Effectiveness of personalized cognitive stimulation in older adults with mild possible cognitive impairment: a 12-month follow-up

Cognitive stimulation in mild cognitive impairment

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ABSTRACT

Objective: The objective of this study was to analyze the long-term effects of a personalized cognitive stimulation (PCS) program in the global cognition, cognitive aspects, activities of daily living (ADLs), anxiety and depression in older adults with possible mild cognitive impairment (MCI). **Methods:** A 12-month follow-up analysis was carried out in a single-blind, randomized clinical trial to research the long-term effects of a 10-week PCS program evaluating the cognitive level, depression, and anxiety of older adults with possible MCI. **Results:** Fifty older adults were assessed 12 months after the CS program; 23 in the intervention group and 27 in the control group. There were significant differences between the groups at 12 months in the global cognition ($p = 0.002$), in global orientation ($p < 0.001$) and in spatial orientation ($p = 0.004$) in favor of the intervention group, measured with the Spanish version of the Mini-Mental Status Examination (MEC-35). **Conclusions:** A PCS program could be effective in improving global cognition, global and spatial orientation. **Clinical implications:** A PCS program based on cognitive levels in older adults with possible MCI achieves improvements in global cognition and global and spatial orientation. PCS programs can be applied successfully by trained occupational therapists.

KEYWORDS: Mild cognitive impairment; cognitive dysfunction; older adults; aging; cognitive stimulation; neuropsychological tests.

Funding details

The authors declared they have not received funds to carry out this study or its publication.

Disclosure statement

The authors report no conflicts of interest in this work.

Introduction

The aging population is a global phenomenon, with 703 million people aged ≥ 65 years in the world in 2019 and a forecast that this figure will double, reaching 1,500 million in 2050 (United Nations, 2019). Cognitive dysfunction is one of the problems associated with aging and constitutes a public health challenge, since the direct cost of care for individuals with mild cognitive impairment (MCI) in primary care is 16% higher than for subjects with normal cognition (Zhu et al., 2013).

MCI is on a continuum between normal cognition and dementia (Sanford, 2017) and is considered as a syndrome that presents a cognitive alteration, but does not interfere with normal functionality (Mora-Simon et al., 2012). It is estimated that MCI has a prevalence between 15–20% in people older than 60 years of age (Petersen, 2016) and that there is an association between persons with MCI and the possibility to suffer concomitant depression or anxiety disorders (Mirza et al., 2017).

Although many researchers have suggested and utilized a variety of criteria for defining cognitive impairment in clinical populations such as Alzheimer disease (AD) (Petersen et al., 1999) and Parkinson disease (PD) (Aarsland et al., 2017), some others have also considered MCI as a preclinical stage of AD. Moreover, the concept of MCI is also widely used in non-clinical populations (i.e., nondemented person) to classify persons who do not fulfill a diagnosis of dementia, but who have a high risk of progressing to a dementia disorder (Winblad et al., 2004), as it is known that the annual rate of conversion to dementia (Marcos et al., 2016) and AD (Petersen, 2016) is 15% and 10%, respectively.

In the scientific literature, different non-pharmacological cognitive interventions has shown to be effective: 1) cognitive training (CT), which is based on cognitive exercises aiming to provide a set of standardized tasks; 2) cognitive rehabilitation (CR), which

consists of individualized interventions based on the assessment and understanding of the patient's cognitive behavioral deficits and 3) cognitive stimulation (CS), which is performed through group activities designed to increase cognitive and social functioning (Clare et al., 2003). Moreover, the current scientific evidence indicates that lifestyle modifications such as physical exercise and the performance of non-pharmacological cognitive interventions are effective in improving the cognition of patients with MCI (Kurz et al., 2011; Reijnders et al., 2013; Sherman et al., 2017; Wang et al., 2020). Besides, this meta-analysis also found that CS was the most effective of six non-pharmacological therapies analyzed and concluded that it had the highest probability of being the optimal non-pharmacological therapy (Wang et al., 2020). Other meta-analysis concluded that CS is effective for improving cognition and quality of life (Kim et al., 2017; Lobbia et al., 2018) in people with dementia.

CS may benefit from tailoring and personalization, as a mode of achieving person-centered care (Félix et al., 2020). Moreover, CS is recognized as a cost-effective intervention, with benefits in cognitive function (Alvares Pereira et al., 2020). However, the existing evidence on the effectiveness in randomized controlled trials (RCT) of CS in older adults with MCI is still limited to its short-term effects in the global cognition (Alves et al., 2014; Gomez-Soria et al., 2020; Polito et al., 2015), executive functions (Djabelkhir et al., 2017; Djabelkhir-Jemmi et al., 2018), memory, processing speed, attention, visuospatial processing, phonemic fluency, categorical fluency (Djabelkhir-Jemmi et al., 2018), basic activities of daily living (BADLs) (Gomez-Soria et al., 2020), instrumental activities of daily living (IADLs) (Alves et al., 2014), ~~a~~nd in self-esteem (Djabelkhir et al., 2017). Therefore, the objective of this study was to analyze the long-term effects (12 months) of a personalized CS intervention in the global cognition, the

cognitive aspects, the BADLs, the IADLs, and in the levels of anxiety and depression in an aging population with MCI.

Methods

Ethical considerations

A 12-month follow-up analysis was carried out in a single-blind, RCT (Gomez-Soria et al., 2020) to research the long-term effects of a personalized CS intervention in older adults with possible MCI. The RCT was approved by the Ethical Committee for Clinical Studies of Aragon (CEICA) with the study registration number PI11/00091. The study followed the Declaration of Helsinki of the World Medical Association Ethical Principles for Human Medical Research 2013 (World Medical Association, 2013). The manuscript followed the recommendation CONSORT 2010 guidelines (Schulz et al., 2010).

Participants

Each participant was informed of the study objectives and signed an informed consent before being enrolled in the study. The inclusion criteria were: 1) aged ≥ 65 years, and 2) diagnosis of possible MCI, defined as 24–27 points by the Spanish version of the Mini-Mental Status Examination (MEC-35), depending on the participant´s educational level (i.e., 24 points for people with low educational levels to 27 points for those with higher educational levels) (Calero-García et al., 2006; Lobo & Dia, 1986; Lobo et al., 1999). Exclusion criteria were: 1) institutionalization, 2) receiving CS in the last year, 3) having less than 60 points on the Barthel Index (BI), 4) deafness, 5) blindness, 6) neuropsychiatric disorders, and 7) motor difficulties (Gomez-Soria et al., 2020).

All the participants were informed about the nature of the study, objectives, and voluntary participation, and that they can depart the study when they want without giving any explanations.

Treatment allocation

Participants were randomized into two groups: the intervention group (IG) and the control group (CG). A stratified randomization was carried out based on the scores obtained from the MEC-35. A therapist independent of the study carried out the randomization.

Study procedure

The study was conducted during primary care consultations at the San José Norte-Centro de Zaragoza Health Center (Spain). For this 12-month follow-up, only the participants who completed the intervention and the medium-term follow-up (6 months) were selected. The occupational therapists (L.R. and G.S.) who performed the 12-month follow-up evaluation were blinded and different from the occupational therapists who performed the intervention.

The intervention was performed using pencil and paper method, accompanied by the red notebook of mental activation (Arilla et al., 2012). The IG received 10 group sessions of 45 min/week, using a personalized CS program based on each participant´s cognitive level. The intervention was personalized, adapting the stimulating activities to the life history, personal preferences, limitations, and potentialities of the patient (Félix et al., 2020). The cognitive stimulation sessions were based on a previous interview that collected information related to the participant´s hobbies, likes, everyday occupation, everyday limitation, previous profession/occupation, life history and neuro-psychological assessment. The proposed activities focused on the patient´s main concerns, his likes, and preferred hobbies (i.e planning a travel they would like to do, providing as many details as possible).The intervention was performed in each subgroup by two trained occupational therapists (I.O. and A.P.) Each session included four parts: (a) reality orientation, (b) explanation of the cognitive aspect that was going to work in each session,

(c) individual practical work, in which four exercises of the cognitive aspect corresponding to each session were performed, and (d) group correction of the practical exercises. The CG did not receive any intervention apart from the periodic standard stimulation, regardless of previous cognitive levels (non-personalized program) that they usually received (Gomez-Soria et al., 2020).

Outcome measures

The main variable was the MEC-35 (Lobo et al., 1999). The secondary variables were the Set-test, Barthel Index (BI), Lawton and Brody scale (L-B), Goldberg anxiety sub-scale and Yesavage geriatric depression scale, and 15-point version (GDS-15). Assessments were always performed at the same time and place to maximally preserve participant conditions.

Spanish version of Mini-Mental Status Examination

Cognitive level was measured by the MEC-35, which is the most widely used cognitive test that has demonstrated its reliability in personalized CS for the detection of cognitive impairment (Calero-García et al., 2007; Lobo et al., 1999). This questionnaire assesses the following cognitive aspects: temporal-spatial orientation, immediate and long-term memory, attention, calculation, language, abstract reasoning, and praxis. Scores vary between 0–35, with 0 being the minimum score and 35 the maximum score (Calero-García et al., 2006). The optimal cut-off point of the MEC-35 to establish the presence of cognitive impairment in a population aged > 65 years is 24 points with a low educational level and 27 points with a medium high level (Calero-García et al., 2006; Vinyoles Bargalló et al., 2002). For the cut-off points of 24 and 27, the sensitivity and specificity of the MEC-35 have been described as 89.8 and 83.9%, respectively (Calero-García et al.,, 2006; Vinyoles Bargalló et al., 2002; Lobo et al., 1979).

Set-test

Verbal fluency was measured by the Set-test in four categories: colors, animals, fruits, and cities. Scores vary between 0–40, with 0 being the minimum score and 40 the maximum score. This test has been proposed as a diagnostic aid in elderly patients with dementia, with a cut-off of 27 points for the elderly, with a lower score indicating dementia. This test has a documented sensitivity of 79% and specificity of 82% (Pascual Millán et al., 1990).

Barthel Index

The independence in ten BADLs was evaluated with the BI. The maximum score is 100 points and scores ≥ 60 indicate mild dependence. This test's sensitivity ranges between 76% (in the item "ambulation + stairs") and 99.8% (in the item "feeding") and its specificity between 46% (in the item "defecation") and 97% (in the item "ambulation + stairs") in scores ≥ 90 points for fragility screening (Bernabeu-Wittel et al., 2019).

Lawton and Brody scale

The autonomy in eight IADLs necessary to live independently was assessed with the L-B. Scores range from 0 (dependent) to 8 (independent). This scale's sensitivity is 57% and specificity, 82%, when an informant observes dependence in three activities (Pfeffer et al., 1982).

Goldberg anxiety sub-scale

Anxiety was measured by the Goldberg anxiety sub-scale, which is a subscale of the Goldberg questionnaire, with nine dichotomic response items (yes/no responses). An independent score is awarded for each scale, with one point for an affirmative answer.

The cut-off value is ≥ 4 for the anxiety subscale, which indicates “probable anxiety”. This scale has a specificity of 91% and sensitivity of 86% (Goldberg et al., 1988).

Yesavage geriatric depression scale, 15-point version

Level of depression was evaluated with the GDS-15 and is considered suitable for seniors in the community. Scores vary between 0–15, with a total score > 5 interpreted as “probable depression”. In older people, for a cut-off of 5 points, sensitivity is 71.8% and specificity is 78.2% (Marc et al., 2008).

Statistical analysis

For the statistical analysis, the program R Version 3.5.1 (R Core Team, 2020) was used. Robust ANOVA statistics were calculated using the MANOVA.RM r package (Friedrich et al., 2018). The level of significance was established at $p < 0.01$. The final power of the study was calculated by applying a repeated measures ANOVA with a mixed design (within-between subjects) on the final scores on the MEC-35 scale accepting a risk $\alpha < 0.05$ and a minimum power of 80%. Considering that the follow-up analysis at 12 months included 50 participants, the resulting power was of 0.936 (ES = 0.049).

The Shapiro-Wilk test was used to determine the non-normal distribution of the quantitative variables. The qualitative variables were described in absolute values and relative frequencies and the quantitative variables with mean and standard deviation.

The presence of significant baseline differences between both groups was tested using Fisher's exact test for qualitative variables or Student's t test for independent samples in the case of age.

Quantitative outcome variables were analyzed using a robust model of repeated measures with two factors, inter (group) and intra (measurements), due to the non-normal

distribution of the variables. The omnibus test reports with its level of significance the robust ANOVA-type statistic (ATS) as well as its version obtained by bootstrapping for the group-time interaction. For post hoc tests, the Mann-Whitney U test with Bonferroni correction was applied between groups. The effect size in the quantitative variables was calculated with the η^2_p statistic obtained by bootstrapping due to the non-normal distribution of the variables, defined as small (0.01–0.06), moderate (0.06–0.14) and large (> 0.14).

The presence of significant changes over time in the total score of the MEC-35 in each group was tested using the Friedman test with post hoc tests with Bonferroni correction. The changes in the MEC-35 dichotomized into scores greater or less than 24 were tested using the Cochran-Mantel-Haenszel test. The final effect size between both groups was tested with Cramer's V, defined as small (0.1–0.3), medium (0.3–0.5) and large (> 0.5).

Results

The baseline characteristics of the 122 recruited older adults are published elsewhere and the IG showed a significant improvement in the global cognition measured with the MEC-35 at both post-intervention and at 6-month follow-up. The BI was found to be higher in the IG, but only in the post-intervention analysis (Gomez-Soria et al., 2020). Of the 65 participants who completed the assessment at six months (28 participants from the IG and 37 from the CG), 15 did not participate in this follow-up; five from the IG (one deceased, one rejected and three not located) and 10 from the CG (two deceased, one rejected, four not located and three institutionalized). Therefore, in the 12-month follow-up, we analyzed 23 participants in the IG and 27 in the CG. There were no significant differences between groups for the clinical-demographic (Table 1) or the outcome variables at baseline. The mean age of the participants was 74.32±5.47 and 78% were women.

[Insert Table 1]

This follow-up study showed a significant group-time interaction (ATS [2,838] = 5.194; p = 0.002; ATSp-boot = 0.043) in the global cognition measured with the MEC-35, with a small significant effect size (η^2p = 0.014; 95% CI= [0.018–0.107]) in favor of the IG. The Friedman test showed significant differences in the MEC-35 scores over time in both the IG (X^2 [33.795] = 3; p < 0.001) and the CG (X^2 [10.316] = 3; p = 0.016). However, the pairwise comparisons only showed significant differences in the IG from baseline at post-treatment (p = 0.001), six-month (p < 0.001) and 12-month (p < 0.001) follow-ups whereas in the CG there were no differences from baseline (Figure 1).

[Insert Figure 1]

The Cochran-Mantel-Haenszel test also showed a significant group-time interaction on the MEC-35 scale, categorized as to having more or less than 24 points (X^2 [1] = 6.562; p = 0.01), with a greater decrease of patients with more than 24 points and an increase of those with less than 24 points in the CG at 12 months, although effect size was small and not significant (Cramer's V = 0.124 [0, 1]). (Table 2).

[Insert Table 2]

The analysis by domains also revealed a significant group-time interaction in the global orientation (ATS [2,925] = 6.731; p < 0.001; ATSp-boot = 0.002) and spatial orientation (ATS [2,963] = 4.561; p = 0.004; ATSp-boot = 0.005), with a small and significant effect size in both cases (η^2p = 0.009; 95% CI = 0.012–0.125 and η^2p = 0.008; 95% CI = 0.016–0.116, respectively), in favor of the IG. Friedman test showed significant differences in both domains in the IG (X^2[15.804] = 3, p = 0.001 and X^2[10.312] = 3, p = 0.016) but not in the CG (X^2[3.102] = 3, p = 0.376 and X^2[7.313] = 3, p = 0.063). In the IG, pairwise comparisons showed significant differences from baseline at post-treatment (p = 0.005),

six-month (p = 0.004) and 12-month (p = 0.043) follow-ups in the global orientation domain whereas only post-treatment differences appeared in the spatial orientation domain (p = 0.031). In the CG, there were no differences from baseline at any time points (Table 3).

[Insert Table 3]

Although there were differences between groups at post-treatment, at 6 months and at 12 months in the global score and the global orientation subdomain, there were no differences within or between groups in the period from the 6- and 12-months follow-up.

No significant differences were obtained in the remaining study variables.

Discussion

This 12-month follow-up study showed that a personalized CS program was effective in improving global cognition and cognitive aspects, such as global and spatial orientation, with significant differences between both groups. To the best of our knowledge, there are no RCT that have analyzed the long-term effects of a personalized CS in older people. We also analyzed the progression of participants in having a score lower to 24 according to the MEC-35, which could be considered equivalent to a preclinical neurodegenerative disease (Lobo et al., 1999). Although there were significant differences between the groups in favor of the IG, the effect size was small and not significant, so no conclusions can be extracted. Future studies should also analyze the effects of CS in the progression of dementia.

Regarding global cognition measured with the MEC-35, the personalized program achieved statistically significant long-term improvements between the groups, although with a small effect size, which implied that the long-term impact of the therapy, although significant, was not very important. However, if our results are compared with other

studies that applied CS, we found a mean improvement of 4.13 points, higher than other studies, which reported mean improvements from 1.91–2.34 points in the short-term (Calero-García et al., 2006; Gomez-Soria et al., 2020), and similar to other studies that reported mean improvements from 2.17–4.24 points in the medium-term (Carballo-García, 2013). Other type of interventions, such as CT, has also shown to have long-term effects in global cognition (Gaitán et al., 2013). Although the mechanisms underlying the observed benefits in this study remain unclear, the improvements in the IG could be due to that cognitive stimulating activities contributed to increase the cognitive reserve, which has shown to be a protective factor (Mazzeo et al., 2019). The cognitive reserve theory postulates that individuals with a greater reserve will cope with brain damage more successfully than those with low levels of reserve (Stern, 2009) and therefore a hypothesis would be that the increase of the cognitive reserve may lead to the slowdown of the deterioration process (Palo Villegas et al., 2020).

Analyzing the cognitive aspects of the MEC-35, we observed statistically significant improvements in global orientation and spatial orientation. The changes in spatial orientation could avoid disconnection from the environment (Palo Villegas et al., 2020). Other study that applied other cognitive intervention, such as CR, also showed significant differences in spatial orientation, although only in the short-term (Retureta Rodríguez et al., 2012). Although we did not find differences in other cognitive aspects, such as language and memory, other studies found differences in language with a greater number of sessions of CS (Justo-Henriques et al., 2019) and with CR (Retureta Rodríguez et al., 2012) in the short-term. Other studies performed with different type of cognitive interventions found differences in memory in the short-term (Hampstead et al., 2012) and medium-term (Hampstead et al., 2012; Kinsella et al., 2016) with CR and differences in the short-term (Hyer et al., 2016) and long-term (Gaitán et al., 2013) with CT.

Regarding verbal fluency, no statistically significant differences were found at 12 months. Other studies that analyzed the short-term effects of CS (Djabelkhir et al., 2017) or the short-term (Talassi et al., 2007) and long-term effects with other cognitive interventions (Park et al., 2019; Rozzini et al., 2007) did not find changes in verbal fluency either. This was also the case for BADLs, where no statistically significant differences were observed, similarly to other studies with other personalized CS programs that did not report improvements in the short-term (Justo-Henriques et al., 2019) and medium-term (Carballo-García et al., 2013; Gomez-Soria et al., 2020). Neither of the other studies based in other cognitive interventions observed differences with other variables in the short-term (Talassi et al., 2007) or long-term (Rozzini et al., 2007). Regarding IADLs, no statistically significant differences were found at 12 months, similarly to other studies that analyzed the effects of CS and showed not to be effective in the short-term (Gomez-Soria et al., 2020; Llanero Luque et al., 2010) and medium-term (Gomez-Soria et al., 2020), as well as studies that evaluated CT that also did not show differences in the short-term (Talassi et al., 2007). Our study did not find any long-term effects of performing a personalized CS program on anxiety and depression, similarly to other studies that found no effects when performing a CS program on anxiety in the short-term (Djabelkhir et al., 2017; Gomez-Soria et al., 2020; Llanero Luque et al., 2010) or medium-term (Gomez-Soria et al., 2020) and on depression in the short-term (Djabelkhir et al., 2017; Gomez-Soria et al., 2020; Llanero Luque et al., 2010) or medium-term (Gomez-Soria et al., 2020). Other studies which that analyzed the effectiveness of other cognitive interventions showed no effects on anxiety in the short-term (Savulich et al., 2017) or on depression in both the short-term (Savulich et al., 2017; Tarnanas, 2014) and long-term (Gaitán et al., 2013).

The number of drop-outs at 12 months were double in the CG compared to the IG. In analyzing the reasons for the drop-outs, the number of them were very similar between groups except for the reason “institutionalized”, which could be due to the worsened status of the participants in the CG because they did not receive the intervention. Despite the high number of drop-outs, the final power of the study at 12-month follow-up was of 0.936, which avoids the risk of underpower.

However, this study had some limitations, as neither the therapists who performed the intervention nor the participants could be blinded. Besides, we could not access the participants’ medical histories or clinical diagnoses, and for this reason we should have labeled the participants of this study as "possible MCI". Moreover, although the initial sample size was high, there were a lot of drop-outs at 12 months, which impedes the generalization of our results. The study’s strengths, however, included its status as a RCT and including a long-term follow-up of 12 months. More RCTs that administer personalized CS with long-term follow-ups are recommended in older people with MCI living in the community to demonstrate the effectiveness of CS.

In conclusion, this RCT has demonstrated that a personalized CS program could be effective in improving global cognition and cognitive aspects, such as global and spatial orientation in the long-term.

Clinical implications

- Personalized cognitive stimulation based on cognitive levels in older adults with possible MCI achieves improvements in global cognition and global and spatial orientation.
- Personalized cognitive stimulation can be applied successfully by trained occupational therapists.

Acknowledgments

The authors would like to thank the study participants for their effort and time; we humbly acknowledge their contributions. We would also like to thank to Dr. Carmen Muro and Dr. Fernando Plo for their collaboration and participation in the different phases of the study.

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Table 1. Socio-demographic and clinical self-reported characteristics of the participants.

		Total (n=50)	**Control Group (n=27)**	**Intervention Group** (n=23)	**[a]p-value**
Age		74.32±5.47	74.70±4.81	73.87±6.23	0.596
Sex, n(%)	Men	11 (22)	9 (33)	2 (9)	0.080
	Women	39 (78)	18 (67)	21 (91)	
Marital status, n(%)	Single	3 (6)	3 (11)	0 (0)	0.267
	Married	29 (58)	16 (59)	13 (57)	
	Widower	15 (30)	6 (22)	9 (39)	
	Separated	3 (6)	2 (7)	1 (4)	
Educational level, n (%)	Primary incomplete	22 (44)	12 (44)	10 (43)	0.085
	Primary complete	22 (44)	9 (33)	13 (57)	
	High school	3 (6)	3 (11)	0 (0)	
	Vocational Training	3 (6)	3 (11)	0 (0)	
Arterial hypertension, n (%)	No	33 (66)	17 (63)	16 (70)	0.848
	Yes	17 (34)	10 (37)	7 (30)	
Mellitus Diabetes, n (%)	No	44 (88)	22 (81)	22 (96)	0.271
	Yes	6 (12)	5 (19)	1 (4)	
Hypercholesterolemia, n (%)	No	29 (58)	14 (52)	15 (65)	0.505
	Yes	21 (42)	13 (48)	8 (35)	
Obesity, n (%)	No	40 (80)	22 (81)	18 (78)	1.000
	Yes	10 (20)	5 (19)	5 (22)	
Stroke, n (%)	No	46 (92)	25 (93)	21 (91)	1.000
	Yes	4 (8)	2 (7)	2 (9)	
Visual disturbance, n (%)	No	4 (8)	3 (11)	1 (4)	0.722
	Yes	46 (92)	24 (89)	22 (96)	
Hearing impairment, n (%)	No	27 (54)	18 (67)	9 (39)	0.096
	Yes	23 (46)	9 (33)	14 (61)	

Data expressed with mean ± standard deviation or with absolute and relative values (%).
[a] significative if $p<0.05$.

Table 2. Differences between groups at 12 months post-intervention in the different outcome variables.

	Intervention Group (n=23)				Control Group (n=27)				Differences between groups 6-12 months (95%CI)	Group:time interaction
	Basal	Post-Intervention	6 months	12 months	Basal	Post-Intervention	6 months	12 months		p-value
MEC-35	25.87±1.058	28.957±2.705	29.652±2.516	30±2.892	25.815±0.962	26±3.823	27.259±3.623	27.481±3.867	-0.126 (-1.605, 1.354)	0.002[a]
Dicthomized MEC-35, n(%)										
<24 points	0 (0)	1 (4)	0 (0)	1 (4)	0 (0)	6 (22)	5 (19)	3 (11)		0.01[a]
>24 points	23 (100)	22 (96)	23 (100)	22 (96)	27 (100)	21 (78)	22 (81)	24 (89)		
Set-Test	36.435±4.294	37.609±4.619	37.783±4.089	37.652±6.492	35.63±4.143	35.963±5.571	35.37±5.779	36.704±4.581	1.464 (-0.636, 3.564)	0.401
Barthel	96.522±6.98	96.739±5.136	95.435±9.159	95.87±8.346	94.63±7.712	93.796±8.643	93.648±9.173	93.889±7.382	-0.194 (-2.309, 1.921)	0.784
L-B	7.304±1.295	7.261±1.287	7.217±1.413	7.261±1.356	7.074±1.269	6.815±1.272	7.111±1.086	7.111±1.311	-0.043 (-0.329, 0.242)	0.52
Goldberg	2.783±1.718	2.739±2.23	2.609±1.889	3.065±2.298	3.315±2.965	2.87±2.744	2.685±2.37	3.019±2.622	-0.123 (-1.385, 1.138)	0.844
GDS-15	2.609±2.536	2.326±2.229	2.217±1.845	2.435±2.356	3.796±3.625	3.87±3.804	3.315±3.866	3.704±3.891	0.171 (-1.061, 1.404)	0.899

MEC-35: Spanish version of the Mini-Mental Status Examination. Barthel: Index of Barthel. LB: Scale of Lawton y Brody. Goldberg: Anxiety subscale of Goldberg questionnaire.
GDS-15: Yesavege Abbreviated Geriatric Depression Scale, of 15-item version.
Data expressed with mean ± standard deviation.
IC95%: confidence interval at 95%
[a] significative if $p<0.05$.

Table 3. Differences between groups at 12 months post-intervention in the different subdomains of MEC-35.

	Intervention Group (n=23)				Control Group (n=27)				Between groups 6-12 months difference (95%CI)	Group:time interaction
	Basal	Post-Intervervention	6 months	12 months	Basal	Post-Intervention	6 months	12 months		p-value
Orientation global	8±1.243	9.13±1.359	9.130±1.10	8.957±1.522	8.556±1.281	8.185±1.52	8.37±1.597	8.481±1.451	0.285 (-0.475, 1.045)	<0.001[a]
Orientation temporary	3.807±0.815	4.435±0.896	4.870±0.344	4.696±0.559	4.037±1.055	4.259±1.023	4.481±0.700	4.667±0.620	0.359 (0.011, 0.708)	0.232
Orientation space	4.130±0.694	4.696±0.703	4.261±1.096	4.261±1.176	4.519±0.643	3.926±1.207	3.889±1.219	3.815±1.178	-0.074 (-0.733, 0.585)	0.004[a]
Fixation memory	3.000±0.000	3.000±0.000	3.000±0.000	3.000±0.000	3.000±0.000	3.000±0.000	3.000±0.000	3.000±0.000		-
Short term memory	1.130±1.100	1.913±0.996	2.435±0.843	2.522±0.730	0.852±0.864	1.296±1.137	1.519±1.014	1.593±1.152	-0.013 (-0.537, 0.512)	0.114
Atention and calculation	4.652±1.668	5.087±1.125	5.348±1.152	5.652±1.465	4.778±1.908	4.815±1.902	5.111±1.826	5.148±1.936	-0.267 (-1.036, 0.501)	0.647
Calculation	3.783±1.242	4.304±0.822	4.217±0.998	4.087±0.949	3.556±1.423	3.259±1.745	3.481±1.397	3.704±1.265	0.353 (-0.339, 1.045)	0.208
Atention	0.870±0.815	0.783±0.85	1.130±1.217	1.522±1.201	1.222±1.155	1.556±1.121	1.630±1.079	1.444±1.219	-0.576 (-1.475, 0.322)	0.203
Languaje and praxis	9.087±1.24	9.87±0.815	9.739±1.322	9.87±0.869	8.667±1.359	8.704±1.409	9.222±1.717	9.185±1.21	-0.167 (-0.843, 0.509)	0.183
Languaje	5.000±1.000	5.435±0.788	5.348±0.775	5.391±0.839	4.519±0.975	4.519±0.975	5.000±1.038	4.741±0.859	-0.303 (-0.753, 0.147)	0.207
Praxis	4.087±0.996	4.478±0.511	4.391±0.722	4.478±0.593	4.148±0.602	4.222±0.751	4.259±0.859	4.444±0.641	0.098 (-0.359, 0.556)	0.548

Data expressed with mean ± standard deviation.

IC95%: confidence interval at 95%
[a]significative if $p<0.05$.