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A Comparative Single-Blind Randomized Controlled Trial With Language Training in People With Mild Cognitive Impairment

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Abstract

Background: Although cognitive training is effective for people with mild cognitive impairment (MCI), it is not clear which format is more effective. **Objective:** To compare the effectiveness of the same language programs when carried out via computer, paper/pencil and orally in people with MCI. **Methods:** Seventy-one participants with MCI were randomly classified in 3 experimental and 2 control groups. The experimental groups attended 48 sessions of language training for 6 months. The control groups attended either unstructured sessions or they were on waiting list. **Results:** Mixed measures analysis of variance, at the follow-up, showed a significant cognitive abilities improvement among the experimental versus control groups. At the end of the language training, the 3 groups presented improvement in cognitive abilities and daily function, while the control groups remained at the same performance level. **Conclusion:** All 3 cognitive language training methods were equally significantly effective.

Keywords

language training, mild cognitive impairment, different format of training, randomized control trial

Introduction

Background

With the aging of the population, the number of people with age-dependent disorders is increasing and the prevalence of Alzheimer's disease (AD) is rapidly growing, expected to nearly triple by 2050.[1] The increasing number of older people with AD is a burden not only to the people who meet the diagnostic criteria but also to their families and to the social system. Therefore, research has focused on identifying approaches that might slow disease progression[2] and developing lifestyle strategies that may delay onset or reduce AD risk.[3,4] Another avenue of investigation is to discover early detection methods for people who may be in the prodromal phase of disease progression, so they may be targeted in treatment when it might be most effective.[5] Mild cognitive impairment (MCI) is a transitional stage between healthy elderly and dementia[6] and is considered to be a prodromal phase of AD. Mild cognitive impairment of amnestic plus multiple domain type (aMCImd) is characterized by several deficits such as attention and executive function decline, verbal or visual memory, and language problems.[7-9] The language deficits have to do with language comprehension,[10] accuracy in syntactic reasoning,[11] and naming a rhyming word. Deficits in performance on a variety of other tests for semantic memory, such as lexical decision, semantic categorization,[12] semantic encoding,[13] and semantic priming,[14] and in productive and receptive discourse-level processing have also been reported in MCI.[15,16] The naming impairment seems to be the most common between other deficits and may originate from disturbances at the level of lexical–semantic processing, that is, a context-dependent impairment of access to, or inability to use, structurally intact semantic representations.[17] Alternatively, word-finding and word comprehension problems may originate from an actual loss in semantic knowledge that gives rise to a

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deficit that is consistent for a given item across a variety of tasks.[18,19]

In addition to assessing knowledge and memory, verbal fluency may also affect other cognitive processes including components of executive function such as divergent reasoning to generate category exemplars, maintaining a cognitive set of the overarching category while flexibly searching subcategories, working memory (WM) for prior responses, and inhibition of noncategory items.[20] Moreover, our recent study has proved that naming abilities seem to be affected in patients with AD, although individuals with MCI tend to exhibit greater impairments in category fluency.[21] Verbal fluency deficits in MCI, especially category fluency, confrontation naming deficits as well as in language comprehension[21] and accuracy in syntactic reasoning,[11] are referred. As the lexical–semantic processing is typically affected early in the disease course, it constitutes a primary target for detection and prognosis of MCI, since there are reductions in lexical activation in MCI as well as impairments in activation of multiple semantic representations.[9] More specifically, "secondary verbs per utterance, percentage of clauses, percentage of right-branching and left-branching clauses, propositions per utterance, conjunctions per utterance, mean duration of pauses, and standardized phonation time have all been reported to show significant differences between healthy older adults and patients with MCI or AD".[22]

Since no literature consensus about pharmacological interventions exists and medical treatment is not recommended for people with MCI,[23-25] it is prominent to develop nonpharmacological therapies that would enhance cognitive abilities and therefore delay the onset of neurodegeneration.[26]

Cognitive training (CT), the most popular nonpharmacological intervention, seems to be the most appropriate method for people with MCI. The basic aim of CT is to practice and enhance specific cognitive abilities that are trained. Many studies exist, providing evidence about the effectiveness of CT. Some among the CT programs were designed to improve a single cognitive ability and some others to improve multiple cognitive domains.[27] Multifaceted cognitive training for attention, memory, abstract thinking and constructional abilities might be effective interventions for people with MCI who present multiple cognitive problems.[28]

Cognitive training is either carried out in groups of 5 to 6 people or individually and the training tasks are mostly based on intelligence components, such as image rerecognition and assignment, pictures sequences, cube tasks, row formation, correct recognition of sets of words or images, perception speed, assignment tasks, speaking tasks, search tasks and so on. Nowadays, it is not clear enough which type of training is more effective. Is the classic cognitive training provided via paper and pencil, oral tasks, or a computer more effective? Although there is a recent study administered in people with MCI, providing evidence about the effectiveness of both versions (computer-based training and paper and pencil training) in a broad range of cognitive functions, such as executive function, attention, and verbal memory,[29] it still remains unclear which means of training is the most effective for people with MCI.

Conceptual Framework

The present single-blind randomized controlled trial tried to evaluate the impact of a language training program in aMCImd, community-dwelling, and Greek-speaking people, aged from 60 to 80 years provided via different means of training (computer based, paper and pencil, and oral). The primary aim was to investigate which format (tasks with paper and pencil, oral, or computer-based tasks) is more effective in people with MCI and to compare these 3 groups with 2 different control groups. The secondary aim was to separately evaluate the program's effectiveness in these 3 groups and to investigate whether the groups could manage to transfer the cognitive benefit to real-life conditions. Additionally, another goal was to generalize the benefit in other cognitive domains such as semantic memory and cognitive parameters of executive function. Our main hypotheses were as follows:

- The 3 experimental groups would present better performance only compared to control groups.
- The paper and pencil group (PP/G) would present better performance than the computer-based program of language tasks group (PC/G), because we assumed that training via paper and pencil is more familiar to older adults older than 65 years, since they use writing for several reasons. Moreover, writing is also a procedure that activates more brain regions than computerized and oral training.
- The participants who participated in these 3 formats of training should present improvements not only in language but also in other cognitive abilities.

Materials and Methods

Participants

This experimental study was carried out between September 2013 and June 2014 in the Day Care Centre of the Greek Association of Alzheimer Disease and Related disorders (Alzheimer Hellas), "Saint Helen" (http://www.alzheimer-hellas.gr/index.php/en/). Inclusion criteria were (1) age more than 60 years, (2) a diagnosis of aMCImd according to Petersen criteria,[30] (3) stage 3 of the disease according to Global Deterioration Scale (GDS),[31] and (4) independent walking. Exclusion criteria were (1) the diagnosis of major neurocognitive disorder according to *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition[32]; (2) affected disorders such as severe depression or anxiety and behavioral problems such as aggressiveness and irritability as that could affect the effectiveness of the CT programs; (3) other neurological disorders such as epilepsy, stroke, or hydrocephalus; (4) uncontrolled hypertension or terminal illness; (5) cardiovascular disease; (6) mental illness; (7) pharmacological treatment with cholinesterase inhibitors, antipsychotic, anticholinergic drugs, and benzodiazepines; and (8) sensory deficits, such as visual and hearing problems. The diagnosis was supported by

Table 1. Demographic Characteristics, M (SD) of group's participants.

Demographic Characteristics	Baseline Scores	Groups M (SD) PC/G, n = 14	PP/G, n = 18	OR/G, n = 10	AC/G, n = 15	C/G, n = 14	*P*
Age		67.86 (9.85)	70.14 (5.54)	71.80 (3.93)	65.73 (6.61)	68.14 (6.90)	.222
Gender M/F (χ^2)		5/9	4/14	5/5	4/11	4/10	.618
Years of education		12.14 (3.25)	11.17 (3.25)	9.70 (5.85)	11.13 (4.47)	10.36 (4.81)	.674
	MMSE[a]	28.07 (1.63)	27.89 (1.28)	26.90 (2.47)	27.20 (1.93)	26.07 (3.05)	.088
	FRSSD[b]	3.43 (1.65)	3.72 (1.60)	4.40 (3.09)	3.93 (1.90)	4.07 (2.09)	.811
	RAVLT 2[a]	44.23 (10.90)	40.28 (10.84)	36.30 (5.94)	37.07 (8.42)	28.50 (12.28)	.051
	RBMT[a]	11.14 (4.21)	10.19 (3.49)	8.20 (4.15)	10.80 (3.23)	10.14 (5.31)	.492
	FAS (X)[a]	7.73 (3.37)	8.76 (2.46)	8.60 (2.63)	8.09 (2.25)	8.50 (3.61)	.903
	FAS (S)[a]	12.18 (3.79)	9.47 (3.37)	8.60 (3.77)	8.55 (3.41)	8.93 (4.26)	.136
	FAS total[a]	10.26 (2.95)	9.16 (3.06)	8.36 (2.96)	8.99 (2.83)	8.66 (3.69)	.674

Abbreviations: AC/G, active control group; C/G, control group; FAS (S), verbal fluency test (letter S); FAS (X), verbal fluency test (letter X); FAS Total, verbal fluency test-total score; FRSSD, Functional Rating Scale for Symptoms of Dementia; MMSE, Mini-Mental State Examination; M (SD), mean (standard deviation); OR/G, oral group; PC/G, computer-based group; PP/G, paper and pencil group; χ^2, Pearson chi square; RAVLT 2, Rey Auditory Verbal Learning Test-Learning Ability; RBMT, Rivermead Behavioral Memory Test-Delayed Recall.

[a]More points/better performance.

[b]Less Points/better performance.

neurological examination, neuropsychological and neuropsychiatric assessment, neuroimaging (computed tomography or magnetic resonance imaging), and blood tests by a consensus of specialized health professionals, experts in neurocognitive disorders.

Of the 150 visitors at the day care center of Alzheimer Hellas, 50 were excluded because they didn't met the criteria (20 met the diagnosis of major neurocognitive disorder, 15 had severe depression or anxiety, 5 had other systematic diseases such as uncontrolled hypertension, 3 had other neurological disorders, and 7 people had serious sensory problems). Thus, 100 participants with aMCImd were randomly assigned into 5 groups. The first experimental group (n = 20) attended a PC/G, the second (n = 20) attended the same tasks via PP/G, and the third (n = 20) performed the same tasks orally (OR/G). The fourth group (n = 20) was an active control group (AC/G) that has followed unstructured sessions with discussion of current events, while the fifth one (n = 20) was a passive control group without any kind of pharmaceutical or cognitive intervention—waiting list (C/G). Only 71 people completed the follow-up and were considered for the analysis (22 males and 49 females with mean [M] standard deviation [SD] of 68.61 [7.00] years old), with 10.99 (4.17) years of education, and with Mini-Mental State Examination (MMSE) of 27.28 (2.16). Participants were matched in age ($P = .222$), gender ($P = .618$), and education ($P = .674$; Table 1).

Randomization, Allocation Concealment, and Blinding

This study aims to minimize the selection bias by using randomization and allocation concealment. Prior to inclusion of participants, a technician performed randomization using an algorithm. Until the completion of the last long-term follow-up, only the project leader and 2 persons responsible for the interviews and focus groups had access to the information on group allocation. Due to the nature of the therapy programs, blinding of the participants and instructors is not possible. However, all the independent evaluators are blinded with respect to group allocation, and the participants are not informed of primary outcome measures or the study hypothesis. To maintain group allocation confidentiality, participants are requested prior to each assessment phase not to reveal allocation or therapy content to the evaluators. Participants scheduled for qualitative studies are told that they must not talk to the evaluators about participation in interviews and neuropsychological assessment. Furthermore, the interviews and focus groups were performed in a way that does not reveal participants' allocation. After the baseline assessment, eligible and consenting people with aMCImd were randomized in each of the 5 groups.

Withdrawals and Discontinuation

The study would stop if any of the following occurs:

- Participant death or discharge.
- Incident dizziness.
- Medical problems related to exercises (auditorial, visual problems, and so on).
- The participant experiences adverse event(s) that require discontinuation in the judgment of the principal investigator or instructor.
- The participant has a need for additional intervention that would interfere with the trial.
- The participant neglects to follow trial instructions.
- The participant has lost more than 5 lessons and has not attended additional lessons to cover this gap.
- The participant or their legally authorized representative request consent withdrawal (Figure 1).

Figure 1. Flow of the sample.

Language Intervention

The study participants attended the CT program, at the Day Care Center of Alzheimer Hellas, at the same time in the morning or afternoon. Cognitive training included tasks, focused in the training and enhancement of semantic expression of language, semantic comprehension of language and phonemic expression of language. The tasks were ecologically valid, as they were derived from activities of daily living (ADLs), and were not similar to the tasks included in the neuropsychological tests. Each set of cognitive tasks had 3 levels of difficulty. In the first session, the participants were evaluated with respect to their language skills in order to initiate with the appropriate difficulty level. The trainees could remain at the same level or proceed to a more difficult one, according to their performance.

Each session comprised 10 tasks. The primary aim of the language tasks was to activate the vocabulary. The 10 tasks are divided into 3 subtasks of semantic expression, 3 subtasks of semantic comprehension and 4 subtasks of phonemic expression of language. However, it is impossible to separate the cognitive skills necessary for the tasks execution. Therefore, the tasks implementation also required several other cognitive abilities, apart from language, such as selective attention and shift of attention, WM, inhibition control and executive function (phonological organization, use of phonological strategies and control of meaning). An illustration of “paper and pencil tasks”, “computer tasks” and “oral tasks” can be found in Figures 2, and 3, respectively.

Examples of the CT Tasks, Third Level of Difficulty

First task: Put the letters in the right order and create the correct words. The words you are going to create are common fruits.

For example, roagne = orange

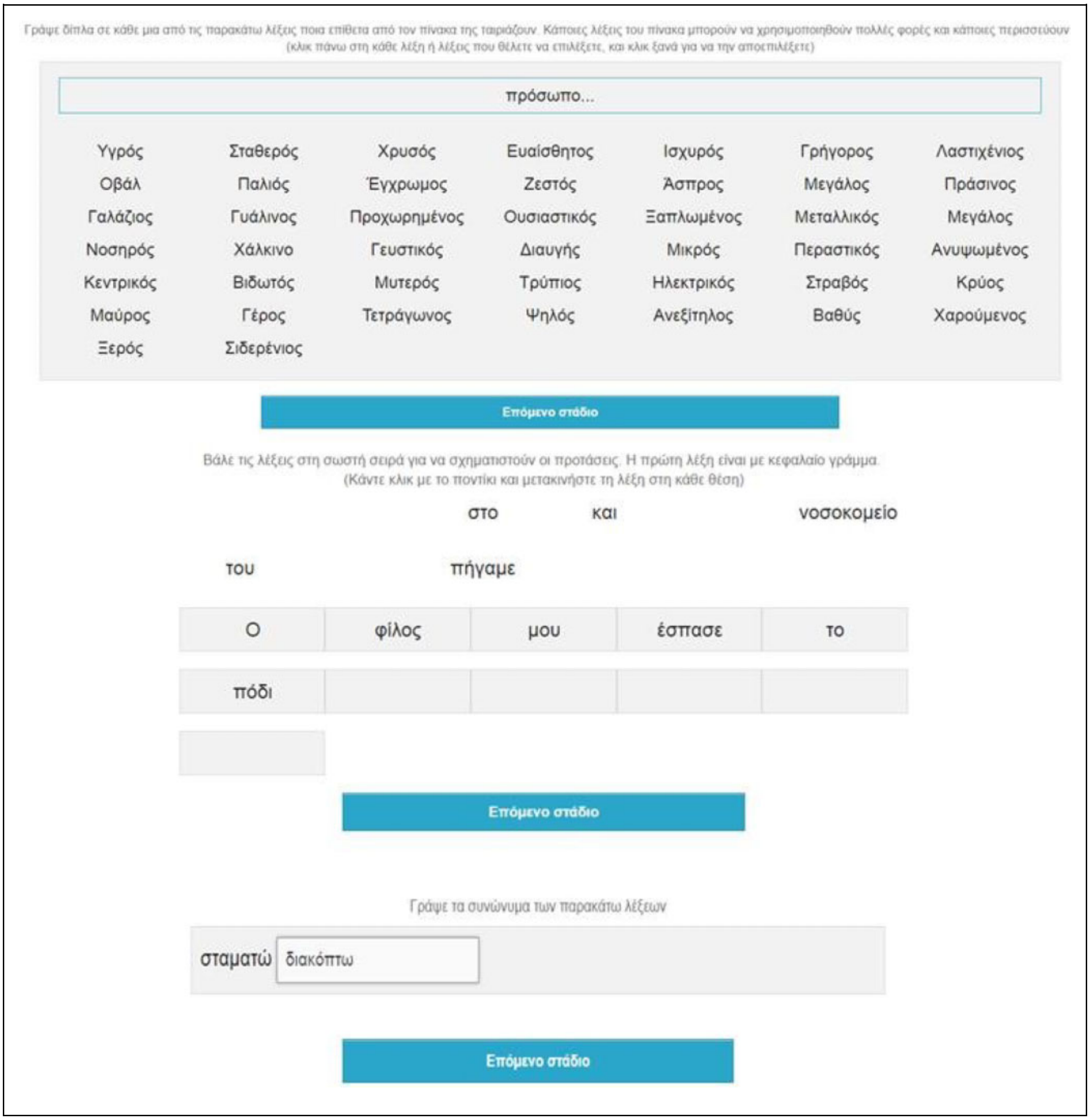

Figure 2. Example photo from computer-based version.

Second task: Put the words in the right order, so as to correctly recreate the sentences. The first word of the sentence is presented with a capital letter.

For example, dirty / has / week / to / Mrs / her / this / is / Mary / house / because / clean / very = Mrs Mary has to clean her house this week because it is very dirty

Third task: Write 7 words for which the initial letter is the letter -a, and the last letter is the letter -s.

For example, animals

The training was provided via different means such as computer, paper and pencil, and oral. The tasks were the same for the 3 groups of CT and they were administered using the same order. The CT included 48 sessions and lasted 6 months. The trainees visited the day care center twice a week and participated in 1-hour sessions. The CT was applied in group sessions. Each group comprised 5 to 10 participants. The program was administered by expert psychologists trained in cognitive interventions.

The participants signed an informed consent and were aware that they could withdraw their consent at any time without their statutory rights or medical care being affected. The study was approved by the Scientific and Ethics Committee of Alzheimer Hellas. All groups underwent a neuropsychological examination 2 weeks prior to initialization of interventions and after 6 months.

Neuropsychological Assessment

The programs effectiveness was examined by neuropsychological assessment performed at baseline and 6 months later, which signified the program's termination. The participants

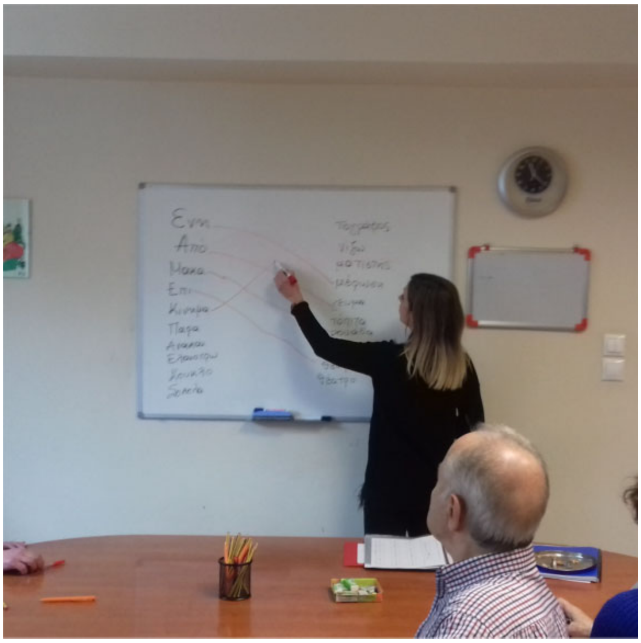

Figure 3. Example photo from oral version.

of each group were examined and followed up at the same time and place, after the competence of the training period.

Neuropsychological assessment included a comprehensive battery of psychometric tests (1) MMSE[33] for the assessment of general cognitive function; (2) Functional Cognitive Assessment Scale[34] for general functional performance; (3) Functional Rating Scale for Symptoms of Dementia (FRSSD) for ADL[35] (evaluates caregiver's opinion about daily function of people with cognitive disorders); (4) Rey Auditory Verbal Learning test (RAVLT)[36] for verbal memory; (5) Rey Osterrieth Complex Figure test[37] for visual memory and visual constructive abilities; (6) Rivermead Behavioral test (RBMT; history subtest),[38] for verbal episodic memory; (7) the total score of Verbal Fluency test (FAS)[39] and its sub scores—the 3 Greek letters used were χ (Chi), S (Sigma), and α (Alpha) for executive function, (8) the Pyramids and Palm Trees (PPT) test (raw score and performance time)[40]; and (9) Boston Diagnostic Aphasia Examination (BDAE; subtests of narrative writing, repetition, phonemic correlation, and reading comprehension of sentences)[41] for language. The GDS[42] was used in order to exclude patients with depression, while the neuropsychiatric inventory[43] was used for the exclusion of people with psychopathological symptoms. We tried to avoid practice effects using different test versions wherever necessary, namely, the Taylor's Complex Figure Test[44,45] for visual memory and visual constructive abilities and California Auditory Verbal Learning[46] for verbal memory.

As far as the language tests are concerned, we have used the Greek version of the abovementioned language tests among the available one. All the specific language tests used (apart from PPT test) were validated for the Greek older population, with the appropriate normative data for people older than 65 years.[39,41] For example, the results of the validation study of BDAE showed that there was a strong correlation between the cognitive status and the BDAE's performance of people with neurocognitive disorders and normal aging.[41] Furthermore, the FAS test was also validated for Greek older adults free of cognitive deficits.[39]

Data Statistical Analysis

The statistical analysis was performed with the IBM SPSS Statistics for Windows, (version 23.0; IBM Corp, Armonk, New York).[47] Demographic characteristics such as age, gender, and education were analyzed at baseline using a univariate analysis of variance (ANOVA) and Fisher exact test when necessary. In order to determine whether significant difference between all groups and times of assessment existed, a mixed-measure ANOVA 5 (between patients factor: group: PC/G-PP/G-OR/G-AC/G-C/G) $\times$ 2 (within patient factor: time of assessment: baseline follow-up) was used. Multivariate ANOVA (MANOVA) and the Scheffe multiple comparisons post hoc criterion were also used. Scheffe test was considered as the best choice for post hoc comparisons, as it tests if all possible comparisons are robust with respect to nonnormality and gives maximum protection against making type I errors which was our main concern in this study. The effect of cognitive training for each group was separately analyzed with repeated measures ANOVA.[48]

Results

The Effect of Group and Assessment Time

Baseline measurements showed that there were no statistically significant differences between all groups in demographic characteristics such as age (P = .222), gender (P = .618) or education (P = .674), and also in the majority of cognitive and functional tests used. The RAVLT (digit span), PPT (time), and BDAE (phonemic comprehension/repetition subtests) were significantly different at baseline; therefore, any significant difference at the follow-up was not taken into account at our final results (Table 1).

Mixed measures ANOVA showed that there was a main effect of time of assessment, $F_{1,71} = 29.3$, $P < .001$, $\eta^2 = .33$, and a significant interaction effect, $F_{4,71} = 4.48$, $P < .001$, $\eta^2 = .23$, on verbal fluency-x (FAS [X]). The subsequent MANOVA with group as the independent variable and performance in 2 times of assessment as the dependent ones, $F_{20,71} = 2.70$, $P < .001$, $\eta^2 = .17$, showed that at the follow-up there was a significant effect of group in verbal fluency-x, $F_{4,71} = 4.90$, $P < .001$, $\eta^2 = .22$. The PP/G was found to score higher than AC/G ($P = .050$) and the OR/G to outperform the AC/G in the same cognitive skill (P = .039; Table 2). Within-group ANOVA (repeated measures) between baseline and follow-up assessment in each group separately showed neither improvement

Table 2. Differences in Performance at the Follow-Up Among the Groups.[a]

Test	P	Group	M (SD)	P
FAS (X)[b]	≤.001	PP/G-AC/G	11.58 (2.87)-8.18 (3.68)	.050
		OR/G-C/G	12.40 (3.94)-8.64 (2.43)	.039
FAS (S)[b]	≤.001	OR/G-C/G	15.30 (5.01)-10.00 (3.23)	.046
FAS Total[b]	≤.001	OR/G-C/G	14.09 (3.68)-9.54 (2.88)	.027

Abbreviations: AC/G, active control group; C/G, control group; FAS (S), verbal fluency test (letter S); FAS (X), verbal fluency test (letter X); FAS Total, verbal fluency test-total score; M (SD), mean (standard deviation); OR/G, oral group; P/C, computer-based group; PP/G, paper and pencil group .
[a] $P = .05$.
[b] More points/better performance.

nor deterioration regarding the 5 groups' performance on the abovementioned ability.

As far as the verbal fluency-s (FAS [S]) is concerned, there was also a main effect of time of assessment, $F_{1,71} = 36.0$, $P < .001$, $\eta^2 = .38$, and a significant interaction effect, $F_{4,71} = 3.70$, $P < .001$, $\eta^2 = .20$. The subsequent MANOVA with group as the independent variable and performance in 2 times of assessment as the dependent ones, $F_{20,71} = 2.70$, $P < .001$, $\eta^2 = .17$, showed that at the follow-up there was a significant effect of group in FAS (S), $F_{4,71} = 3.23$, $P < .001$, $\eta^2 = .16$. The OR/G scored higher than the C/G ($P = .046$; Table 2). Within-group analysis between baseline and follow-up showed neither improvement nor deterioration regarding the 5 groups' performance at the abovementioned ability.

Regarding the total verbal fluency (FAS total), a main effect of time of assessment, $F_{1,71} = 74.4$, $P < .001$, $\eta^2 = .56$ and a significant interaction effect, $F_{4,71} = 6.87$, $P < .001$, $\eta^2 = .32$, were also noticed. The subsequent ANOVA, $F_{20,71} = 2.70$, $P < .001$, $\eta^2 = .17$, showed that at the follow-up there was a significant effect of group in FAS total, $F_{4,71} = 4.03$, $P < .001$, $\eta^2 = .12$. The OR/G outperformed the C/G ($P = .027$; Table 2). Repeated measures between baseline and follow-up assessment showed that after the language training, the PC/G improved, $F_{1,14} = 7.80$, $P < .001$, $\eta^2 = .43$, in FAS total ($P = .019$). The PP/G was also found to score higher at the follow-up assessment than at baseline, $F_{1,18} = 36.4$, $P < .001$, $\eta^2 = .69$ ($P = .000$). Finally, the OR/G also showed improvement, $F_{1,10} = 35.49$, $P < .001$, $\eta^2 = .79$ ($P = .000$), in FAS total. The AC/G and the C/G stabilized their performances and showed neither improvement nor deterioration (Table 3).

As far as the other cognitive abilities that were assessed are concerned, there was neither a main effect of time of assessment nor a significant interaction effect or a significant effect of group. However, it was considered appropriate to examine what is happening in each group separately. Therefore, the within-group ANOVA between baseline and follow-up assessment showed that at the end of the language training the PC/G showed deterioration, $F_{1,14} = 8.17$, $P < .001$, $\eta^2 = .38$, in phonemic correlation (BDAE; $P = .013$), whereas the PP/G showed improvement, $F_{1,18} = 5.27$, $P < .001$, $\eta^2 = .23$ ($P =$

Table 3. Difference in Groups' Performance Between Baseline and Follow-Up.[a]

Test	Baseline, M (SD)	Follow-Up, M (SD)	P
MMSE[b]			
PC/G	28.07 (1.63)	28.92 (1.32)	.089
PP/G	27.89 (1.28)	28.33 (1.37)	.119
OR/G	26.90 (2.47)	26.70 (2.54)	.591
AC/G	27.20 (1.93)	27.40 (1.99)	.638
C/G	26.07 (3.05)	26.92 (2.73)	.125
FRSSD[c]			
PC/G	3.43 (1.65)	3.78 (1.42)	.389
PP/G	3.72 (1.60)	2.88 (1.81)	.012
OR/G	4.40 (3.09)	3.30 (2.86)	.066
AC/G	3.93 (1.90)	3.73 (1.94)	.629
C/G	4.07 (2.09)	3.78 (2.75)	.740
RAVLT 1[b]			
PC/G	5.79 (1.76)	5.07 (2.09)	.239
PP/G	4.56 (1.19)	4.38 (2.00)	.692
OR/G	4.30 (1.33)	5.70 (2.05)	**.025**
AC/G	3.93 (1.38)	4.33 (1.91)	.458
C/G	4.21 (1.71)	5.14 (2.56)	.115
RAVLT 2[b]			
PC/G	44.23 (10.90)	43.35 (10.11)	.874
PP/G	40.28 (10.84)	39.44 (11.70)	.730
OR/G	36.30 (5.94)	42.60 (9.86)	**.011**
AC/G	37.07 (8.42)	39.00 (12.76)	.505
C/G	28.50 (12.28)	43.00 (11.31)	.058
RBMT[b]			
PC/G	11.14 (4.21)	13.00 (3.86)	**.036**
PP/G	10.19 (3.49)	10.17 (2.66)	.982
OR/G	8.20 (4.15)	9.65 (4.35)	.275
AC/G	10.80 (3.23)	10.06 (.95)	.438
C/G	10.14 (5.31)	10.06 (3.69)	.853
FAS (X)[b]			
PC/G	7.73 (3.37)	11.63 (3.61)	**.014**
PP/G	8.76 (2.46)	11.58 (2.87)	**.001**
OR/G	8.60 (2.63)	12.40 (3.94)	**.002**
AC/G	8.09 (2.25)	8.18 (3.68)	.923
C/G	8.50 (3.61)	8.64 (2.43)	.832
FAS (S)[b]			
PC/G	12.18 (3.79)	13.72 (3.92)	.281
PP/G	9.47 (3.37)	11.88 (4.25)	**.001**
OR/G	8.60 (3.77)	15.30 (5.01)	**.002**
AC/G	8.55 (3.41)	10.72 (3.92)	.091
C/G	8.93 (4.26)	10.00 (3.23)	.189
FAS Total[b]			
PC/G	10.26 (2.95)	12.66 (3.50)	**.019**
PP/G	9.16 (3.06)	12.17 (2.87)	**.000**
OR/G	8.36 (2.96)	14.09 (3.68)	**.000**
AC/G	8.99 (2.83)	10.35 (3.26)	.088
C/G	8.66 (3.69)	9.54 (2.88)	.105
BDAE 1[b]			
PC/G	11.93 (1.49)	11.28 (1.20)	.082
PP/G	12.22 (1.11)	12.83 (1.38)	**.037**
OR/G	12.60 (.96)	13.00 (.94)	.343
AC/G	11.36 (1.44)	12.20 (1.26)	.208
C/G	12.93 (1.20)	12.35 (1.44)	.055
BDAE 2[b]			
PC/G	7.14 (1.61)	5.71 (1.85)	**.013**
PP/G	5.78 (1.70)	6.27 (1.40)	**.035**

(continued)

Table 3. (continued)

Test	Baseline, M (SD)	Follow-Up, M (SD)	P
OR/G	5.20 (2.15)	5.90 (2.02)	0.173
AC/G	6.07 (1.68)	6.60 (1.72)	.082
C/G	5.29 (1.77)	5.35 (1.64)	.861
PPT[c]			
PC/G	241.57 (52.72)	269.85 (94.52)	.322
PP/G	396.50 (145.18)	326.00 (79.93)	**.019**
OR/G	318.40 (73.55)	251.80 (59.64)	**.000**
AC/G	317.42 (103.08)	297.33 (141.11)	.429
C/G	314.78 (107.48)	293.28 (114.17)	.569

Abbreviations: AC/G, active control group; BDAE, Boston Diagnostic Aphasia Examination; BDAE 1, Repetition; BDAE 2, Phonemic Correlation; C/G, Control group; FAS (S), verbal fluency test (letter S); FAS (X), verbal fluency test (letter X); FAS total, verbal fluency test-total score; FRSSD, Functional Rating Scale for Symptoms of Dementia; MMSE, Mini-Mental State Examination; M (SD), Mean (Standard Deviation); OR/G, oral group; PC/G, computer-based group; PP/G, paper and pencil group; RAVLT 1, Rey Auditory Verbal Learning Test-Digit Span; RAVLT 2, Rey Auditory Verbal Learning Test-Learning Ability; RBMT, Rivermead Behavioral Memory Test-Delayed Recall; PPT, Pyramids and Palm Trees Test-Time.
[a] $P = .05$.
[b] More points/better performance.
[c] Less Points/better performance.
[d] It should be stated that the bold-faced values indicate the statistically significant differences between the baseline and follow-up assessments.

.035). The OR/G, AC/G, and the C/G stabilized their performances and showed neither improvement nor deterioration between the 2 assessments. As regards the repetition of BDAE, the within-group analysis showed that at the end of the language training, the PP/G improved their performance, $F_{1,18} = 5.13$, $P < .001$, $\eta^2 = .23$, ($P = .037$). The other 4 groups (PC/G, OR/G, AC/G, and C/G) showed neither improvement nor deterioration at the same ability (Table 3).

The PP/G also improved, $F_{1,18} = 6.68$, $P < .001$, $\eta^2 = .28$, in semantic memory (PPT-performance time; $P = .010$), while the OR/G was found to score higher than the baseline assessment, $F_{1,10} = 36.5$, $P < .001$, $\eta^2 = .80$ (performance time-PPT; $P = .012$), as well. The PC/G, AC/G, and C/G showed neither improvement nor deterioration (Table 3).

The PC/G showed a significant improvement, $F_{1,14} = 5.49$, $P < .001$, $\eta^2 = .29$, in verbal memory (RBMT; $P = .036$), whereas the PP/G showed improvement, $F_{1,18} = 8.01$, $P < .001$, $\eta^2 = .32$, in ADLs (FRSSD; $P = .012$; Table 3). Finally, the OR/G after the language training was improved, $F_{1,10} = 7.23$, $P < .001$, $\eta^2 = .44$, in digit span (RAVLT; $P = .025$), and, $F_{1,10} = 10.08$, $P < .001$, $\eta^2 = .52$, in learning ability (RAVLT; $P = .011$). The AC/G and the C/G stabilized their performances and showed no significant differences between the baseline and follow-up assessment (Table 3).

Discussion

The primary aim of this study was to compare the effectiveness of the same language program when carried out via computer, paper and pencil, or orally and to also compare the effectiveness of these 3 experimental groups to 2 different control groups, an active and a passive one. The secondary aim was to evaluate the language training program impact in people with aMCImd. Our basic hypothesis was that the experimental groups would have higher scores than control groups, whilst our second hypothesis was that the PP/G would have better performance than the PC/G. Furthermore, our third hypothesis was that a well-structured language training program could not only enhance language cognitive skills in people with aMCImd, but also transfer the benefit of language programs in other not directly practiced cognitive domains, such as in executive function and ADL.

According to the results, our first hypothesis seems to be confirmed, since at the end of the training sessions, the experimental groups (at least the PP/G and the OR/G) showed better performance compared to the AC/G and the control one in verbal fluency skills. Regarding the effectiveness of the experimental groups in comparison to C/G, our results are in agreement with many other studies that support the idea that cognitive training is effective for people with MCI.[49-52] For example, Herrera et al assessed the effectiveness of a 12-week memory-attention training program based on recognition in people with MCI. The results have shown that the intervention group, compared to AC/G, showed improvement in trained skills during the intervention such as episodic recall and recognition. Besides, in their study in contrast to ours, the cognitive training concerned attention skills and not language; nevertheless, the experimental group showed better results than active control, which is in accordance with our study, proving that cognitive training is effective for people with MCI, compared to controls. Another study, the study of Gooding et al in 2016, compared 2 experimental groups with an AC/G.[52] The first experimental group consisted of people with MCI who were administered computerized cognitive training, while the second was a group that was administered traditional computerized training plus a program that incorporated motivational teaching and rehabilitation techniques. The training programs lasted 16 weeks and the participants completed 30 hours of training. The results showed that the experimental groups presented greater preservation of functioning in general cognitive performance than the AC/G. The computerized training, plus the motivational teaching strategies program, outperformed the AC/G in verbal learning and verbal memory, while the traditional computerized training group also performed better than the AC/G. Therefore, the study concludes that although the computerized cognitive training is beneficial for people with MCI, the most benefit may be offered when incorporated into a therapeutic milieu rather than administered alone.

On the other hand, the Rose et al study in 2015 administered a prospective memory training program using the Virtual Week computer game.[51] The intervention lasted over a month, and the participants were healthy elderly who completed 12 hourly sessions. Training group was compared to a no-contact and an AC/G. At the end of the training, the computerized memory training group improved in comparison to controls in performance on real-world prospective memory and ADLs. The study supports the idea that short-term training with the Virtual

Week game can produce cognitive and neural plasticity that may result in real-world benefits. In contrast to our study, the experimental groups have not outperformed the C/Gs in ADL, but this was expected since we used language training and not prospective memory training. Prospective memory seems to be associated with WM and executive function; therefore, the primary training effect is more likely to be transferred into real life.[53] Moreover, in comparison to our study, the training group was healthy elderly and the training sessions lasted only 1 month.

Finally, Li et al in their study in 2017, administered a multimodel cognitive training program in people with MCI.[50] The results showed that the multimodel cognitive training helped patients with MCI to gain cognitive benefits compared to C/G, in memory, visual spatial abilities and executive function after 6 months of training. Although the abovementioned studies refer to practice of general cognitive functions and not only practice of language skills, as our study refers, the aforementioned studies indicate that cognitive training (orientated either in language skills or in other cognitive functions) is effective for healthy elderly individuals, people with subclinical cognitive decline, and MCI compared to controls a result consistent with our initial hypothesis.

As far as our second hypothesis is concerned (the PP/G would show better performance than the PC/G), our results did not confirm our hypothesis. The PP/G was not outperformed by the PC/G, neither in language skills nor in other cognitive abilities. Our secondary hypothesis relied on the fact that the act of writing with paper and pencil is a quite different task than the keyboard writing. That is because the hand writer, in order to write a word, has to actively produce the letters, since he has to form every single letter on his own.[54] Therefore, the writers who use paper and pencil have to pay higher visual attention to the writing process.[55] In contrast, the PC writing demands only identification of the letters, since the letters are presented.[56] Consequently, the act of handwriting seems to activate more brain regions such as posterior cortical regions in the left hemisphere and central motor and sensory regions[56], and potentially promotes greater brain changes than the computerized and oral training. Our results seem to be in contrast with other studies supporting the idea that the computer condition might be inferior to the paper and pencil condition. The study of Tsolaki et al in 2017, for example,[29] compared 65 people who participated in a traditional cognitive training program provided via paper and pencil versus 59 people with MCI who participated in a computer-based training. Their results showed that at the end of the training (after 12 months), although computer-based training was effective in people with MCI, the administration of the traditional cognitive training via paper and pencil improved a greater range of cognitive abilities. However, in contrast to our study, in the study by Tsolaki et al the basic aim was the enhancement of attention and executive function abilities and not the language skills. However, as indicated by the final group results, our hypothesis that the paper and pencil tasks' versions would be superior to the others is not supported, since there were no statistically significant differences between PP/G compared to PC/G.

The third aim of the study was to evaluate the program's effectiveness to enhance specific language skills and to generalize the benefit in other cognitive domains. At the end of the training, only the PP/G showed improvements in directly trained abilities, such as verbal repetition and phonemic correlation. The OR/G showed language stability, while the PC/G at the end of the training showed stability and a slight deterioration in verbal repetition. However, these findings seem rational, since verbal repetition was not particularly trained in the computer format in the same way as was trained for example in OR/G, besides the fact that the training tasks were the same at the 3 formats.

As far as the generalization of the program's effectiveness in other cognitive domains than language, such as in semantic and episodic verbal memory and in cognitive parameters of executive function is concerned, all the experimental groups (PC/G, PP/G and OR/G) showed improvement in verbal fluency. Although verbal fluency as an executive aspect of language was an ability that was trained during the program, it was not one of its main aims. The most impressive fact was that although no significant language improvement was noticed at least for all the experimental groups, all the training groups have shown improvement in other general cognitive abilities that were not directly practiced during the intervention. To be more precise, the PC/G showed improvements in verbal fluency, which is an ability of executive functions indirectly trained during the intervention. Moreover, an improvement was also noticed in episodic verbal memory. Results from other studies of computer-based programs support that PC training is beneficial for people with MCI[57] and potentially leads to generalization of cognitive effect when these programs are focusing at specific cognitive abilities.[58,59]

The PP/G and the OR/G also showed improvements in verbal fluency, while the OR/G group showed additional improvement in semantic memory (completion time), WM (digit span), and verbal memory (learning ability). The OR/G, similar to the other 2 experimental groups, has generalized the effectiveness in other cognitive domains that were not trained directly during the program. Furthermore, as we can notice, the OR/G showed greatest generalization in more cognitive domains of the 3 groups. A possible explanation may be that although the 3 experimental groups were matched in the majority of the cognitive functions, the participants recruited for the OR/G had notably lower performance than the other experimental groups in the post abilities that showed improvement after the training (although no statistically significant). Therefore, it is rational for the OR/G to present larger improvement than the other groups, since they had greater improvement potentials.

Finally, as regards whether the groups could manage to transfer the cognitive benefit to real-life conditions, as a part of our third aim, the PP/G showed improvement in ADL. The transference of program's benefit in real life is always the ultimate goal of every intervention in people with cognitive deficits, and it was achieved for the PP/G. This result is also confirmed from other studies, which support that cognitive interventions may have an impact on ADLs in people with MCI.[60,61] The paper and pencil training seems to be more familiar to the elderly individuals aged 65 and older, since they use writing for several reasons such as in for remembering their dates, the list for shopping, or their obligations in everyday life. Therefore, it is probable that people with MCI allocated in PP/G showed improvement in daily function, since writing is strongly connected with their ADLs.

Limitations of the Study

Our study has 2 basic limitations. The first one concerned the absence of a second neuropsychological follow-up at least 6 months after the end of the language training. According to our knowledge, there is little research concerning the duration of the maintenance of the cognitive benefits yielded from the language training over time. Therefore, a second follow-up would be possible to provide more evidence. These results would be very important, since they could confirm that people with MCI have potential to benefit from the training and maintain the good results over time, especially when the training is over. A second limitation of the present study is the small number of the sample allocated in each group. Therefore, further studies are needed to provide more evidence about the effectiveness of the language training carried out via different means of training. The next step of our study would be the increase of the sample in each group, which may lead to more reliable conclusions.

Conclusion

According to our knowledge, till today, there are no studies assessing the effectiveness of a pure language training program in people with MCI. Our study is the first that demonstrates evidence regarding the effectiveness of a language training program, not only to enhance specific language skills but also to generalize the primary trained benefit in cognitive domains, not directly trained for people with MCI.

Besides the fact that it was not possible in our study to give strong evidence concerning which language training format (PC/G, PP/G, OR/G) is the most effective, however, it provides evidence that when the training is performed via paper and pencil or orally, it is more probable for the participants to show improvement in many more cognitive abilities than computer-based training improvements could offer. As our study showcased, the paper and pencil version was more effective regarding the transfer of the cognitive benefit to ADL. This is likely due to the fact that older people do not consider computers as part of their lives. Although the computer-based cognitive training in MCI is usual nowadays and its effectiveness is well established, more studies are necessary in order to investigate the effectiveness of this means of training in comparison to the traditional one. Despite the fact that the use of computer-based cognitive training is a low-cost solution and is recommended for people who do not have access to day care centers, the paper and pencil tasks and the personal interaction between the psychologist and the participant seem to play an important role for the program's effectiveness.

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