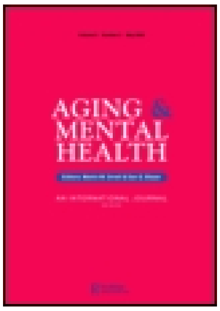

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The effects of a computer-based cognitive and physical training program in a healthy and mildly cognitive impaired aging sample

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The effects of a computer-based cognitive and physical training program in a healthy and mildly cognitive impaired aging sample

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Objectives: The Long Lasting Memories (LLM) program concerns a newly integrated platform which combines cognitive exercises with physical activity within the context of advanced technologies. The main objective of this study was to present the preliminary results that determine the possible effectiveness of the LLM program in the improvement of cognitive functions and symptoms of depression in healthy elderly and subjects with mild cognitive impairment (MCI).
Method: Fifty healthy and MCI subjects participated in the study. All of them received one hour's physical training and 35 minutes' cognitive training, 3 times a week, during the 12 weeks of the program. Before and after the intervention all participants were assessed using a battery of neuropsychological tests.
Results: The results showed a significant improvement after the LLM training in global cognitive function, in verbal memory, in attention, in episodic memory and symptoms of depression.
Conclusion: This study indicates that LLM is a promising solution for older adults with and without cognitive impairment, maintaining their wellbeing with few professional and technical requirements.

Keywords: Alzheimer's disease; mild dementia; mild cognitive impairment; cognitive stimulation; physical activity

Introduction

The potential impact of cognitive and physical training in older adults has been a topic of increasing interest. Aerobic and cognitive activity appears to moderate the decline of cognitive function associated to older adults with and without cognitive impairment (Netz, Dwolatzky, Zinker, Argov, & Agmon, 2011). Under the study of the factors that underlie the effects of physical activity on the brain, several mechanisms have been identified (Greenwood & Parasuraman, 2010). (1) Neurogenesism: research has shown that physical exercise increases proliferation and survival of new neurons in the dentate gyrus of the hippocampus of adults (Chae et al., 2012; Dery et al., 2013; Speisman, Kumar, Rani, Foster, & Ormerod, 2013). (2) Synaptic plasticity: exercise alters the length and complexity of dendrites and of the density of the spines found on dendrites. These exercise-induced dendritic changes can improve the efficiency of communication between neurons and the functioning brain areas of healthy individuals and subjects with neuropathologies (Eadie, Redila, & Christie, 2005). (3) Neurotrophins and cerebral blood flow: physical exercise is associated with higher cerebral blood flow (Pereira et al., 2007), as well as with the release of brain-derived neurotrophic factor (BDNF) (Coelho et al., 2013) and insulin growth factor (IGF-1), both of which are assumed to be involved in synaptogenesis, angiogenesis, and neurogenesis (Lista & Sorrentino, 2010).

Cognitive training is the most frequently reported form of cognition focus intervention. It involves sessions with practice on tasks targeting aspects of cognition, such as attention, memory and language (Martin, Clare, Altgassen, Cameron, & Zehnder, 2011). The effects of cognitive training on the brain have been studied in two directions: by synaptic plasticity and compensatory plasticity. The neuronal process of synaptic plasticity is assumed to occur in response to learning, daily experience or consistent use of certain functions. In this change, the source or cause of change is introduced externally to the brain, in the form of stimuli to the neural system (Kim & Kim, 2013). Compensatory plasticity addresses the brain's capability for adaptation with remaining resources. In cases of brain damage or neural degeneration, the brain actively changes internally, to adapt and reorganize cortical maps, or alter its structure and functions (Stern, 2006).

Many studies have used traditional methods to train cognitive functions in healthy elderly (Ball et al., 2002; Buiza et al., 2008; Craik et al., 2007; Tsai, Yang, Lan, & Chen, 2008) and subjects with mild cognitive impairment (MCI) (Belleville et al., 2006; Greenaway, Hanna, Lepore, & Smith, 2008; Hampstead, Sathian, Moore, Nalisnick, & Stringer, 2008; Wenisch et al., 2007). In addition, there has been a growing number of longitudinal cohort studies that have suggested that individuals who take part in a greater number of physical activities are at lower risk

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of developing cognitive impairment and dementia (Barnes, Yaffe, Satariano, & Tager, 2003; Geda et al., 2010; Larson et al., 2006). Randomized control trials also show significant evidence of the possible influence of exercise in the improvement of cognitive functions in MCI and age-related cognitive decline (Brown, Liu-Ambrose, Tate, & Lord, 2009; Geda et al., 2010; Lautenschlager et al., 2008; Liu-Ambrose et al., 2010; Scherder et al., 2005; Williamson et al., 2009).

Although these studies provide encouraging findings, traditional interventions may not always be accessible on a large scale for the older population (Faucounau, Wu, Boulay, De Rotrou, & Rigaud, 2010). Therefore, the development of technological applications for the intervention of older adults is increasing (Caprani, Greaney, & Porter, 2006; González Palau et al., 2012). For instance, there is an increasing number of studies that involve computer-based cognitive training programs (Barnes et al., 2009; Cipriani, Bianchetti, & Trabucchi, 2006; Gunther, Schafer, Holzner, & Kemmler, 2003; Rozzini et al., 2007; Smith et al., 2009; Talassi et al., 2007) and that have created a wide range of new possibilities for treatment.

The effects of cognitive and physical training have typically been investigated by separate research groups. However, findings suggest that interventions targeting multiple domains may be more effective than those that treat each domain independently (Schneider & Yvon, 2013). The Long Lasting Memories (LLM) European project comprises the validation of an integrated technology platform that combines cognitive exercises with physical activity. This unprecedented approach to simultaneous cognitive and physical stimulation aims to deliver an effective solution to reduce cognitive decline in healthy aging, MCI or mild dementia. The main objective of this study is to analyze the preliminary results that determine the possible effectiveness of the LLM cognitive and physical training program in the improvement of cognitive functions and symptoms of depression in a healthy and MCI Spanish population.

The hypothesis of this study was that both healthy and MCI participants would benefit from the intervention. Thus, performance on the primary outcome measures that were targeted by the training was expected to increase when comparing pre- to post-intervention scores. It was predicted that the magnitude of the intervention effect would be similar across the two groups. Finally, it was hypothesized that personal factors such as age or education would influence the efficacy of the training.

Method

Participants

Fifty elderly people recruited from two community centers participated in the study. The centers were located in the city of Zamora, in Spain. Eleven participants had a diagnosis of MCI and 39 were healthy elderly people. In each case MCI was diagnosed using Petersen's criteria (Petersen et al., 1999). Information for these diagnoses was obtained in structured interviews with participants and with members of the family on demographic variables, on personal and family medical history. Participants also received a battery of cognitive tests that included the Montreal Cognitive Assessment test (MoCA) (Nasreddine et al., 2005), the Clock Drawing Test (Cacho, Garcia-Garcia, Arcaya, Vicente, & Lantada, 1999), the Rey Auditory Verbal Learning Test (RAVL) (Rey, 1964), the Instrumental Activities of Daily Living Scale (IADL) (Lawton & Brody, 1969) and the Trail Making Test (TMT A and B) (Parkington & Leiter, 1947).

Participants with MCI were included in the study if they showed a memory deficit (amnestic single domain MCI subtype) or if they showed deficits of memory in addition to other domains (amnestic multiple domain MCI subtype). Participants with amnestic single domain MCI showed impaired performance on the memory tasks only (more than 1.5 SD below age/education norms), whereas patients with amnestic multiple domain MCI showed impairment on the memory task (more than 1.5 SD below age/education norms), as well as on any of the other cognitive tasks mentioned above (defined as performance that is more than 1.5 SD below norms). We excluded patients with AD on the basis of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria, as well as patients with other forms of dementia.

All current subjects who were ≥60 years old, fluent in Spanish and not currently enrolled in another research study, were invited to participate. Older adults with severe depression or other relevant psychiatric or neurological diagnosis, unstable medication or severe irreversible vision/hearing problems that made it impossible to keep up with all the components of the LLM service, were excluded from the study. Figure 1 shows the recruitment process.

Participants were briefed on the goals and procedure of this study. An informed consent form was distributed, with general information, which was mandatory to sign before proceeding with the program.

Materials

After the first interview each subject was asked to return for a brief second day of testing, where they received a battery of cognitive measures that included the following.

(1) The Mini Examen Cognitivo (MEC 35) (Lobo, Esquerra, Gomez Burgada, Sala, & Seva, 1979): The MEC 35 is the Spanish version of the Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975). The test consists of a series of questions and tests, each of which scores points if answered correctly. If every answer is correct, a maximum score of 35 points is possible. The MEC 35 tests a number of different mental abilities, including a person's memory, attention and language.
(2) The Digit Span Test of the Wechsler Memory Scale III (WMS III) (Wechsler, 2004): The Digit Span Test is a measure of attention and working memory. During the test a sequence of numbers is

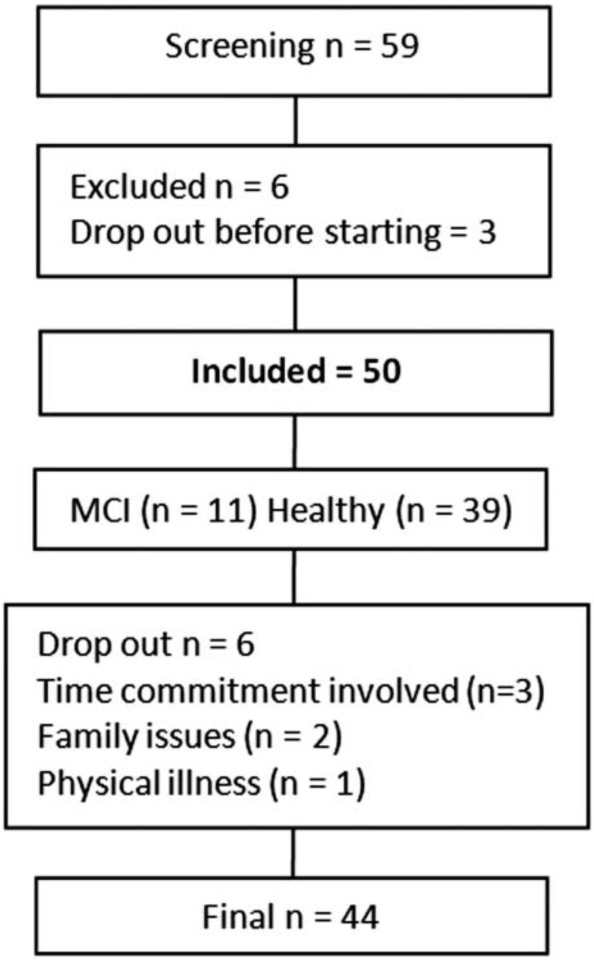

Figure 1. Recruitment process and number of participants involved in the study.

read out to the participant. The participant is then asked to repeat the numbers that were read. The length of the digit sequence is increased across trials until there is a failure across two consecutive trials of a particular length. In the reverse trial of the Digit Span the experimenter reads a series of numbers and the participant is asked to repeat the sequence in reverse order. This sequence is also continued until the participant fails twice in a particular length trial. The Digit Span test is scored by the amount of numbers the person was able to remember in each test.

(3) Logical Memory subtests of the WMS III (Wechsler, 2004): In the WMS-III Logical Memory subtest, story A is read once to the examinee, who then orally provides any information recalled. Story B is read twice to the participant, with any recalled information provided after each reading. The examiner records the number of free recall units and thematic units, which represent more general information, that are provided by the examinee. In the original test, following 30 minutes of other testing, the participant is asked to provide any information recalled from Story A and then Story B. The recall and thematic unit scores are again recorded. Fifteen yes/no recognition memory questions are then asked about each story and the recognition memory scores are recorded. In our sample, only immediate trials of story A and B were administered. We used only immediate trials since the Hopkins Verbal Learning Test – Revised (HVLT-R) was also added to the battery and assesses delay recall.

(4) The Color Trail Test 1 and 2 (CTT 1 and 2) (D'Elia, Satz, Uchiyama, & White, 1996): The CTT is similar to the TMT but was developed to be free from the influence of language and cultural bias. It assesses sustained attention and executive functions in adults. In the test, numbered circles are printed with pink or yellow backgrounds. For Part 1, the respondent uses a pencil to rapidly connect circles numbered 1–25 in sequence. For Part 2, the respondent rapidly connects numbered circles in sequence, but alternates between pink and yellow. The length of time to complete each trial is recorded, along with qualitative features of performance.

(5) The Hopkins Verbal Learning Test Revised (HVLT-R) (Brandt & Benedict, 2001): The HVLT-R measures memory in addition to the rate of verbal learning over three successive learning and recall trials. A 12-item list of words is presented orally at a rate of one word every 2 seconds, and the participant recalls as many words as possible in any order immediately after the presentation. Each list consists of three semantic categories with four words in each category. Three successive presentations and recall tests are administered. After the third learning trial, the participant is instructed to remember the words. After a 20-minute delay, the participant again recalls the words in any order. The delay free recall is followed by a 24-word recognition trial. Twelve are the target list words, six are the categorically related non-target words and six are the unrelated non-target words. The HVLT-R has a number of alternate forms. Form 1 of the HVLT-R was used for the pre-test procedure and form 4 was used for the post-test procedure.

(6) The Geriatric Depression Scale (GDS) (Yesavage et al., 1982): The GDS scale is a basic screening measure for depression in older adults. The 15-item version is most widely used with self report or informant report, and takes 5/10 minutes to complete. Of the 15 items, 10 indicated the presence of depression when answered positively, while the rest indicated depression when answered negatively.

This same battery was repeated during the post-test procedure. Before beginning the training participants were also asked to provide information about the frequency of the physical and cognitive activities they performed per week. These questions included the number of days that they did sports or other exercise, the frequency of cognitive activities that they performed, such as reading, and if they knew how to use and frequently used a PC.

The pre-test was conducted between 1 and 2 weeks prior to the intervention, while the post-test was conducted between 1 and 2 weeks following the end of the intervention. For each time-point, measures were taken in one testing session that lasted approximately 60 minutes. The examiners who conducted the testing in the pre- and post-intervention were different from the instructors who administered the program and from those who had made the diagnoses. The examiners were unaware of the participants' cognitive status.

Procedure

All assessments and treatments were conducted at the community centers where participants usually went. LLM's Spanish prototype was based on the integration of the LLM cognitive training component (CTC) and the physical training component (PTC) which perform complementary and interactive tasks to provide the system's services.

Cognitive training component (CTC)

The CTC was designed to support the cognitive training procedure provided by the Gradior software (Franco, Orihuela, Bueno, & Cid, 2000). Gradior is a neuropsychological assessment system and a multi-domain cognitive training program including attention, perception, episodic memory and working memory tasks. Principles of feedback and difficulty adaptation are used to enhance plasticity and motivation. In response to correct and erroneous responses, verbal-auditory feedback is given. Adaptation of task difficulty is provided by initially setting the difficulty level according to pre-test performance. Afterwards, the task difficulty can be adjusted by the professional according to each patient's individual performance. User-friendliness is given by using a touch screen display. All participants received 40 minutes of cognitive training, three times a week, during the 12-week program. The training included exercises of perception (six trials), attention (seven trials), episodic memory (four trials) and working memory (two trials).

Physical training component (PTC)

All physical exercises were implemented in the FitForAll (FFA) platform (Bamidis et al., 2011). FFA is a game platform that can help elderly people to keep fit and maintain their wellbeing through an innovative, low-cost ICT platform, such as Wii Balance Board. Participants start on the light intensity level with a target heart rate (HR) of 50%–60% of maximum heart rate (HR_{max}) and can proceed to the very hard level with a target HR of 80%–90% of HR_{max} within the training period. The program has four levels of difficulty which are assigned to the subject according to their physical possibilities. In consultation with a therapist, participants decide every two weeks either to proceed to the next level of intensity or to remain at the present level of intensity. The design of one training session involves the following modules: (1) a warm-up period (5–10 minutes), through aerobic exercises like hiking or cycling; (2) the main component (30–35 minutes) through exercises of endurance, strength and balance; (3) a cool down period (5 minutes) that includes stretching and cool-down training exercises to recover normal cardiac levels. All participants performed one-hour session of FFA, three times a week, during the 12-week program.

The cognitive sessions and the physical sessions were conducted on the same day. Participants performed the cognitive training first and the sessions of physical training afterwards. In order to ensure a minimal consistency of the LLM application, the upper and lower limits of sessions were established for each component. Participants whose data did not remain within the lower limit were considered dropouts.

The suggested schedule was created taking into consideration the results of previous research (Heyn, Johnson, & Kramer, 2008). The upper and lower limits established were 32–40 weeks, with a frequency of 2–4 sessions per week. The intensity established for the physical exercise sessions was of 40–80 minutes per session and that of the cognitive training sessions was of 30–50 minutes.

It is important to mention that, even though the study lasted 12 weeks, the trial sites and the participants have the opportunity, after the post-test, to continue with the training. Actually, both trial sites continued providing the program to the participants and also offered the LLM to other users of the community that were interested in it.

Statistical analyses

Descriptive statistics (mean and standard deviation) were calculated for all screening/baseline outcome measures. Mixed Analyses of Variance (ANOVA) were performed on the scores of the primary outcome measures, with the Diagnosis (healthy – MCI) as between subject factor and Time (pre-test–post-test) as the repeated factor. Bivariate associations were performed between socio-demographic characteristics, frequency of cognitive and psychical exercise performed before the beginning of the LLM training and cognitive measures for the complete sample. Multivariate linear regression analysis was performed in order to evaluate which factors might account for the results of the training program. Socio-demographic variables at baseline that significantly correlated with the scores obtained by participants on the main outcome measures at the end of training were included in this analysis.

All statistical analyses were performed with the Statistical Package for Social Sciences (SPSS) version 18.0

Results

Demographic characteristics of the sample

Socio-demographic characteristics for participants of the entire sample and split by type of group are given in Table 1. The sample was Spanish with a mean education of 9.14 (±3.25). The overall sample had more females (80.5%) and had a mean age of 73.43 (±7.51) years. Half

Table 1. Demographic characteristics of the sample.

	All (n = 50)	Healthy (n = 39)	MCI (n = 11)
Age (M, SD)	73.43 ± 7.51	72.29 ± 7.09	74.60 ± 8.62
Education (M, SD)	9.14 ± 3.25	9,64 ± 3.30	8.41 ± 3.12
Gender% female	80.5	80.0	80.0
Gender% male	19.5	20.0	20.0
Marital status			
Single%	18.1	13.4	21.6
Married%	29.7	36.9	23.5
Divorced%	2.3	2.0	2.9
Widow%	50.0	47.7	52.0
Country residence/nationality% Spain/Spanish	100	100	100

(50.0%) of the sample had been widowed, 29.7% were married and 18.1% were single.

The mean number of sessions attended by participants was 32.9 (±3.10). Forty-four subjects successfully completed the study while 6 (12.0%) elderly people dropped out. Subjects who dropped out did not differ from those who completed the study in terms of age, sex, education, symptoms of depression or cognitive function scores ($p < .01$). The primary reasons for dropping-out included the time commitment involved ($n = 3$), family issues ($n = 2$) or physical illness ($n = 1$) not induced by the program.

Outcome measures

Table 2 reports the means and standard deviations for each test according to the different clinical groups. The ANOVA analyses showed a significant main effect of Time on MEC 35 scores ($F(1,48) = 4.465$; $p = .04$; $\eta\rho^2 = .085$). The Diagnosis by Time interaction did not reach significance ($F(1,48) = 0.015$; $p = .902$). Thus, the intervention improved global cognitive function in both MCI and healthy participants.

In memory tests, the analysis evidenced a significant main effect of time on the HVLT-R recognition subtest ($F(1,46) = 8.21$; $p = .006$; $\eta\rho^2 = .152$), delay recall ($F(1,46) = 24{,}35$; $p < .0001$; $\eta\rho^2 = .346$) and free recall subtests ($F(1,46) = 80.98$; $p = .004$; $\eta\rho^2 = .163$). A significant main effect of Time was also found on the WMS III, subtest of logical memory ($F(1,46) = 5.083$; $p = .02$; $\eta\rho^2 = .100$ and $F(1,46) = 14.1$; $p < .0001$; $\eta\rho^2 = .235$). The Diagnoses by Time interaction did not reach significance. Thus, the intervention improved verbal and episodic memory in both MCI and healthy participants.

In attention, the analysis revealed a significant main effect of Time (pre-test–post-test) on CTT1 scores ($p = .04$). The Diagnosis by Time interaction did reach significance indicating that the intervention improved processing speed only in healthy participants ($F(1,46) = 6.06$; $p = .013$; $\eta\rho^2 = .126$).

Finally, a significant main effect of Time was found on the GDS ($F(1,48) = 16.1$; $p < .0001$; $\eta\rho^2 = .262$). The Diagnosis by Time interaction did not reach significance. Thus, the intervention decreases symptoms of depression in both MCI and healthy participants.

Correlation of variables

Bivariate analyses showed that the years of education, the age and the frequency of physical and cognitive activities correlated with most of the cognitive measures ($p < .001$). Age had the strongest negative correlation with global cognitive function (MEC 35: $r = -.350$; $p < .001$),

Table 2. Means and standard deviations obtained at pre-test and post-test in healthy aging and MCI.

	Group							
	Healthy				MCI			
	Pre-*t*-test		Post-test		Pre-*t*-test		Post-test	
Test	Mean	SD	Mean	SD	Mean	SD	Mean	SD
MEC 35	30.91	3.05	31.84	2.50	29.61	3.534	30.44	3.823
HVLT-R Recognition	10.19	1.19	10.61	1.45	10.06	2.53	11.22	0.943
HVLT-R Free Recall	18.00	5.69	19.32	5.02	14.50	4.85	18.33	6.61
HVLT-R delay recall	4.71	2.88	6.32	2.77	3.00	3.23	6.00	2.97
CTT1 (time in seconds)	85.48	32.17	78.78	56.60	87.71	35.01	99.61	52.17
CTT 2 (time in seconds)	161.61	65.01	147.44	77.79	185.41	67.39	196.17	95.65
WMS III digit span forward	6.84	1.37	7.47	1.64	6.17	1.33	5.78	1.39
WMS III digit span backward	4.59	2.40	4.09	1.46	3.50	1.38	3.50	.98
WMS III logical memory/units recalled	26.63	10.40	29.06	10.06	20.50	10.38	22.78	12.69
WMS III logical memory/ thematic units recalled	10.97	4.50	13.03	3.56	7.89	4.17	11.28	4.62
GDS 15	5.44	5.02	2.50	2.55	5.00	3.85	2.39	2.09

verbal memory (HVLT-R total recall: $r = -.397$; $p < .001$; delay recall: $r = -.387$; $p < .001$) and episodic memory tests (WMS: $r = -.408$; $p < .001$) indicating that an increase in age is associated with a decrease in the cognitive performance of the participants. Age also had a positive correlation with CTT 1 ($r = .535$; $p < .001$) and CTT 2 ($r = .503$; $p < .001$). In this test, higher values are related to poorer performance. The multiple linear regression analysis evidenced that the best model was accounting for 48.8% of the explained variance (beta standardized coefficient) and included two variables: age and the frequency of cognitive activities performed by the participants before the beginning of the program. Years of education and frequency of physical activity performed before the beginning of the LLM program did not significantly improve the model despite the fact that they correlated significantly with the predicted variables.

Discussion

The LLM program involves an integrated technology platform which combines cognitive exercises with physical activity. LLM intends to respond to the need for research in effective solutions for the prevention and the treatment of cognitive decline in a European population. Moreover, the project considers the difficulty health care systems have in dealing with the increasing demands resulting from the progressive ageing of our societies (Moniz-Cook, Vernooij-Dassen, Woods, & Orrell, 2011).

In this context, intervention programs based on new technological systems play a key role. The validation of these solutions would enable the prevention and the treatment of cognitive decline while reducing the costs of time, personnel and resources required by the elderly population (Faucounau et al., 2010; Franco et al., 2000; Gonzalez Palau et al., 2013).

Previous studies conducted on older adults have pointed to the beneficial effects of aerobic activity and cognitive training on brain function (Erickson & Kramer, 2009; Foster, Rosenblatt, & Kuljis, 2011; González Palau et al., 2012). Consistent with these, the preliminary results of the LLM study showed an improvement after the training in global cognitive function and verbal memory, which involved recognition, free recall and delay recall, in attention, in episodic memory and in symptoms of depression. In accordance with our hypothesis, this suggests that brain plasticity might be present in older adults and that cognitive decline may be reversible in healthy aging and MCI populations.

Brain plasticity is a multifaceted concept that involves the ability to change neurons and networks in response to experience (Greenwood & Parasuraman, 2010). The preliminary results of our study demonstrate, as expressed above, the potential of older adults to improve performance after the training (Jones et al., 2006). However, this improvement was also influenced by the age and the cognitive activity that the participants performed before the beginning of the study. Although older adults benefit from the training, younger adults benefit even more from it. This apparent age-related reduction in cognitive plasticity is consistent with our hypothesis and with other studies where young-old exhibited greater training-related gains than old–old (Singer, Lindenberger, & Baltes, 2003).

In addition, the impact of the LLM on community MCI participants is of extreme importance. Subjects with an MCI usually present impairment in explicit long-term memory (Petersen & Negash, 2008), and in episodic and semantic memory tasks (Cuetos, Rodriguez-Ferreiro, & Menendez, 2009; Perri, Carlesimo, Serra, & Caltagirone, 2009). However, verbal memory and episodic memory were the functions that showed the greatest improvements after the LLM treatment in MCI participants. These results suggest that cognitive plasticity could be preserved in this population (Clare et al., 2009; Fernández-Ballesteros, Zamarrón, Tárraga, Moya, & Iñiguez, 2003) and that the LLM program is effective in improving functions that are frequently impaired in MCI.

It should be mentioned that in this study the effective sizes provided evidence of small to modest improvements in cognitive functions. In elderly populations, previous meta analyses that studied the influence of physical activity on cognition also reported small (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008; Etnier, Nowell, Landers, & Sibley, 2006) to moderate (Colcombe & Kramer, 2003; Heyn, Abreu, & Ottenbacher, 2004) effects sizes when compared to other disciplines and other groups of subjects. In agreement with recent studies with active control conditions that analyzed the effects of cognitive and physical training (Theill, Schumacher, Adelsberger, Martin, & Jancke, 2013), and found similar effects sizes, these effects could be the result of the rather short duration of intensity of the training programs. To provide a stronger effect, it may be necessary to lengthen the training sessions or at least to increase the frequency of the sessions.

Moreover, we agreed that when valuing the magnitude of an intervention, the costs and benefits that are associated with it should be considered. An increase in cognitive functions with a small or modest effect size can be very important in this clinical group, provided that the intervention does not involve a high cost (i.e. financially speaking or with regard to personnel time and effort), and provided that the program can be applied at a large scale and, even more so, if the effect produced by the intervention increases over time.

Finally, previous studies have found that computer-based cognitive training could be effective in reducing symptoms of depression (Rozzini et al., 2007; Talassi et al., 2007). We obtained similar results when analyzing the community population. Our group evidenced a significant reduction in symptoms of depression in healthy and MCI participants after the LLM program.

There are a few limitations in this study that should be considered for future research. In the first place, most of the subjects performed the same number of training sessions, and therefore it was not possible to determine the optimal amount of LLM training for each group of subjects and whether the results vary with treatment of a greater (or lesser) duration or intensity (e.g., weekly sessions).

Second, most of the participants performed the physical training as well as the cognitive training. Future studies could analyze the impact of each one of these programs on cognitive functions and their difference with regard to the integral LLM solution. Third, although the design was planned to analyze an experimental group and a control group, the characteristics of the sample made it impossible to compare the results of community population with a control group. Future lines of analysis could include this variable, and corroborate the important results found in this population.

More research is needed to determine the long-term effects of combined cognitive and physical training. Given the theoretical reflections of training effects on neural activity and changes, it would be of great importance to investigate neuronal changes associated with combined cognitive and physical training. Only this way can the potential for cognitive plasticity be completely examined.

To conclude, the preliminary results of the LLM study are promising. This research is important when considering that we have so far been unable to find other studies on a Spanish population that assess the impact of physical and cognitive training along with new software technologies. The present research generates new knowledge that could help to create effective strategies for cognitive intervention and to reduce the risks of cognitive decline and the development of degenerative diseases.

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