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Controlling Memory Impairment in Elderly Adults Using Virtual Reality Memory Training: A Randomized Controlled Pilot Study

Gabriele Optale, MD,[1,2] Cosimo Urgesi, PhD,[3,4] Valentina Busato, MS,[5] Silvia Marin, MS,[1,2] Lamberto Piron, MD,[6,7] Konstantinos Priftis, PhD,[6,7] Luciano Gamberini, PhD,[7] Salvatore Capodieci, MD,[1] and Adalberto Bordin, MD[5]

Abstract

Background. Memory decline is a prevalent aspect of aging but may also be the first sign of cognitive pathology. Virtual reality (VR) using immersion and interaction may provide new approaches to the treatment of memory deficits in elderly individuals. *Objective*. The authors implemented a VR training intervention to try to lessen cognitive decline and improve memory functions. *Methods*. The authors randomly assigned 36 elderly residents of a rest care facility (median age 80 years) who were impaired on the Verbal Story Recall Test either to the experimental group (EG) or the control group (CG). The EG underwent 6 months of VR memory training (VRMT) that involved auditory stimulation and VR experiences in path finding. The initial training phase lasted 3 months (3 auditory and 3 VR sessions every 2 weeks), and there was a booster training phase during the following 3 months (1 auditory and 1 VR session per week). The CG underwent equivalent face-to-face training sessions using music therapy. Both groups participated in social and creative and assisted-mobility activities. Neuropsychological and functional evaluations were performed at baseline, after the initial training phase, and after the booster training phase. *Results*. The EG showed significant improvements in memory tests, especially in long-term recall with an effect size of 0.7 and in several other aspects of cognition. In contrast, the CG showed progressive decline. *Conclusions*. The authors suggest that VRMT may improve memory function in elderly adults by enhancing focused attention.

Keywords

memory impairment, virtual reality, memory training, cognitive dysfunctions, rehabilitation

Introduction

The process of aging is associated with functional deficits in episodic memory, attention, language, visuospatial abilities, and executive function abilities. Similar changes are also observable in elderly people with mild cognitive impairment,[1] which may progress into Alzheimer's disease (AD).[2] Aging, however, is not inexorably linked to cognitive decline.[1] Indeed, there are still many doubts about the potential evolution of cognitive deficits and their possible treatment. The American Academy of Neurology has encouraged the clinical evaluation and monitoring of elderly patients affected by cognitive deficits and has recommended the identification of potential treatments that prevent progression to dementia.[3] Recent studies have documented the efficacy of cognitive training in enhancing the memory and attention abilities of aged individuals who have not had cognitive decline.[4-9] Here, we explored the possibility of stimulating an improvement in memory in aged individuals with memory impairment (MI) by taking advantage of the immersive and interactive therapeutic possibilities of systems that employ virtual reality (VR).

[1]Association of Medical Psychotherapists, Venice, Italy
[2]Psychosexology, ASL12, Mestre, Venice, Italy
[3]University of Udine, Udine, Italy
[4]IRCCS "Eugenio Medea", Polo Friuli Venezia Giulia, San Vito al Tagliamento, Pordenone, Italy
[5]Consorzio Sociale CPS gestore centro servizi "Anni Sereni" Rest-Home, Scorzè, Venice, Italy
[6]IRCCS San Camillo Hospital, Venice, Italy
[7]University of Padua, Padua, Italy

Corresponding Author:
Gabriele Optale, Via Grimani 3, 30035, Mirano (VE), Venice, Italy
E-mail:optale@tin.it

VR is an experiential interface in which the components of perception (visual, tactile, and kinesthetic) are the bases for interactivity, encouraging a sense of "being there"—that is, the sensation of being actually inside the virtual environment.[10,11] VR immersion frees the person from external distraction, and the interaction with the VR world encourages selective attention. VR has been used in other medical-psychological fields (eg, in patients with specific phobias such as fear of heights and fear of flying),[12,13] in motor-function rehabilitation (eg, post–brain damage),[14-16] and in a 65-year-old woman experiencing an impairment in memory-related cognitive processes.[17] In the present study, we tested the efficacy of a program of VR memory training (VRMT) in a group of rest-home residents, who can be easily observed over time.

Methods

Participants

We recruited 36 (24 female and 12 male) of the 159 residents of the "Anni Sereni" rest-care home in Scorzè (Venice, Italy) for the study (Figure 1). Inclusion criteria were the following: (*a*) age 65 years or older; (*b*) availability during the training and testing phases; and (*c*) presence of memory deficits as documented by a corrected total score at the Verbal Story Recall (VSR) Test[18] below the cutoff value (15.76). Exclusion criteria were the following: (*a*) serious sensorimotor deficits that would prevent participation in the training; (*b*) psychiatric disorders; (*c*) participation in previous cognitive training; and (*d*) serious medical conditions (ie, cancer, stroke, or other brain diseases). Recruitment was performed through presentations to participants and their relatives, and all participants provided written informed consent. The procedures were approved by the local ethics committee and were in accordance with the guidelines of the Declaration of Helsinki. Owing to logistical considerations, recruitment was conducted in 3 replicates each lasting 3 months, and 12 participants were recruited in each replicate. One experimental group (EG) participant and 2 control group (CG) participants died before completing the booster training. Furthermore, 2 EG participants left the rest home and went back to their families before completing the booster phase. Because we aimed to investigate the effects of both the initial and the booster training phases, the 5 participants yielding incomplete data were not included in the analyses. Thus, the final sample comprises 15 EG and 16 CG participants (31 participants in total; Figure 1).

One EG participant was left-handed, and the remaining participants were right-handed. The EG and CG participants were matched for age (EG: mean = 78.5, standard deviation [SD] = 10.9; CG: mean = 81.6, SD = 5; $t_{29} = 1$, $P = .325$), education (EG: mean = 5.3, SD = 2.4; CG: mean = 6, SD = 3.5; $t_{29} = 0.61$, $P = .544$), and gender distribution (EG: 10 women and 5 men; CG: 11 women and 5 men; $\chi^2 = 0.02$, $P = .9$).

Study Design

A randomized controlled single-blind procedure was used, in which the examiner administrating the clinical and neuropsychological tests remained unaware of the participants' allocations to the EG or CG. For each replicate, half of the participants were randomly allocated to the EG, whereas the remaining participants were allocated to the CG (Figure 1). The EG received the VRMT, whereas the CG received equivalent individual face-to-face training sessions using music therapy.[19] Both groups participated in recreational-expressive activities (reading/discussing newspapers and magazines, watching TV documentaries, creative and painting workshops) and assisted-mobility activities during the training. The experimental and control interventions consisted of an initial training phase lasting 3 months and a booster training phase during the following 3 months. In the initial training phase, participants were treated for 3 sessions per week over 3 months for a total of 36 sessions; in the booster training phase, participants underwent 2 sessions per week over 3 months for a total of 24 sessions per week. Each session of the experimental and control training lasted approximately 30 minutes and was conducted on separate days. The clinical and neuropsychological evaluation was performed before the onset of the training (pretraining), at the end of the initial training phase (posttraining), and at the end of the booster training phase (postbooster).

Interventions

The VRMT consists of auditory and VR experience sessions. During the initial training phase, 3 sequential auditory sections were administered alternating with 3 VR sessions every 2 weeks, and the cycle was repeated every 2 weeks. During the 3-month booster training phase, 1 auditory and 1 VR session were administered every week. Each auditory and VR session lasted approximately 15 minutes and was followed, after a pause of 1 minute, by 15 minutes in which the participant was invited to make an oral summary of the experience.

In the auditory sessions, the participant (blindfolded) listened via headphones to 3 stories told by 2 voices (1 male and 1 female) and accompanied by 3 different musical backgrounds. The musical backgrounds were custom created for the present study in the light of studies using music therapy in neurological disorders,[20] thus, avoiding any possible familiarity arising from known contexts. Lulled by the soothing, calming music, the participant may concentrate entirely on the semantic contents of the audio experience.

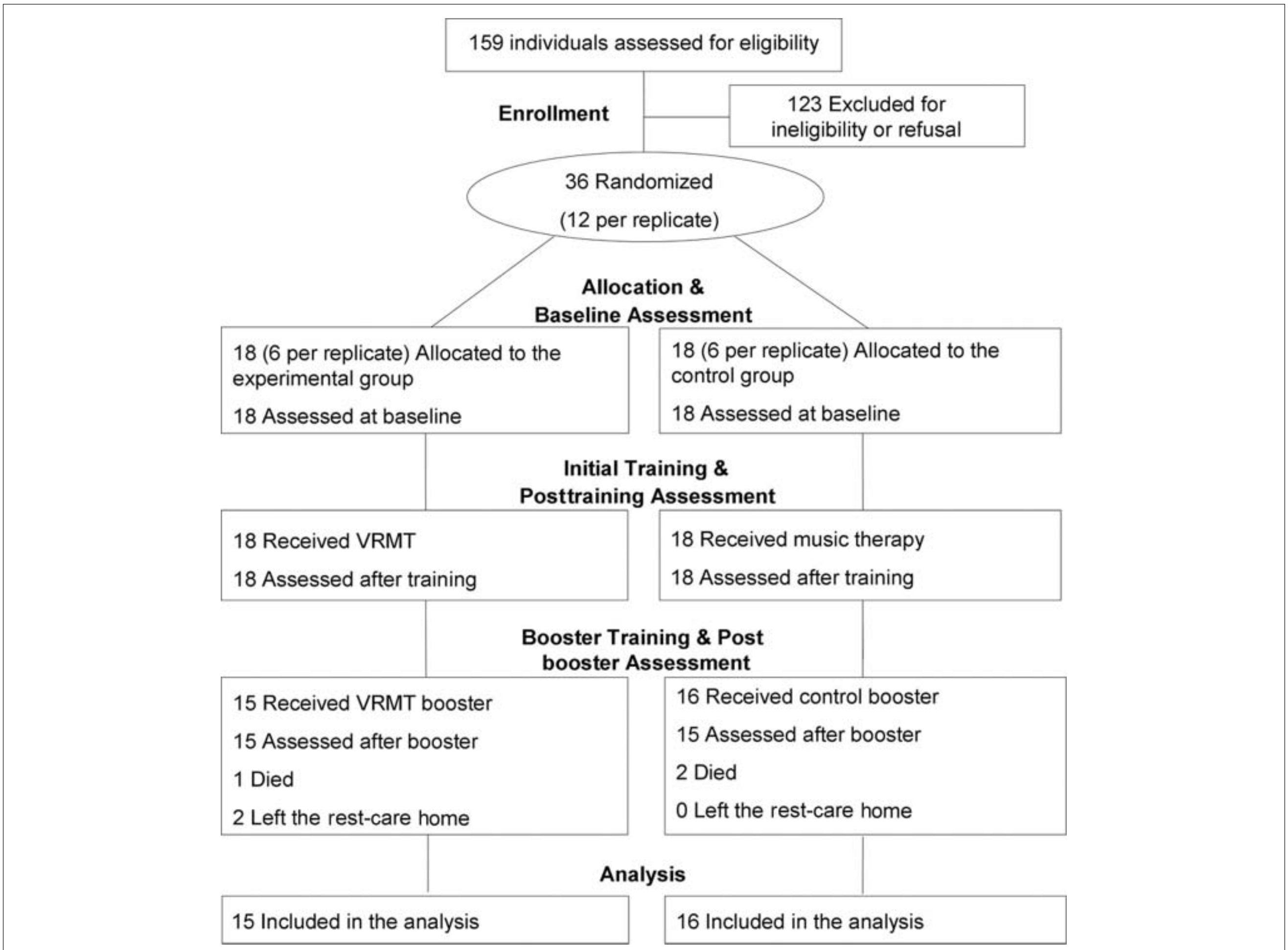

Figure 1. Flow of participants through the study

In the VR sessions, the participant is asked to concentrate attention on paths that lead to the activation of AVI film frame clips (eg, a view of a garden swing in motion or a seagull in flight) lasting about 15 seconds and constituting the end of a session (Figure 2). In the VR world, the participant moves as if gently strolling by pushing the joystick forward. The VR experiences include several tests of the participant's capacity to remember the paths taken and their orientation. These paths are individualized with color or form indicators. Even if the participants feel themselves unobserved, their movements and what they see can be followed on a computer monitor. Thus, the operator can simultaneously observe and, if necessary, intervene. Should the participant take a wrong turn and proceed to the wrong path, he or she is automatically transported back to the point immediately prior to the error. In creating the VR world, we paid particular attention to gradually increasing the complexity of the stimuli. Furthermore, to link the therapeutic sessions to the participant's real life and to encourage his or her independent, conscious reintegration into daily life, the VRMT begins with auditory and VR sessions that take place in familiar settings such as the childhood family home or a green park full of paths leading the participant to various destinations, or as he or she walks through the streets of a modern city. The VR experiences are accompanied by the same musical backgrounds used in the auditory sessions. This allowed continuity in the music-acoustic background across the 2 types of sessions, helping the participant to concentrate on the images and the interaction.

The control treatment consisted of individual face-to-face training sessions of music therapy.[19] Using music therapy in the CG group allowed us to have an active control for the experimental treatment. It also allowed us to control for any effects of using musical stimulation in the VRMT and, thus, isolate the specific VR effects. The music therapy was inspired by the creative music therapy approach in which the therapist encourages the participant to sing and play a variety of instruments. The different sessions are based on the themes

Figure 2. The virtual reality environment

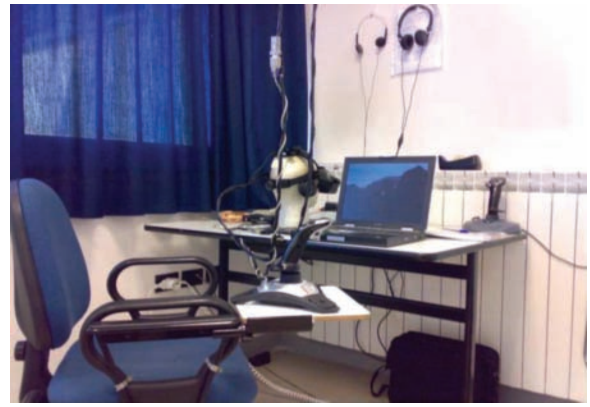

Figure 3. The virtual reality system

of "matching," "pacing," and "leading," in which the therapist starts from some rhythmic behaviors of the participant to improvise music and encourages the participant to do the same and to continue on his or her own with music improvisation. Because improvisation is a key element of creative music therapy,[19] each session is tailor-made to each individual participant. Each CG participant took part in the same number of sessions as the EG participants, that is, 3 sessions every week in the initial training phase and 2 sessions every week in the booster training phase. Each session lasted approximately 30 minutes and was administered on separate days.

The VR System

The VR experiences are administered through a head-mounted display V6. The VR system runs on a notebook PC (minimum requirements Pentium III, 850 MHz, 128 MB RAM, graphic accelerator, 8 MB VRAM). On the head-mounted display, there is a motion tracking sensor (InterTrax gyroscopic tracker). A joystick provides an easy interface. Directional change is effected merely by turning the head or rotating the swivel chair (an ordinary office desk chair) on which the participant sits comfortably (Figure 3). The direction of the movement is determined by the rotation of the participant's head with the introduction of a device to limit movement to the horizontal plane. The virtual environment was created using the Virtools platform with a VR development kit, using Windows XP.

Outcome Measures

We measured the effects of the treatments on general cognitive abilities, verbal memory, executive functions, and visuospatial processing by administering a series of neuropsychological tests before and after the initial and booster training phases (Table 1). General cognitive abilities were measured using the Mini Mental State Examination (MMSE)[21,22] and the Mental Status in Neurology.[23] Short-term verbal memory abilities were measured with the Digit Span (DS) Test[24] and long-term verbal memory with the VSR Test,[18] which requires the participant to repeat a short tale immediately after having heard it and after a 10-minute interval. The scores obtained by each participant in the immediate and delayed recall were collapsed and analyzed. Executive functions were evaluated with the Phonemic Verbal Fluency (PVF) Test,[18] the Dual Task Performance (DTP)[25] Test, and the Cognitive Estimation Test (CET).[26] The PVF requires the participant to produce in 1 minute all the words he or she can remember, starting with the letters C, P, and S. The DTP requires the participant to memorize a triplet of consonants for 10 or 30 seconds while making mental calculations. The scores in the 2 parts of the test (10- and 30-second performances) were collapsed together into a compound score. The CET evaluates the strategies adopted by the participant to respond to questions to which people do not usually know exact answers but that can be answered using general knowledge. The Trail Making Test[27] was also part of the evaluation protocol but could not be administered to most participants and was not included in the final analysis. Visuospatial processing abilities were evaluated with the Clock Drawing Test (CDT).[28] Higher scores on all the neuropsychological tests indicate better performance.

The generalization of the effects to daily-life functioning was evaluated with indexes of autonomy in the Activities of Daily Living Functions and Mobility (ADL-F and ADL-M, respectively)[29,30] and in the Instrumental Activities of Daily Living (IADL).[31] Higher scores in the ADL and IADL tests indicate higher dependency. The effect of the treatments on mood was evaluated using the Geriatric Depression Scale (GDS),[32] in which higher scores indicate increasing depressive disturbance.

Data Analysis

The scores of the 12 outcome measures were corrected for age, gender, and education as appropriate. The scores of the

Table 1. Comparisons of the EG and CG at the Baseline Neuropsychological Evaluation

	EG (n = 15), Mean (SD)	CG (n = 16), Mean (SD)	t_{19}	*P*
General cognitive abilities				
Mini Mental State Examination/30	22.9 (5)	20.99 (4.75)	1.09	.285
Mental Status in Neurology/10	3.07 (2.81)	3.81 (2.71)	–0.75	.459
Verbal Memory				
Digit Span	4.87 (1.25)	4.44 (0.81)	1.14	.263
Verbal Story Recall/28	6.1 (4.9)	7.25 (4.14)	–0.71	.485
Executive functions				
Phonemic Verbal Fluency	5.73 (4.44)	3.59 (3.15)	1.55	.132
Dual Task Performance/18	4.4 (5.29)	2.63 (3.5)	1.11	.277
Cognitive Estimation Test/5	2.23 (1.21)	2.06 (1.17)	0.40	.692
Visuospatial processing				
Clock Drawing Test/10	2.27 (2.22)	1.75 (2.26)	0.64	.526
Daily living activities				
Activities of Daily Living–Functions/60	11.67 (8.85)	18.88 (17.07)	−1.46	.155
Activities of Daily Living–Mobility/40	9.07 (7.36)	15.69 (14.21)	−1.61	.118
Instrumental Activities of Daily Living/8	2.8 (1.57)	1.94 (1.48)	1.57	.126
Depression				
Geriatric Depression Scale/15	5.47 (3.78)	3.31 (3.32)	1.69	.102

Abbreviations: EG, experimental group; CG, control group; SD, standard deviation.

EG and CG at the pretraining evaluation were preliminarily compared using the independent sample *t* test (2-tailed) to confirm the comparability of the 2 groups. The effect of the treatments was tested by entering the scores obtained by the 2 groups at the 12 outcome measures into a series of a 2-way mixed-model analyses of variance (ANOVAs), with group (EG and CG) as the between-subjects variable and time (pretraining, posttraining, postbooster) as the within-subjects variable. A significance threshold of $P < .004$ was set for all ANOVA effects using a Bonferroni correction procedure to protect against false positives in multiple testing. Planned comparisons were used for repeated-measure pairwise comparisons. Cohen's *d* was calculated to estimate the effect sizes for the EG improvements from the pretraining to the posttraining and from the posttraining to the postbooster evaluation.

Results

Baseline

Table 1 shows that nonsignificant differences were observed before training between the EG and the CG scores in any neuropsychological test or in the ADL-F, ADL-M, IADL, and GDS. Participants in both the EG and CG presented various degrees of cognitive decline as assessed with the MMSE. The corrected MMSE score of the EG and CG participants ranged from 9.7 to 29.3 and from 13.1 to 29, respectively, with 9 EG and 12 CG participants presenting a score below the cutoff value (23.8).[22]

The results of the ANOVAs comparing the changes of the 2 groups from pretraining to the posttraining and postbooster evaluations are reported below for each outcome measure. Table 2 lists the effect sizes for the EG changes after the initial and booster VRMT training.

Table 2. Effect Size of the EG Changes After the Initial and Booster VRMT Sessions[a]

	Training	Booster
General cognitive abilities		
Mini Mental State Examination	0.48	0.26
Mental Status in Neurology	0.45	0.07
Verbal Memory		
Digit Span	0.24	0.14
Verbal Story Recall	0.7	0.32
Executive functions		
Phonemic Verbal Fluency	0.3	0.11
Dual Task Performance	0.31	0.17
Cognitive Estimation Test	0.42	0.14
Visuospatial processing		
Clock Drawing Test	0.44	–0.32
Daily living activities		
Activities of Daily Living–Functions	–0.33	0.4
Activities of Daily Living–Mobility	–0.59	0.05
Instrumental Activities of Daily Living	–0.12	0.26
Depression		
Geriatric Depression Scale	0.75	0.3

Abbreviations: VRMT, virtual reality memory training; EG, experimental group.
[a]The effect size is defined as the Cohen's *d* for the changes of the EG after the initial VRMT phase with respect to the baseline and after the booster VRMT phase with respect to the first posttraining evaluation. Positive values indicate increased scores in the measures of general cognitive and neuropsychological abilities and decreased scores in the tests for daily living activities and depression.

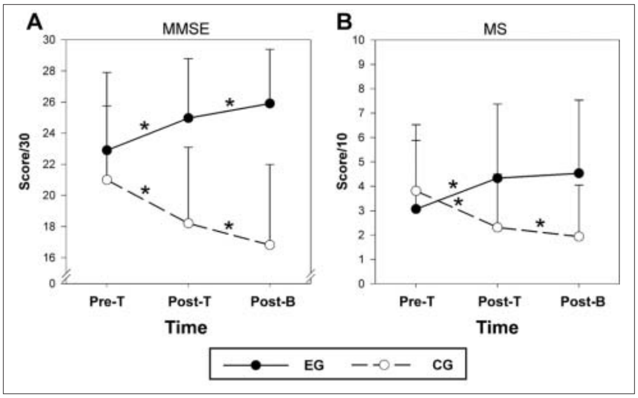

Figure 4. General cognitive abilities: A, Mini Mental State Examination (MMSE); B, Mental Status in Neurology (MS). Mean scores obtained by the experimental group (EG) and control group (CG) at the pretraining (Pre-T), posttraining (Post-T), and postbooster (Post-B) evaluations are reported. Error bars indicate standard deviations. $^*P < .05$.

General Cognitive Abilities

The ANOVA of the MMSE scores (Figure 4A) revealed a nonsignificant main effect of time ($F_{2,58} < 1$) but significant effects of group ($F_{1,29} = 15.12$; $P = .0006$) and of the interaction between group and time ($F_{2,58} = 23.01$; $P < .0001$). Pairwise repeated-measures contrasts revealed that the EG participants' scores improved from pretraining to the posttraining ($F_{1,29} = 6.85$; $P = .014$) and from the posttraining to the postbooster evaluation ($F_{1,29} = 4.46$; $P = .044$). In contrast, the scores of the CG participants decreased after the initial ($F_{1,29} = 13.35$; $P = 0.001$) and booster training phases ($F_{1,29} = 10.41$; $P = .003$).

The ANOVA on the Mental Status in Neurology scores (Figure 4B) revealed nonsignificant main effects of time ($F_{2,58} < 1$) and group ($F_{1,29} = 1.98$; $P = .17$), whereas their interaction was significant ($F_{2,58} = 30.16$; $P < .0001$). The EG participants' scores improved after the initial ($F_{1,29} = 10.12$; $P = .003$) but not after the booster phase ($F_{1,29} = 1.71$; $P = .201$). The scores of the CG participants presented a gradual decline that was significant from the pretraining to the posttraining evaluation ($F_{1,29} = 15.15$; $P < .001$) and from the posttraining to the postbooster evaluation ($F_{1,29} = 6.43$; $P = .017$).

Verbal Memory

The ANOVA of the DS results (Figure 5A) revealed that the main effect of time was nonsignificant ($F_{2,58} = 1.01$; $P = .37$), whereas the main effect of group ($F_{1,29} = 10.19$; $P = .003$) and the interaction ($F_{2,58} = 17.4$; $P < .0001$) were significant. The EG participants improved after the initial ($F_{1,29} = 4.46$; $P = .043$) and booster phases ($F_{1,29} = 4.46$; $P = .043$). In contrast, the DS scores of the CG participants decreased from the pretraining to the posttraining evaluation ($F_{1,29} = 16.73$; $P < .001$) but remained stable after the booster ($F_{1,29} < 1$).

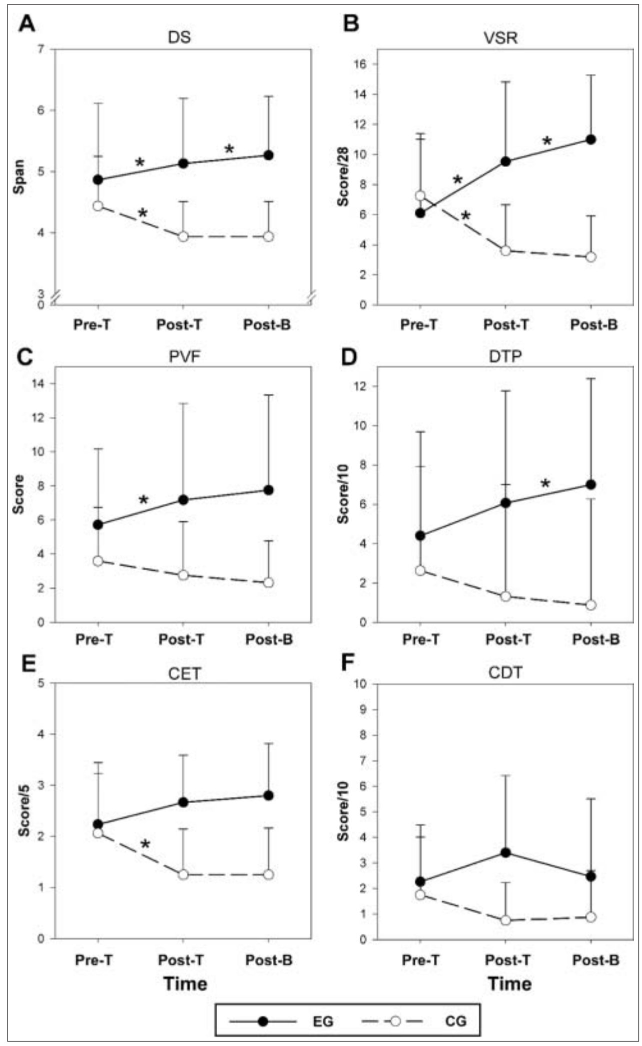

Figure 5. Neuropsychological abilities: A, Digit Span (DS); B, Verbal Story Recall (VSR); C, Phonemic Verbal Fluency (PVF); D, Dual Task Performance (DTP); E, Cognitive Estimation Test (CET); F, Clock Drawing Test (CDT). Mean scores obtained by the experimental group (EG) and control group (CG) at the pretraining (Pre-T), posttraining (Post-T), and postbooster (Post-B) evaluations are reported. Error bars indicate standard deviations. $^*P < .05$.

In a similar vein, the ANOVA on the VSR Test (Figure 5B) revealed a nonsignificant main effect of time ($F_{2,58} < 1$) but significant effects of group ($F_{1,29} = 9.77$; $P = .004$) and of the interaction between group and time ($F_{2,58} = 36.66$; $P < .0001$). The EG improved after the initial ($F_{1,29} = 15.02$; $P < .001$) and booster phases ($F_{1,29} = 12.26$; $P = .002$). In contrast, the performance of the CG participants decreased from the pretraining to the posttraining evaluation ($F_{1,29} = 18.17$; $P < .001$), whereas it remained stable after the booster ($F_{1,29} = 1$; $P = .325$).

Executive Functions

The ANOVA on the PVF scores (Figure 5C) revealed nonsignificant main effects of time ($F_{2,58}$ < 1) and group ($F_{1,29}$ = 7.36; P = .011) but a significant interaction ($F_{2,58}$ = 14.6; P < .0001). The EG participants' scores improved after the initial VRMT phase ($F_{1,29}$ = 9.26; P = .005), whereas they did not change after the booster ($F_{1,29}$ = 3.16; P = .086). In contrast, the scores of the CG participants remained stable after the initial ($F_{1,29}$ = 3.23; P = .083) and booster training phases ($F_{1,29}$ = 2.02; P = .166).

The ANOVA on the DTP scores (Figure 5D) showed a nonsignificant main effect of time ($F_{2,58}$ < 1) and group ($F_{1,29}$ = 8.98; P = .0055), whereas their interaction was significant ($F_{2,58}$ = 10.92; P = .0001). The scores of the EG participants remained stable after the initial training ($F_{1,29}$ = 2.02; P = .166) but increased after the booster ($F_{1,29}$ = 6.44; P = .017). The scores of the CG participants did not change after the initial ($F_{1,29}$ = 2.4; P = .132) and booster phases ($F_{1,29}$ = 1.51; P = .229).

The ANOVA on the CET scores (Figure 5E) revealed significant effects of group ($F_{1,29}$ = 11.12; P = .0024) and interaction ($F_{2,58}$ = 10.26; P = .0002) but a nonsignificant effect of time ($F_{2,58}$ < 1). The EG participants remained stable after the initial ($F_{1,29}$ = 2.6; P = .117) and booster training ($F_{1,29}$ = 1.35; P = .255). In contrast, the CG participants presented a significant decline from the pretraining to the posttraining evaluation ($F_{1,29}$ = 9.76; P = .004), but they remained stable after the booster ($F_{1,29}$ < 1).

Visuospatial Processing

The ANOVA on the CDT (Figure 5F) revealed that the main effects of group ($F_{1,29}$ = 5.27; P = .029) and time ($F_{2,58}$ < 1) and their interaction ($F_{2,58}$ = 3.14; P = .051) did not reach the Bonferroni-corrected significance threshold.

Daily Living Activities

The ANOVA on the ADL-F (Figure 6A) revealed that the main effects of group ($F_{1,29}$ = 2.38; P = .134) and time ($F_{2,58}$ < 1) and their interaction ($F_{2,58}$ = 3.22; P = .047) did not reach the Bonferroni-corrected significance threshold. Nonsignificant effects were, similarly, obtained from the ANOVA on the ADL-M (Figure 6B; group: $F_{1,29}$ < 1; time: $F_{2,58}$ = 1.18, P = .315; interaction: $F_{2,58}$ = 1.5, P = .231) and IADL measures (Figure 6C; group: $F_{1,29}$ = 2.12, P = .156; time: $F_{2,58}$ =1.72, P = .189; interaction: $F_{2,58}$ = 1.05, P = .362).

Depression

The ANOVA on the GDS score (Figure 6D) revealed nonsignificant main effects of time ($F_{2,58}$ < 1) and group

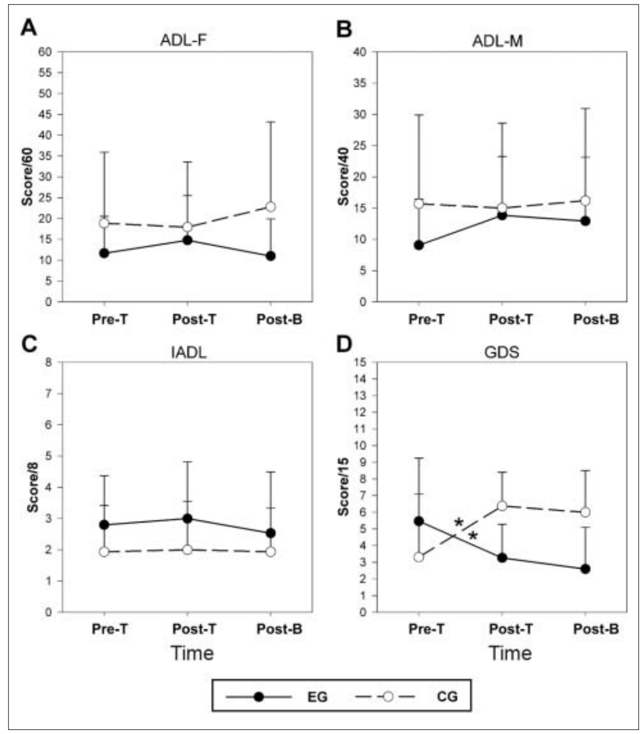

Figure 6. Daily living activities and depression: A, Activities of Daily Living–Functions (ADL-F); B. Activities of Daily Living–Mobility (ADL-M); C. Instrumental Activities of Daily Living (IADL); D. Geriatric Depression Scale (GDS). Mean scores obtained by the experimental group (EG) and control group (CG) at the pretraining (Pre-T), posttraining (Post-T), and postbooster (Post-B) evaluations are reported. Error bars indicate standard deviations. *P < .05.

($F_{1,29}$ = 1.82; P = .187), whereas their interaction was significant ($F_{2,58}$ = 15.79; P < .0001). The EG participants' depression values decreased after the initial training ($F_{1,29}$ = 5.61; P = .025) but not after the booster ($F_{1,29}$ = 1.35; P = .255). On the other hand, the CG participants had increased depression values after the initial training phase ($F_{1,29}$ = 11.59; P = .002) but not after the booster ($F_{1,29}$ < 1).

Follow-up Covariance Analysis

In a supplementary analysis, we tested whether the reduction of the subjectively reported depression symptoms could explain the EG improvements in cognitive abilities. We entered the differences between the pretraining and posttraining scores of the EG and CG participants into 3 multivariate analyses of covariances (MANCOVAs), one for each cognitive domain, with group as the between-subject variable and the GDS score changes as a continuous predictor. A nonsignificant effect of the changes in GDS score was obtained on the changes observed in any cognitive domain (all F < 1), whereas the effect of group remained significant after controlling for the main effect of the covariate in the analysis of the changes in general cognitive abilities ($F_{2,27}$ = 17.74; P < .0001) and verbal memory ($F_{2,27}$ = 14.03; P < .0001) but not in the executive functions ($F_{3,26}$ = 17.74; P = .035) and visuospatial processing ($F_{2,27}$ = 6.6; P = .016).

Discussion

We tested the efficacy of a program of VRMT in enhancing cognitive functioning of elderly adults with MI. We found that the participants who received the VRMT presented an improvement of general cognitive functioning and verbal memory after the initial training phase. The largest effects were observed in long-term memory, in keeping with the cognitive abilities stimulated by the auditory session of the VRMT. The improvements in executive functions abilities, in contrast, were small and did not survive corrections for the reduced depression scores of the EG participants. Furthermore, despite the spatial nature of the VR sessions, no effect was observed on the visuospatial abilities as tapped by the CDT. This drawing test, however, requires constructional praxis abilities and thus may not have been adequate to test for possible improvements of the EG in spatial orienting. The booster sessions consolidated the effects of the training, although the effects were smaller and limited to the MMSE, short-term and long-term memory, and DTP. The beneficial effects did not extend to the patients' autonomy in daily living activities as measured with the ADL-F, ADL-M, and IADL. In sum, the VRMT was effective in improving the general cognitive and verbal memory abilities of elderly participants with MI in contrast to the otherwise progressive cognitive decline observed in the control participants.

The improvements of the EG as compared with the CG participants are unlikely to be, at least exclusively, a result of placebo effects. We did not use a structured posttraining placebo questionnaire but showed that the EG improvements in general cognitive and verbal memory abilities could not be explained by the EG decreases and the CG increases in reported depression, which should be maximally affected by placebo effects. Thus, although we could not rule out placebo effects, the VRMT may have added to the EG performance beyond placebo effects.

The generalization of the improvements presented by the EG participants to different cognitive abilities may be explained by hypothesizing that the VRMT boosted focused attention, that is, the ability to concentrate and selectively respond to one specific visual, auditory, or tactile stimulus; to one aspect of the stimulus; or to a specific spatial location while ignoring others.[33] Attention abilities may decline in elderly adults and in patients suffering from AD,[34,35] causing ineffective processing and memorization of sensory stimuli. We suggest that the repeated exposure of elderly adults with MI to the VRMT may stimulate their attention system thanks to the peculiarity of the immersion in and interaction with the VR experience. In the immersive–interactive experience of VR, the participant, freed from external distractions, is able to exercise constant selective attention directed toward concluding the experience ("finishing the session"). It has been shown that types of training focused on a particular goal promote the learning and the development of the cognitive and perceptual motor skills that are specifically required to achieve that goal.[36] Furthermore, the abilities to classify and respond to external stimuli depend on previous experiences[37] and may consolidate through constant repetition of the same experience. These changes in cognitive functions are allowed by the brain's plasticity in response to changes in the environments,[38,39] which may persist in all phases of life.[40] Indeed, studies of aging with animal models have shown that immersion in new, enriched environments may lead to a refinement of sensory and motor cortices and improve memory and learning abilities, probably by inducing synaptic structural changes.[41]

During the VRMT, participants are presented with repeated, multimodal (auditory and visual) stimulation in enriched environments and are required to perform functional realistic tasks. This may enforce a continuous integration between the actual percepts and the mental representations of the aspects of the stimuli memorized during previous experiences. During the debriefing at the end of the VRMT experiences, we noticed that the EG participants, in each successive therapeutic cycle, focused their attention on new details of the stimulation, which had been hitherto disregarded. These new details could be associated with the memory representations of the environments formed in previous experiences, leading to a continuous memory updating that increased the quantity of personal memories of participants and, as a consequence, their self-confidence. Furthermore, the repetition of this memory updating process may have stimulated the development of a self-directed memory strategy[42] through a trial-and-error learning procedure. This type of learning is based on implicit, nondeclarative memory processes, which are relatively spared in AD patients.[43]

The beneficial effects of the immersion in new "virtual" environments were demonstrated in computer gamers, who present improved performance, as compared with nonplayers, in different attentional and perceptual abilities, including visual attention,[44] attentional capture,[45] and visual contrast sensitivity.[46] Indeed, training in video games may enhance the attentional resources and allow a better distribution of the processing resources to different stimuli and tasks, inducing a generalized improvement in cognitive functioning in real-world tasks also.[47] The present study confirms and extends the results of previous trials using computerized cognitive training in elderly adults[5,6,8,9] in showing that the beneficial effects of cognitive training are not only limited to the trained functions but extend to other cognitive abilities. Furthermore, whereas previous trials have been conducted in elderly adults not experiencing a relevant cognitive decline, more than half of the EG and CG participants in this study had cognitive decline, and all of them had memory deficits. Thus, the present study shows that the particular nature of the VRMT may allow memory function training even with those affected by severe MI.

The intention of the VRMT was to stimulate focused attention of elderly MI sufferers, perhaps by triggering plastic changes of the brain that could compensate for mild-moderate deficits. The generalized improvements in cognitive and memory abilities evidenced by the neuropsychological tests may suggest a successful transfer to the real world of the skills acquired in the VR. Studies using VR in neurorehabilitation have already shown transference of improvements from the virtual to the real world.[48-50] The results of the ADL-F, ADL-M, and IADL evaluation in the present study, however, failed to support such a transfer to real-word abilities. This is in keeping with the results of the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study,[4] in which the improvements in cognitive tests did not transfer to self-reported and performance-based measures of daily functions. Whereas the participants of the ACTIVE study were unimpaired in daily living activities, the deficits presented by several participants of our study rule out the possibility that the negative results could be a result of ceiling effects. We suggest, instead, that the instruments used measured mainly praxis abilities and were not adept at detecting changes in the cognitive functions necessary to other, more cognitive everyday activities (eg, watching a movie) or to social relationships.

In conclusion, the beneficial effects observed in cognitive functions support the efficacy of using VR in memory training with elderly adults and suggest that our VRMT protocol can be a valid and integral part of a rehabilitative strategy aimed at encouraging memory recovery. Future studies, however, are needed to confirm the results on larger samples, to investigate the durability of the effects, and to document the transfer to other daily living activities not examined in the present study.

Declaration of Conflicting Interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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