Topics in Geriatric Rehabilitation

EFFECTIVENESS OF COGNITIVE STIMULATION PERSONALIZED BY THE PRE-EXISTING COGNITIVE LEVEL IN OLDER ADULTS: A RANDOMIZED CLINICAL TRIAL

--Manuscript Draft--

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Corresponding Author:	Pablo Herrero, PhD University of Zaragoza Zaragoza, Spain SPAIN
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	University of Zaragoza
Corresponding Author's Secondary Institution:	
First Author:	Estela Calatayud, OT, PhD
First Author Secondary Information:	
Order of Authors:	Estela Calatayud, OT, PhD
	Carolina Jiménez-Sánchez, PT, MSc
	Sandra Calvo, PT, PhD
	Natalia Brandín-de la Cruz, PT, MSc
	Pablo Herrero, PhD
	Isabel Gómez-Soria, OT, PhD
Order of Authors Secondary Information:	
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Calatayud, Estela PT, MSc, PhD[1]; Jiménez-Sánchez, Carolina PT, MSc[2]; Calvo, Sandra PT, MSc[2]; Brandín-de la Cruz, Natalia PT, MSc[2]; Herrero, Pablo PT, MSc, PhD[1*]; Gómez-Soria, Isabel PT, MSc, PhD[1]

[1]*Universidad de Zaragoza. Departamento de Fisiatría y Enfermería. Facultad de Ciencias de la Salud, Zaragoza, España.*

[2]*Universidad San Jorge. Campus Universitario, Autov. A23 km 299, 50830. Villanueva de Gállego, Zaragoza, España.*

*** Correspondence:**

Pablo Herrero, PhD. Universidad de Zaragoza. Departamento de Fisiatría y Enfermería. Facultad de Ciencias de la Salud. C/ Domingo Miral s/n, CP 50009 Zaragoza. Email: pherrero@unizar.es

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Abstract.

This randomized clinical trial analyzed if a personalized cognitive stimulation based in the individual´s pre-existing cognitive levels may be more effective in the short and long term than a standard cognitive stimulation programme. 288 older adults were randomized into an intervention and a control group, stratified according to their cognitive levels. There were significant differences between groups with a small effect size at post-intervention (10 weeks), follow-up I (26 weeks) and follow-up II (52 weeks) ($p<0.001$, $0.2<r<0.4$) and in the cognitive category ($p<0.001$). The personalization of cognitive stimulation is effective to maintain normal cognitive functioning and to delay cognitive decline.

Keywords: Cognitive impairment; Cognition; Healthy aging; Occupational therapy; Elderly.

INTRODUCTION

The world's population is suffering an unprecedented demographic change. The older people in Europe (defined as those aged 65 years or more) will increase significantly, reaching 129.8 million by 2050. Besides, more than two thirds of this population are projected to have an old-age dependency ratio above 50%. This growing number has a range of consequences, being one of the principal areas of concern the cost of providing adequate health and long-term care, as very old people tend to consume proportionally more social services.[1]

Given the demographic change faced by the world population with a higher life expectancy, it is possible that a large number of older adults will have risk of cognitive decline.[2] Several epidemiological studies point out that between 12% and 18% of people over the age of 60 years will suffer mild cognitive impairment (MCI) in the next 25 years.[3] The MCI, which is an intermediate state between normal cognition (NC) and dementia, is also considered as an early predictor of dementia.[4]

It has been reported that the direct cost of care of individuals with MCI in Primary Care is 16% higher than in subjects with NC[5], with recent studies highlighting that although the transition from MCI to NC is quite common[6], approximately half of the patients diagnosed with MCI could develop Alzheimer's within 3 to 5 years.[7] Different factors have been identified to prevent the progression of cognitive decline or to revert it, such as the improvement of lifestyle, the performance of physical activity and the implementation of personalized interventions through the creation of healthy environments and cognitively engaging, as it encourages the development of skills and personal attitudes.[8,9]

A recent systematic review recommends to conduct more clinical trials with longitudinal follow-ups that can address the question of whether cognitive interventions impact upon or alter the trajectory of non-normal cognitive decline.[10] Moreover, recent publications show the need to identify factors that allow professionals to provide more effective treatment options[11] based on individual characteristics of the study population (age, education, general cognitive ability, initial performance...) and if so, how[12] the pre-existing cognitive level may help to provide this effective personalized intervention.[13] Because of the aforementioned identified needs, the main aim of this study was to analyze if a personalized intervention based in the individual´s pre-existing cognitive levels may be more effective in the short and long term than a general cognitive training programme.

MATERIALS AND METHODS

Design

A randomized controlled clinical trial was designed to analyze the therapeutic effect of a personalized cognitive training programme based on pre-existing cognitive level measured by the cognition mini-exam (MEC_{35}). This study followed the CONSORT guidelines. All participants signed an informed consent form before their participation. The study was approved by the Ethics Committee of Aragon (reference no. PI11/090) and followed the clinical practice principles of the Declaration of Helsinki.

Participants

Participants were people attended in the Primary Care consultations who received the usual medical and nursing care at the San José Norte-Centro de Zaragoza Health Center in Zaragoza (Spain). Participants were recruited in two ways: referrals from family physicians (who previously received a clinical information session on the study), and information received through informational posters placed at medical consultations.

Inclusion in the study was based on the following criteria: 1) aged ≥65; and 2) between 20 and 35 points evaluated with the MEC_{35}. Individuals were excluded if they 1) had received cognitive stimulation in the last year; 2) were institutionalized; 3) obtained a Lawton-Brody index ≥3; 4) more than 6 points on the abbreviated Goldberg anxiety scale; 5) ≥12 points on the abbreviated questionnaire of depression of Yesavage; 6) <60 points on the Barthel Index; 7) presented deafness; 8) presented blindness; 9) presented neuropsychiatric disorders; or 10) motor disturbances. The withdrawal criteria consisted of the failure to attend assessments or decision to abandon, death or entry into a Geriatric Centre.

All the participants were informed about the nature of the study, objectives, and voluntary participation, and that they can abandon 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 in the MEC_{35} scale (validated Spanish version of the Mini-Mental State Examination (MMSE))[14]: normal cognition (30-35); borderline (25-29); mild cognitive impairment (20-24). A therapist who was independent of the study carried out the randomization.

Intervention

The intervention was carried out at La Caridad Foundation in Zaragoza (collaborating entity). All participants, who were blinded to the group allocation, were treated by two skilled occupational therapists.

The treatment of the IG consisted of a standardized programme of cognitive stimulation whose novelty lies in the customization of the program based on pre-existing cognitive level of patients, evaluated by the MEC_{35}. This programme allows to work on

pathological aging and consists of 40 activities divided into 4 exercises of the following cognitive aspects: memory, orientation, language, praxis, gnosis, calculation, perception, logical reasoning, attention-concentration, and programming (Figure 1).

Cognitive and occupational elements such as the degree of difficulty involved in the activity, the amount of elements contained, the help offered by the occupational therapist, the facilitating cues and the maximum time established for every activity and level were considered in the design of the programme. The occupational elements (profession, interests, and roles) allowed the participants to express different levels of complexity and increase their personal satisfaction.

The intervention was administered in groups, with a practical session of 45 minutes performed once a week during 10 weeks.[15] Before starting, the participants received a theoretical explanation about the aspect that was going to be worked. At the end of the session, the group shared what they had worked on.

[insert Figure 1]

The CG ~~control group~~ did not receive any cognitive intervention during the study~~apart from the periodic standard stimulation regardless of previous cognitive levels (non-personalized programme), that they usually received.~~

Outcomes measures

Participants who confirmed their willingness to participate, and fulfilled the inclusion criteria, were enrolled in the study, and assessed for all outcome measures at baseline (Pre), at 10 weeks (Post), at 26 weeks (Follow-up I), and at 52 weeks (Follow-up II). Baseline data included sociodemographic and clinical data (Table 1). Different occupational therapists who were blinded to the group allocation performed each

evaluation. Evaluators who performed the interventions carried out a 20-hours specific theoretical-practical training to guarantee the homogeneous application of the evaluation. Assessments were always performed at the same time and at the same place to maximally preserve participant conditions. Besides, other factors like changes in the medication were also controlled.

Primary outcomes were the changes in the cognitive level, evaluated with the MEC_{35}. Secondary outcomes included the abbreviated form of the Goldberg Scale, the Yesavage Scale, and the Set-test.

The cognition mini-exam (MEC_{35})[14] is the most used short cognitive test to study the cognitive abilities in primary care. This scale comprises 11 items that evaluates cognitive impairment by assessing five cognitive areas: orientation (temporal and spatial), attention and calculation, word recall, language, and visuospatial abilities. The maximum MEC score is 35 points, and scores lower than 30 points suggest the presence of cognitive impairment. Classification is based on the scores, with people considered to have normal cognitive function scoring 30–35 points, borderline cognitive deficits 25–29 points, mild cognitive impairment 20–24 points, moderate cognitive impairment 15–19 points, and severe cognitive impairment $\leq$14 points. The MEC_{35} has a sensitivity of 85-90% and a specificity of 69%.

The abbreviated Goldberg Anxiety Scale[16] allows the measurement of anxiety in people over 65 years. It examines four fundamental psychiatric areas: depression, anxiety, social inadequacy, and hypochondria. It contains 9 questions and the cutoff point to establish whether a person suffers from anxiety is 4. It has a sensitivity of 83.1%, a specificity of 81.8%.

The Yesavage Scale[17], also known as GDS-15, evaluates the depressive symptoms present in the elderly. The reduced version, composed of 15 dichotomic response (yes or no) items, with scores ranging from 0 to 15 was used. The cut-off points are as follows: from 0 to 4 points is considered normal (there is no depression), from 5 to 12 points means moderate depression and more than 12 points means severe depression. This test has a sensitivity of 80% and a specificity of 75%.

The Set-test[18] evaluates the verbal fluency in 4 categories: colors, animals, fruits, and cities. It has been proposed as a diagnostic aid in dementia in elderly patients. The cut-off value was 29 in adults and 27 in elderly people. A lower score is indicative of dementia. Sensitivity was 79% and specificity 82%, with 20% of incorrectly classified patients.

Sample size

The sample size calculation was performed with G*3 Power 3.1 (Heinrich-Heine University Düsseldorf, Germany). The calculations were based on a standard deviation (SD) 5.2 points, a between-group difference of 2 points (it was the minimal detectable change [MDC] of the MEC_{35})[19], an alpha level of 0.05, and power of 80%. A total sample of 144 participants was estimated. Considering a drop-out rate of 50% based on previous studies done with this type of population, an initial sample of 288 participants is necessary to reach 144 participants in the 52-week follow-up.

Statistical analysis

Data were analyzed with the Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM Corporation, Armonk, NY). The Kolmogorov-Smirnov test was performed to determine normal data distribution. Data are presented as mean ± standard deviation, median with interquartile range or number (percentage). Baseline measurements were compared between the two groups using the Mann–Whitney U test or the Chi-square test.

Spearman's rank correlation coefficients (rho) were carried out to analyze the relationship between MEC_{35} scores, Set-test scores, level of anxiety, level of depression, and socio-demographic data. The strength of correlations was interpreted as low (0.00-0.25), fair (0.25-0.50), moderate to good (0.50-0.75) and good to excellent (>0.75).[20]

Mann–Whitney U test for nonparametric data and Chi-square test for categorical variables were performed to compare the two groups differences. Wilcoxon test for nonparametric data and marginal homogeneity test for categorial variables were applied to highlight the within-group differences. A p-value < 0.05 was considered statistically significant.

Between-group and within-group effect sizes were calculated using Cohen's r. An effect size of less than 0.2 reflects a negligible mean difference; between 0.2 and 0.5, a small difference; between 0.5 and 0.8, a moderate mean difference; and 0.8 or greater, a large difference.[21]

RESULTS

Three hundred and fifty-six participants were screened for eligibility. Two hundred eighty-eight (73.93±6.04 years; 70.04% female) satisfied the eligibility criteria and agreed to participate. The reasons for ineligibility can be found in the flow diagram (Figure ~~1~~2). Participants were randomly allocated to the IG and to the CG. Table 1 shows the baseline participant characteristics, with no statistically significant differences between groups.

[insert Figure ~~1~~2]

[insert Table 1]

Pearson rho values between the clinical variables (cognition level, semantic verbal fluency, anxiety, and depression) and sociodemographic variables (age, gender, marital status, educational level, physical work demand, mental work demand, and living) are presented in Table 2. Cognition level showed a fair correlation with semantic verbal fluency (rho=0.488, $p<0.001$), age (rho=-0.331, $p<0.001$), educational level (rho=0.262, $p<0.001$), and a low correlation with mental work demand (rho=0.232, $p<0.001$), gender (rho=-0.192, p=0.002), and level of depression (rho=-0.123, p=0.045). Semantic verbal fluency demonstrated fair correlation with age (rho=-0.344, $p<0.001$) and low correlation with educational level (rho=0.151, p=0.013) and mental work demand (rho=0.148, p=0.016). Correlation between anxiety and depression was moderate (rho=0.533, $p<0.001$). Anxiety showed to have a low correlation with gender (rho=0.194, p=0.001), physical work demand (rho=-0.167, p=0.006) and marital status (rho=0.126, p=0.040), whilst depression showed a low correlation with marital status (rho=0.242, $p<0.001$), gender (rho=0.232, $p<0.001$), and educational level (rho=-0.125, p=0.041).

[insert Table 2]

Tables 3 shows the within- and between-groups differences in every assessment of the MEC_{35} scores. There were statistical differences with a small effect size between-groups at post-intervention (10 weeks), follow-up I (26 weeks) and follow-up II (52 weeks) ($p<0.001$, $0.2<r<0.4$). Furthermore, in the within-group analysis, the MEC_{35} scores of the IG increased significantly ($p<.001$) with a moderate effect size ($0.5<r<0.8$) after intervention in all assessments in relation to pre-intervention assessment. There were no significant changes at any time points for CG ($p>0.05$).

[insert Table 3]

An analysis of the intervention considering the classification in the MEC_{35} categories (normal, borderline, mild and moderate) was carried out (Table 4). Results show the change of category of the participants, with significant differences between-groups and within-groups in favour of the IG ($p<0.001$). Regarding categories before intervention, there were 70 (48.6%) participants in the "normal" category, 59 (41.0%) in the "borderline" category and 15 (10.4%) in the "mild" category for IG and 49 (39.8%) participants in the "normal" category, 53 (43.1%) in the "borderline" category and 21 (17.1%) in the "mild" category for CG. Considering dropouts, after intervention, the number of participants for IG was 104 (72.2%) for "normal" category, 31 (21.5%) for the "borderline" category, 8 (5.6%) for "mild" category and 1 (0.7%) for "moderate" category. In the case of the CG, there were 60 participants (48.8%) in the "normal" category, 41 (33.3%) in the "borderline", 18 (14.6%) in the "mild" and 4 (3.3%) in the "moderate" category. At follow-up assessments, the number of participants in each category were respectively for the IG and CG groups the followings: for follow-up I, 81 (80.2%) and 47 (55.9%) for "normal", 18 (17.8%) and 23 (27.4%) for "borderline", 1 (1%) and 13 (15.5%) for "mild" and 1 (1%) and 1 (1.2%) for "moderate"; for follow-up II, 61 (82.4%) and 39 (60.9%) for "normal", 11 (14.9%) and 20 (31.2%) for "borderline", 2 (2.7%) and 3 (4.8%) for "mild" and 0 (0%) and 2 (3.1%) for "moderate".

[insert Table 4]

In relation to semantic verbal fluency, anxiety and depression, there were no significant differences for any inter-group and intra-group comparisons at any time points ($p>0.05$).

DISCUSSION

This research showed that the addition of a personalized cognitive stimulation program, according to the patients' pre-existing cognitive level, led to significant global cognitive improvements according to the MEC_{35} in the post-intervention (10 weeks), follow-up I (26 weeks) and follow-up II (52 weeks). Besides, the differences between groups were over the MDC which shows that there was a real change. In addition, the category analysis showed that participants who received personalized cognitive stimulation also achieved an improvement in the category, compared to participants in the CG~~control group~~ who did not. These results are in line with other authors who defend that the type of strategy used is not as important as the adaptation of interventions to the participant´s cognitive level[22], the training of all cognitive areas[15] or the difficulty of the context.[23]

Participants who received the personalized intervention not only improved after treatment, but also maintained the improvements 26 and 52 weeks later. This improvement occurred regardless of their cognitive baseline level, which is supported by the scientific literature, which shows that cognitive stimulation is effective in the various phases of aging from normal to pathological.[24] Besides, the group with cognitive impairment improved more than the others, possibly due to the greater existing room for improvement.[25,26]

This study also showed that the group that received the personalized cognitive stimulation program had a higher rate of maintenance of normal cognitive function. Maintaining the normal cognitive function as long as possible as well as delaying the cognitive decline when this has started is an indicator of successful aging and of the effectiveness of the stimulation received.[27] According to the existing evidence, these cognitive benefits may have been achieved by brain plasticity[28] present in the elderly and by the cognitive reserve capacity that helps to create a deeper learning curve with systematic practice.[29]

Regarding clinical variables, this study showed a direct and significant correlation between cognitive level and semantic verbal fluency, similarly to other authors who show that semantic loss is associated with early neurodegeneration[30,31], which would increase the risk of cognitive impairment and prodromal dementia. In the case of anxiety and depression, which tend to occur in a combined way in the elderly[32] and are associated with marked cognitive decline[33], we only found the association of cognitive decline with depression, but not with anxiety.

In relation to the sociodemographic variables, this study showed two other associations, although low. The cognitive level was found to be related to the age and the educational level. Similar results have been found in other studies which show that the cognitive level decreases as age increases[25] and the years of formal education decrease.[34,35] Depression was also found to be related to the marital status and the gender. The literature also endorses this association, stating that the prevalence of depressive symptoms is higher in women, and in people who live alone and are not married, due to a lack of social support.[32]

Finally, in this study we have detected a relationship between the cognitive demands of the job occupation and the baseline cognitive level, similar to what was found by Chung et al., who showed that occupations with higher levels of mental demands increased cognitive functioning and that this was likely to translate into less cognitive decline after retirement.[36] Evidence supports that higher scores in reserve proxies are associated with a lower risk of progression of normal cognition at the onset of clinical symptoms[36,37]. For this reason, certain aspects such as the influence of the cognitive reserve capacity (educational level, occupations in the population of middle age, and participation in cognitive stimulating activities throughout life) should be taken into account when implementing cognitive stimulation programs.

The study presented some limitations such as having part of the population with a high score in some outcome measurements (ceiling effect) and not controlling other factors that can influence the incidence of cognitive deterioration (physical exercise, self-perception of health, etc.). Besides, there was a high rate of dropouts, although this didn´t impact the analysis as the study detected the intervention effect, avoiding the risk of underpower. However, also presents some strengths such as being an RCT, implementing a personalized cognitive stimulation program based on pre-existing cognitive levels and occupational characteristics of the elderly, and having carried out the intervention in a health center that does not have occupational therapy professionals. Future studies should analyze the longer-term cognitive effects by categories in this population, as well as the evolution of anxiety and depressive symptoms, introducing multimodal interventions.

In conclusion, this randomized clinical trial has demonstrated that the personalization of cognitive stimulation by pre-existing cognitive levels in older adults is effective to maintain normal cognitive functioning and to delay cognitive decline. This study has also identified that baseline characteristics such as the educational and work level, psychological aspects, verbal fluency, age and gender are associated with the improvements of a personalized cognitive intervention and should be considered when designing a personalized intervention.

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Author Contributions

E.C. conceived and designed the study. E.C., I. and were involved in data collection. C.J.S, P.H. and were involved in data analysis. E.C, S.C, P.H. and C.J.S were involved in drafting the article. All authors approved the final version of the manuscript accepted for publication.

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Field Code Changed

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Figure 1

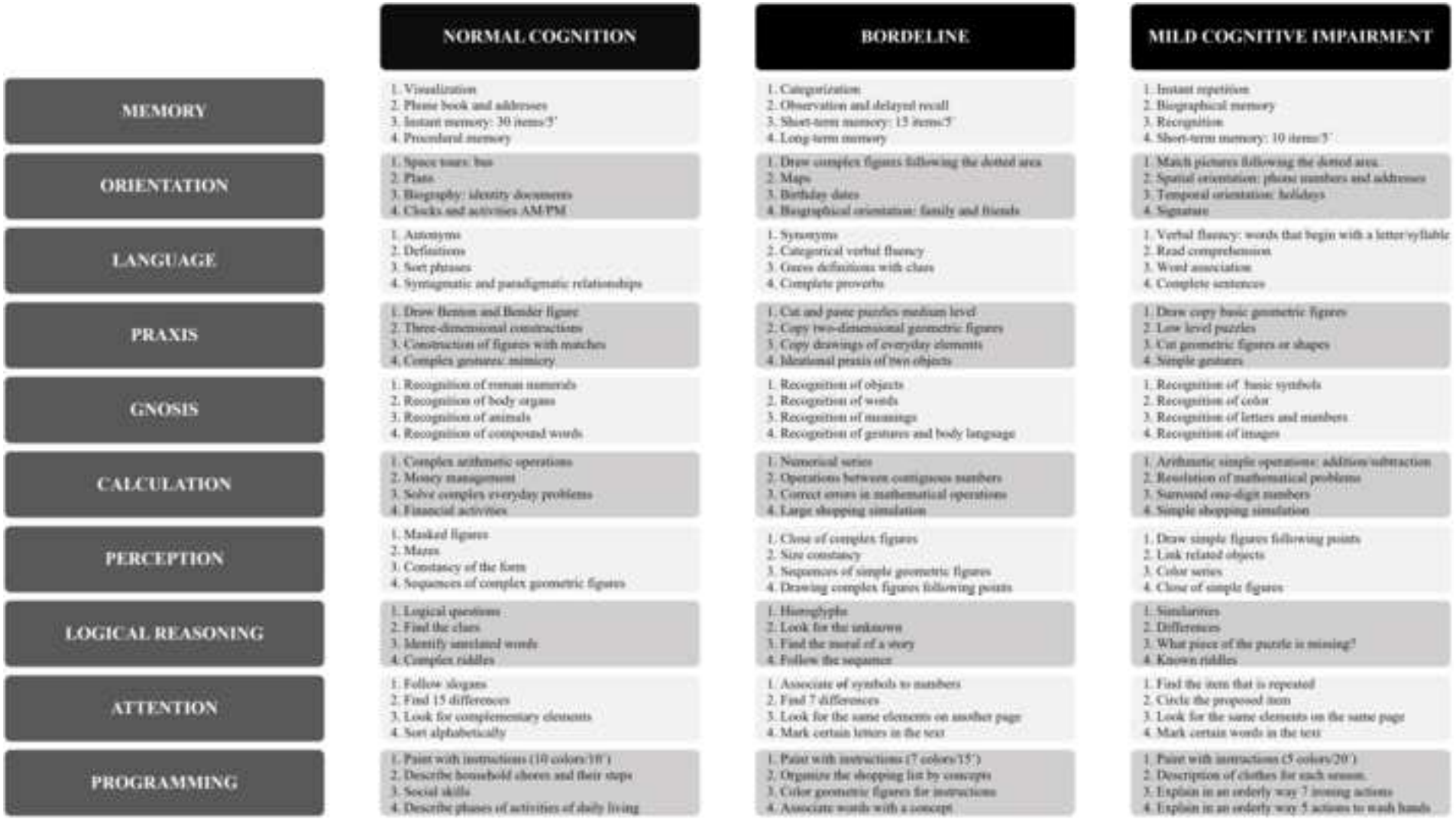

Figure 2

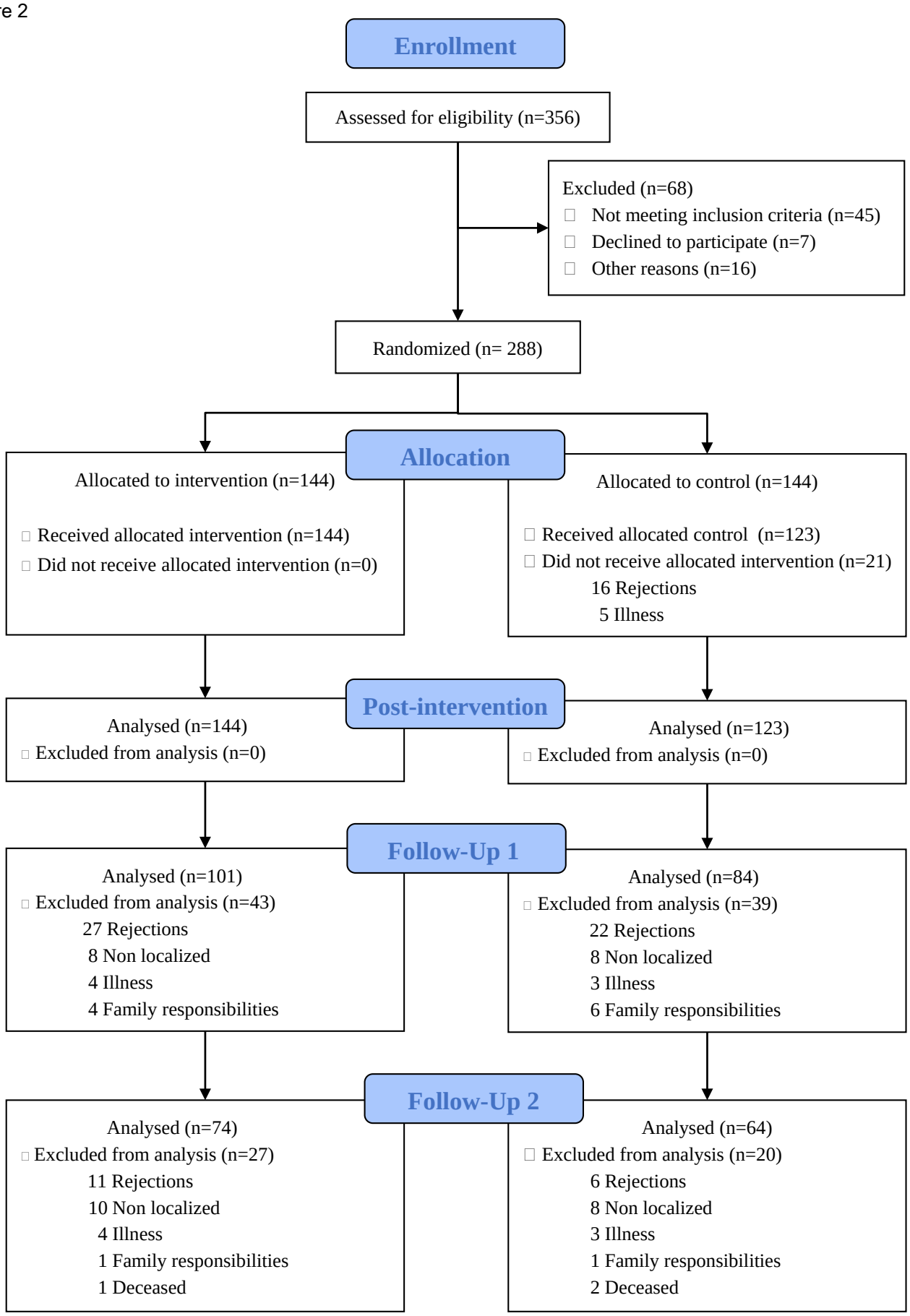
Enrollment
Assessed for eligibility (n=356)
Excluded (n=68)
Not meeting inclusion criteria (n=45)
Declined to participate (n=7)
Other reasons (n=16)
Randomized (n= 288)
Allocation
Allocated to intervention (n=144)
Received allocated intervention (n=144)
Did not receive allocated intervention (n=0)
Allocated to control (n=144)
Received allocated control (n=123)
Did not receive allocated intervention (n=21)
16 Rejections
5 Illness
Post-intervention
Analysed (n=144)
Excluded from analysis (n=0)
Analysed (n=123)
Excluded from analysis (n=0)
Follow-Up 1
Analysed (n=101)
Excluded from analysis (n=43)
27 Rejections
8 Non localized
4 Illness
4 Family responsibilities
Analysed (n=84)
Excluded from analysis (n=39)
22 Rejections
8 Non localized
3 Illness
6 Family responsibilities
Follow-Up 2
Analysed (n=74)
Excluded from analysis (n=27)
11 Rejections
10 Non localized
4 Illness
1 Family responsibilities
1 Deceased
Analysed (n=64)
Excluded from analysis (n=20)
6 Rejections
8 Non localized
3 Illness
1 Family responsibilities
2 Deceased

Table 1. Description of the Study Population				
Socio-demographic and clinical characteristics		***Intervention Group (n=144)***	***Control Group (n=123)***	***p-value***
Age		72.94±5.66 73[64-87]	75.08±6.27 75[64-89]	0.067[a]
Gender	Male	36 (25.0%)	44 (10.6%)	0.055[b]
	Female	108 (75.0%)	79 (64.2%)	
Marital status	Single or divorced or separated	8 (5.6%)	13 (10.6%)	0.307[b]
	Married or living with couple	97 (67.4%)	80 (65.0%)	
	Widowed	39 (24.1%)	30 (24.4%)	
Educational level	Primary school	115 (79.9%)	97 (78.9%)	0.840[b]
	Secondary school or higher	29 (20.1%)	26 (21.1%)	
Physical work demand	Low	26 (18.1%)	29 (23.6%)	0.455[b]
	Moderate	65 (45.1%)	48 (39.0%)	
	High	53 (36.8%)	46 (37.4%)	
Mental work demand	Low	79 (54.9%)	75 (61.0%)	0.578[b]
	Moderate	58 (40.3%)	42 (34.1%)	
	High	7 (4.9%)	6 (4.9%)	
Living	Alone	28 (19.4%)	24 (19.5%)	0.453[b]
	As a couple/children	98 (68.1%)	77 (62.6%)	
	Other conditions	18 (12.5%)	22 (17.9%)	
Cognition level (MEC_{35})		29.09±3.51 29[24-34]	28.79±3.75 29[23-35]	0.104[a]
Semantic verbal fluency (Set-test)		37.57±3.65 39[23-40]	36.72±4.12 39[22-40]	0.071[a]
Anxiety (Goldberg Scale)		2.90±2.49 3[0-9]	3.00±2.57 2.5[0.5-8.5]	0.761[a]
Depression (Yesavage Scale)		2.70±2.58 2[0-12]	3.38±3.03 3[0-14]	0.102[a]

Values are presented as Mean±Standard Deviation (SD), Median [min- max] and Number (Percentage).
[a]Mann–Whitney U test. [b]Chi-square test.

Table 2. Correlation coefficients (r) between variables at baseline.

	Age	Gender	Marital status	Educational level	Physical work demand	Mental work demand	Living	Depression	Anxiety	Set-test
MEC_{35}	**-0.331****	**-0.192****	-0.035	**0.262****	-0.071	**0.232****	0.030	**-0.123***	-0.023	**0.488****
Set-test	**-0.344****	0.042	0.058	**0.151***	-0.092	**0.148***	-0.023	-0.027	0.025	-
Anxiety	-0.098	**0.194****	**0.126***	-0.058	**-0.167****	-0.113	-0.013	**0.533****	-	-
Depression	-0.023	**0.232****	**0.242****	**-0.125***	-0.107	-0.048	0.048	-	-	-

Abbreviations: MEC, Mini-Exam Cognitive; IG, intervention group; CG, control group.

Statistically significant Spearman r values are in bold.

*Significant correlation (P<0.05).

**Significant correlation (P<0.01).

Table 3

Table 3. Comparison of MEC_{35} scores between- and within-groups

Variable		Descriptive data				Within-groups analysis									Between-groups analysis								
		Pre	Post	Follow-up I	Follow-up II	Post-Pre IG n=144 CG n=123			Follow-up I-Pre IG n=101 CG n=84			Follow-up II-Pre IG n=74 CG n=64			Post (n=267)			Follow-up I (n=185)			Follow-up II (n=138)		
		Mean±SD Median [min-max]	Mean±SD Median [min-max]	Mean±SD Median [min-max]	Mean±SD Median [min-max]	Mean difference (95% CI)	P-value	Effect size	Mean difference (95% CI)	P-value	Effect size	Mean difference (95% CI)	P-value	Effect size	Mean difference (95% CI)	P-value	Effect size	Mean difference (95% CI)	P-value	Effect size	Mean difference (95% CI)	P-value	Effect size
MEC_{35}	IG	29.09±3.51 29[24-34]	30.78±3.44 32[19-35]	31.57±3.13 32[25-35]	31.97±2.73 33[23-35]	**1.69 (1.29 to 2.08)**	**<0.001[a]**	**0.590[c]**	**2.06 (1.56 to 2.55)**	**<0.001[a]**	**0.650[c]**	**2.54 (1.93 to 3.16)**	**<0.001[a]**	**0.716[c]**	**2.21 (-3.16 to -1.25)**	**<0.001[b]**	**0.271[c]**	**2.16 (-3.23 to -1.08)**	**<0.001[b]**	**0.283[c]**	**2.10 (-3.20 to -1.00)**	**<0.001[b]**	**0.314[c]**
	CG	28.79±3.75 29[23-35]	28.57±4.31 29[15-35]	29.41±4.07 31[20-35]	29.87±3.67 30[17-35]	-0.22 (-0.13 to 1.08)	0.280[a]	0.121[c]	0.63 (-0.06 to 1.32)	0.150[a]	0.182[c]	0.61 (-0.12 to -1.34)	0.091[a]	0.211[c]									

Abbreviations: MEC, Mini-Exam Cognitive; IG, intervention group; CG, control group.

Values are presented as Mean±Standard Deviation (SD), Median [min- max] and Confidence Intervals (CI). Statistically significant differences and relevant effect sizes are in bold.

[a]Wilcoxon test. [b]Mann–Whitney U test. [c]Effect size expressed as r.

Table 4

Table 4. Comparison of MEC_{35} categories between- and within-groups

Group	Categories	Pre (n=267)	Post (n=267) n (%) IG n=144 CG n=123				P-value		Follow-up I (n=185) n (%) IG n=101 CG n=84				P-value		Follow up-II (n=138) n (%) IG n=74 CG n=64				P-value	
			N	B	M	Mo	Within-groups	Between groups	N	B	M	Mo	Within-groups	Between groups	N	B	M	Mo	Within-groups	Between groups
IG	N	70	68 (97.1%)	2 (2.9%)	0 (0.0%)	0 (0.0%)	<0.001[a]	<0.001[b]	47 (92.2%)	4 (7.8%)	0 (0.0%)	0 (0.0%)	<0.001[a]	<0.001[b]	33 (94.3%)	2 (5.7%)	0 (0.0%)	0 (0.0%)	<0.001[a]	<0.001[b]
	B	59	36 (61.0%)	22 (37.3%)	1 (1.7%)	0 (0.0%)			32 (74.4%)	11 (25.6%)	0 (0.0%)	0 (0.0%)			27 (75.0%)	8 (22.2%)	1 (2.8%)	0 (0.0%)		
	M	15	0 (0.0%)	7 (46.7%)	7 (46.7%)	1 (6.7%)			2 (28.6%)	3 (42.9%)	1 (14.3%)	1 (14.3%)			1 (33.3%)	1 (33.3%)	1 (33.3%9	0 (0.0%)		
CG	N	49	40 (85.1%)	8 (12.8%)	1 (2.1%)	0 (0.0%)	0.197[a]		32 (88.9%)	3 8.3%	1 2.8%	0 (0.0%)	0.317[a]		28 (93.3%)	2 (6.7%)	0 (0.0%)	0 (0.0%)	0.127[a]	
	B	53	17 (32.1%)	28 (52.8%)	7 (13.2%)	1 (1.9%)			14 (36.8%)	17 44.7%	7 18.4%	0 (0.0%)			11 (37.9%)	16 (55.2%)	1 (3.4%)	1 (3.4%)		
	M	21	3 (13.0%)	5 (30.4%)	10 (43.5%)	3 (13.0%)			1 (10.0%)	3 30.0%	5 50.0%	1 (10.0%)			0 (0.0%)	2 (40.0%)	2 (40.0%)	1 (20.0%)		

Abbreviations: MEC, Mini-Exam Cognitive; IG, intervention group; CG, control group. N, normal; B, borderline; M, mild; Mo, moderate.
Values are presented as Number (Percentage).
[a]Marginal homogeinity test. [b]Chi-square test.