groups. The FAB's score is higher in the experimental group after the treatment, thus indicating an improvement in the executive functions after our new VR training.

The greatest limitation that we can highlight in this work is the small sample size, and the representativity of the sample.

At the moment, we have only 14 subjects, but the number will be expanded in the coming months. The other limitation is related to the gender balance. In the VR group there is only one female subject. During the further recruitment this factor will be balanced.

At the same time, a motor rehabilitation program was developed. A stationary bike was integrated in the CAVE to promote the dual-task ability and another task to improve balance [34, 35].

Moreover, within the project a low-end device for a similar training is developing. The purpose of this new implementation is providing a program for home rehabilitation. The system will be designed to be used together by the patient and the caregiver at home without the therapist's support. Extending the training beyond the duration of the hospital journey could guarantee greater stability of improvements over time.

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