Am J of Geriatric Psychiatry 28:5 (2020) 518–529

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ajgponline.org

Regular Research Article

Effects of Cognitive Rehabilitation on Cognition, Apathy, Quality of Life, and Subjective Complaints in the Elderly: A Randomized Controlled Trial

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ARTICLE INFO

Article history:
Received March, 14 2019
Revised October, 17 2019
Accepted October, 17 2019

Key Words:
Cognitive rehabilitation
elderly
apathy
quality of life
subjective complaints
randomized controlled trial
Rehacop

ABSTRACT

Objective: *To determine the efficacy of a new-generation integrative cognitive rehabilitation (CR) program (Rehacop) on cognition, clinical symptoms, quality of life (QoL), and subjective complaints in the elderly.* ***Design:*** *A randomized controlled trial study with a cohort of elderly people over 55 years of age.* ***Setting:*** *Communities of the Basque Country (Spain).* ***Participants:*** *A total of 124 elderly participants (aged 79.00 ± 8.85 years) were randomized in the Rehacop group (RG) (n = 62) and control group (CG) (n = 62).* ***Intervention:*** *The RG attended 39 CR sessions for 3 months (3 sessions/week, 60-minute/session) with the Rehacop program. The CG performed occupational tasks with the same frequency and duration as the RG.* ***Methods:*** *Participants underwent a neuropsychological assessment at baseline and post-treatment which included cognitive, clinical, and functional tests. In addition, participants and their formal caregivers completed a subjective complaints questionnaire. The data were analyzed according to the intention to treat analysis and with participants who completed the study. This study was registered at clinicaltrials.gov (NCT03435029).* ***Results:*** *The RG showed significant improvements compared to the CG in neurocognition (ANCOVA timexgroup interaction effect size* $(\eta_p^2) = 0.05$, *90% confidence interval (CI) = 0.00–0.12). The RG also reduced apathy* ($\eta_p^2 = 0.06$, *90% CI = 0.01–0.15) and participants' subjective complaints* ($\eta_p^2 = 0.11$, *90% CI = 0.03–0.21) and improved QoL* ($\eta_p^2 = 0.08$, *90%*

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Preliminary data were presented at the XVII Zahartzaroa Congress in an oral presentation, May 17–19, 2018, Bilbao, Spain.

https://doi.org/10.1016/j.jagp.2019.10.011

CI = 0.01−0.17). ***Conclusions:*** *Participants who attended the intervention improved their cognition, QoL, and reduced apathy and subjective complaints after treatment. These findings provide a new understanding of the benefits of CR in the elderly.* (Am J Geriatr Psychiatry 2020; 28:518−529)

INTRODUCTION

Age-related cognitive decline (ARCD) is a common cognitive disturbance in the elderly[1,2] and is part of the natural aging process. It is characterized by poor performance in memory, processing speed (PS), visuospatial skills, language, and executive functioning (EF).[3−5] Several studies have also related cognitive decline in aging to mood disorders such as apathy[6,7] or depression.[8,9] Furthermore, they have been related to disability in daily living activities (ADL)[6] and both are considered risk factors for progression to dementia,[6,8,10,11] reflecting the need to address them in treatment protocols.[6,12] Cognitive decline in the elderly also affects other variables such as quality of life (QoL), which tends to become poor as deterioration increases,[13] as well as cognitive complaints, being memory complaints the most prevalent in the elderly.[14]

Due to the growing interest in ARCD over the last decades, several studies focusing on cognitive rehabilitation (CR) have emerged.[15−18] Meta-analyses have shown the direct effects of CR on improving attention, verbal memory, working memory (WM), EF, and PS performance in aging.[19−27] Another meta-analysis[23] has also shown both "near-transfer" and "far-transfer," that is to say, improvements in cognitive or functional variables that had not been directly worked. Despite this, these reviews reveal several difficulties when comparing studies, since few randomized control trials that met the search criteria, such as the CONSORT guidelines, were available.[19,21]

The effectiveness of CR in clinical symptoms has also been studied in older adults. Specifically, depression has been widely studied in aging due to its prevalence in the elderly[28] and its close relationship with memory complaints.[29] Nevertheless, CR has not been shown to improve depressive symptoms in older adults according to the Cochrane meta-analysis.[21] However, in a specific study in the elderly, the authors revealed that participants showed significantly fewer depressive symptoms following the intervention.[30]

CR has also been shown to improve functional variables such as QoL or subjective complaints in the elderly.[23,31] However, QoL improvement has been shown in pathologic samples[13,23] and improvement in subjective complaints[20] has been associated only with memory complaints.[14,32−34]

Despite this previous evidence, there is no consensus on the gains of CR and how this should be carried out.[20,21,35] In addition, most intervention programs for the elderly have focused only on specific domains such as memory, reasoning, or PS.[19] To date, as far as the authors are aware, no study has evaluated the effects of CR on cognition, fatigue, depression, apathy, neuropsychiatric behaviors or QoL in the elderly, nor on subjective complaints reported by both the elderly and their formal caregivers.

The Rehacop is a comprehensive rehabilitation program theoretically sustained, subdivided into eight modules which address both cognitive intervention and functionality, and psychoeducation.[36] This program has proven its efficacy in schizophrenia,[37,38] Parkinson's disease,[39,40] and multiple sclerosis.[41]

Therefore, the primary aim of the present study was to evaluate the efficacy of the Rehacop in improving cognitive performance in the elderly. The secondary aim was to analyze whether the Rehacop might reduce clinical symptoms and improve QoL. Additionally, the effect of the Rehacop on cognitive and functional subjective complaints was also examined for both the elderly and their formal caregivers.

METHODS

Participants

One hundred and forty participants were recruited from different day centers (centers where the elderly in Spain spend the day attending different activities like group physical activity, gardening, crafts, or reading the newspaper, with a wide range of services provided by nurses, gerontologists, and sports trainers). The recruitment was carried out from September

2012 to November 2016 in the Basque Country (Spain). The inclusion criteria were as follows: 1) age over 55 years; 2) signing informed consent; 3) normal overall cognitive functioning, as determined by a score on the Mini-Mental Status Exam (MMSE),[42] which was above the 10th percentile for participant age and education level;[43] and 4) independence in ADL according to the Likert-type semistructured interview, conducted by the clinicians responsible for the day centers. Exclusion criteria included: 1) history of neurologic condition (neurodegenerative disease, dementia, traumatic brain injury, or cerebrovascular disease); 2) diagnosis of psychiatric disorder or significant neuropsychiatric symptoms (The Neuropsychiatric Inventory Questionnaire [NPI-Q][44] >4); 3) illiteracy; and 4) relevant physical impairment. Of the initial sample of 140 participants, 10 did not meet the inclusion criteria, 6 declined to participate, and 5 participants were excluded for protocol violation (incorrect or missing tests; see Fig. 1 for the flow diagram). The final sample included 119 participants (40 males, 79 females) aged between 56 and 95 years (M = 79.25, SD = 8.78 years).

Procedure

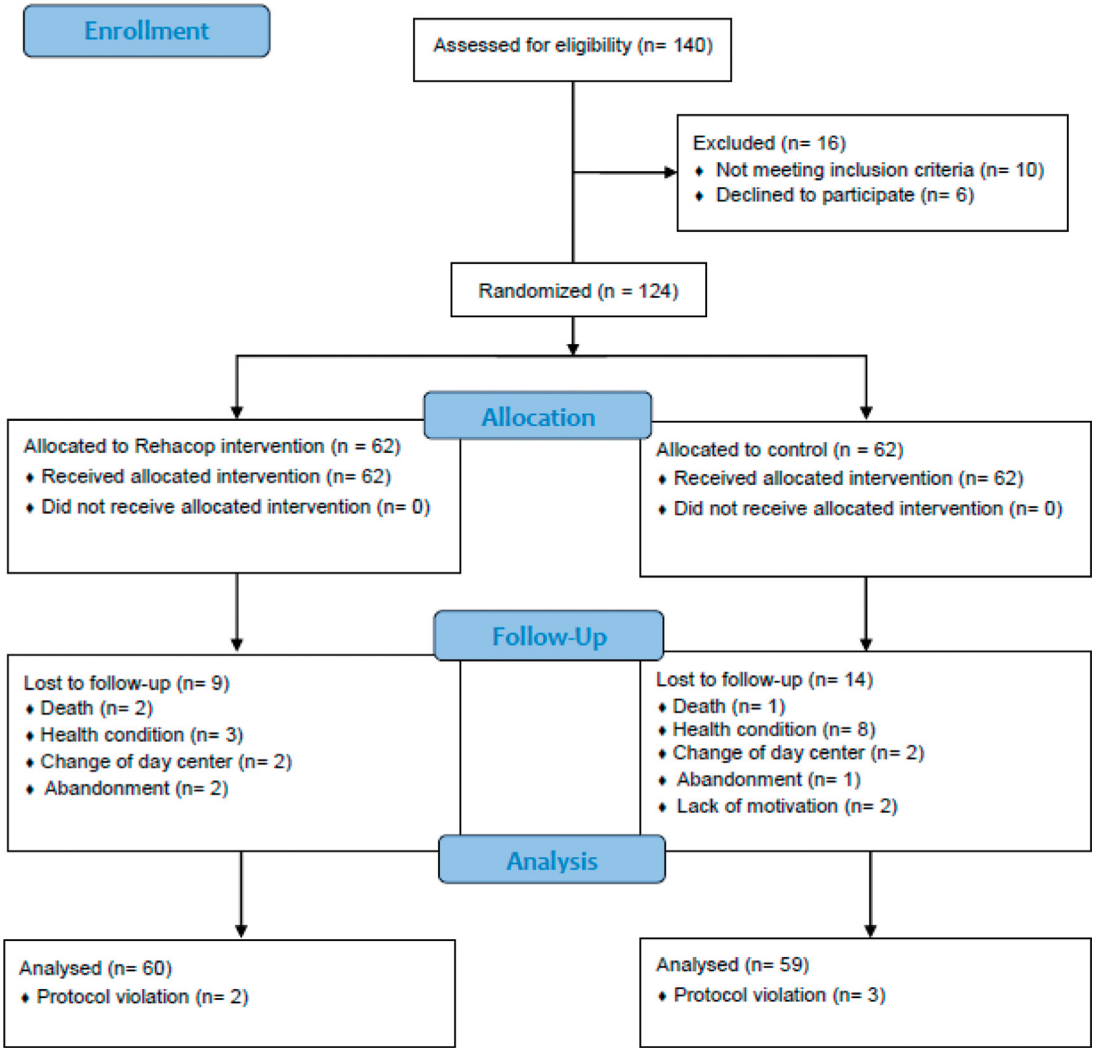
A priori power analysis using G*Power 3.1[45] software was conducted before recruitment was fulfilled to determine the sample size based on a previous study.[38] The results obtained stablished that a sample size of 104 subjects, 52 per group, was sufficient to attain an effect size of $\eta^2 = 0.08$ to detect between-group differences in cognitive performance, with 85% power and a 5% level of significance. The study design was a single blind, parallel-group randomized controlled trial with equal randomization. All users of day centers were invited to participate in the study and were blinded to treatment condition. All participants underwent a clinical interview, an evaluation of their general cognitive status with the MMSE[42] and the Montreal Cognitive Assessment (MoCA),[46] and an estimation of their premorbid IQ with The Word Accentuation Test (TAP)[47] and the Assessment Battery of Reading Processes (PROLEC).[48] The presence of neuropsychiatric symptoms was examined using the NPI-Q,[44] and the cognitive reserve was measured with the Cognitive Reserve Questionnaire.[49] A neuropsychological assessment was also conducted with the scales described in the primary outcome measure. Additional clinical scales for apathy, depression and fatigue, and functional scales (QoL and subjective cognitive and functional questionnaire for participants and caregivers) were administered. Participants were assessed twice: first, at baseline (T_0) and second, in the first week after treatment was completed (T_1). All the tests and questionnaires were completed by the participants except for the version of the subjective questionnaire for formal caregivers, which was completed by the caregivers themselves. The participants were randomly allocated to an experimental group or an active CG on a 1:1 ratio (Fig. 1) using an online computer-generated group (randomizer.org).

OUTCOME MEASURES

Primary Outcome Measure

The primary outcome measure was an overall neurocognition composite score based on the main cognitive domains (attention, verbal fluency, verbal and visual learning and memory, visual perception, visuoconstructive abilities PS, WM, and EF). The tests and subtest included in neurocognition were the following: Digits forward and backward subtest from the Wechsler Adult Intelligence Scale-III (WAIS-III),[50] total score of the Brief Test of Attention (BTA),[51] the Calibrated Ideational Fluency Assessment (CIFA)[52] (words beginning with "p" in 3 minutes, animals, and supermarkets in 1 minute), the Stroop Test (word-color),[53] learning and delayed recall scores of the Hopkins Verbal Learning Test-Revised (HVLT-R)[54] (parallel versions 2 and 4 corresponding to basal and post-treatment assessment), learning and delayed recall scores of the Brief Visual Memory Test-Revised (BVMT-R)[55] (version 1), the Trail Making Test (part A),[56] the Salthouse Perceptual Comparison Test (SPCT),[57] incomplete letters and cube analysis of the Visual Object and Space Perception Battery (VOSP),[58] and free drawing of the Clock Drawing Test (CDT).[59] The neurocognition composite score reached satisfactory internal consistency (Cronbach's $\alpha = 0.89$). MoCA,[46] the Taylor Complex Figure Test (TCF),[60] and Modified Wisconsin Card Sorting Test (M-WCST)[61] were added to the protocol after starting the study. As the missing data from each test were greater than 50%, it was not included in the analyses.

FIGURE 1. CONSORT 2010 flow diagram. CONSORT: Consolidated Standards of Reporting Trials.



Secondary Outcome Measure

The secondary outcome measures included analysis of subjective complaints, as well as analysis of clinical variables and QoL.

Subjective complaints from participants and formal caregivers were assessed with the Subjective Questionnaire on Cognitive and Functional Complaints.[36] This questionnaire consists of two versions: the first is administered to the patient whereas the second is completed by the formal caregiver. Each part comprises 35 items divided into 6 subscales (attention, memory, language, EF, social cognition, and ADL). Higher scores indicate a higher frequency of subjective complaints. The reliability of the participants' version and the caregivers' version of the test was acceptable $\alpha = 0.84$ and $\alpha = 0.85$, respectively. These questionnaires are included in the Rehacop therapist manual.[36]

The secondary outcome measures also included analyses of apathy, fatigue, depression, neuropsychiatric behaviors, and QoL. The Spanish version of the Lille Apathy Rating Scale (LARS)[62] was used to evaluate apathy. Lower scores indicate fewer apathy symptoms (ranging from −36 to 36). Fatigue was measured using the general index of the

Multidimensional Fatigue Inventory (MFI).[63] Higher scores indicate greater fatigue (ranging from 0 to 140 points). Depression was measured with the Spanish version of the Geriatric Depression Scale.[64] Higher scores indicate more depressive symptoms (ranging from 0 to 15). Neuropsychiatric behaviors were analyzed using NPI-Q.[44] This questionnaire includes 10 neuropsychiatric behaviors assessed in terms of severity and frequency on a scale of 0−120 points. Higher scores indicate greater neuropsychiatric behaviors. QoL was measured using the Satisfaction With Life Scale (SWLS).[65] Higher scores indicate higher life satisfaction (ranging from 0 to 35).

Intervention

The experimental group (n = 62) received CR sessions with the Rehacop program. The CG (n = 62) performed different occupational tasks (reading and commenting on the newspaper, drawing, gardening, singing, and crafts) in group format led by a psychologist with the same frequency and duration as the experimental group. Once the post-treatment assessments were completed, the CG was invited to perform CR in accordance with ethical standards.

The Rehacop is a CR program structured in cognitive domains with five levels of difficulty.[36] It is theoretically based on strategies of rehabilitation (restoration, compensation, and optimization). The Rehacop uses a bottom-up approach. Top-down training with the ADL module is used later to help with the generalization of gains to the participant's life. It is a 5-month intervention allowing either an individual or group approach. It is structured hierarchically into four cognitive modules (attention and concentration, learning and memory, language, and EF), three modules of functionality (social cognition, social skills, and ADL), and one psychoeducation module.

This study uses a shortened version (a 3-month version in contrast to the original 5-month version) of the Rehacop program in order to train the most affected cognitive domains in the elderly. The RG took part in 39 sessions divided into: attention and concentration (sustained, selective, alternating, and divided attention) over 4 weeks; learning and memory (verbal and visual memory and learning strategies) 3 weeks; language (verbal fluency, syntax, grammar, vocabulary, and comprehension) 3 weeks; EF (objectives planning and attainment, verbal reasoning, categorization, and conceptualization) 3 weeks, and PS training was given transversely throughout the course of the sessions with time limits for some exercises. Some examples of the tasks performed are: selective attention training: after being shown 2 almost identical images, participants had to find the 10 differences between them; learning and memory training: after receiving psychoeducation on memory strategies, participants had to memorize lists of words which had to be organized according to categories. Nine RGs (with up to eight participants each) were formed. RG sessions were conducted by one qualified neuropsychologist per group, using the same instructions and material three times a week in 60-minute sessions over a 3-month period. The rehabilitation sessions were performed at the day centers.

In cases where a participant failed to attend a session, an appointment was set with her/him in order to review the tasks and clear up any possible queries. A correction feedback session with the participant was made to discuss their performance as well as any difficulties or strategies. However, the attendance rates for the RG and CG was not systematically registered.

Ethics Statement

The study protocol was approved by the Ethics Committee of the University of Deusto (Bilbao). All participants were volunteers and gave their informed consent to participate in the study, which was conducted in accordance with the Helsinki Declaration.[66] This study was registered at clinicaltrials.gov (NCT03435029).

Statistical Analyses

Data analysis was carried out using IBM SPSS[67] (v23). The normal distribution of the data was analyzed using Kolmogorov-Smirnov. Differences between groups at baseline in sociodemographic, cognitive, QoL, and clinical variables were tested with the Mann-Whitney *U* test or 2-tailed *t* test. Categorical data were analyzed using the chi-squared test (χ^2). All variables showed a non-normal distribution except TAP, verbal fluency, fatigue, BTA, and participants' subjective complaints. All cognitive raw scores were converted to z-scores (Tables 2 and 3). The TMT-A

score was adjusted so that higher scores indicated better performance. The z-scores were pooled into a neurocognition composite score which was based on the average of the following tests and subtests included in the protocol, that is: total BTA score; total score of the forward digits and total score of the backward digit of the WAIS-III; total number of words beginning with the letter "p" in 3 minutes and total number of words for animals and supermarket categories in 1 minute in the CIFA; total learning score and total long-term recall score in the HVLT-R; total learning score and total long-term recall score in the BVMT-R; total free drawing score in the CDT; total letters score and total cube analysis score in the VOSP; TMT-A time; total SPCT score; and the total word-color trial score in the Stroop Test.

Missing data were imputed using multiple imputation with the Expectation-Maximization (EM) algorithm.[68,69] The Little's MCAR revealed the missing data were completely missing at random. The missing data on neurocognition ranged from 0% to 18.5% at baseline and 14.03% to 17.6% at post-treatment. The range of missing data for clinical and functional variables ranged from 14.3% to 26.1% at baseline and 14.03% to 40.3% at post-treatment.

Statistical analyses were run twice: first, according to the ITT analysis, and second, only with participants who had completed the study (per protocol analysis [PP]). In the ITT analysis, the differences in primary and secondary outcomes between groups at baseline and post-treatment were analyzed using two (group) by two (time) repeated measures ANCOVA in order to assess time according to group interaction after controlling for the participants' complaints scores at baseline. In the PP analyses, repeated measures ANCOVA was used to determine the intervention's efficacy (timexgroup interaction) in the primary and secondary outcomes after controlling for the apathy scores at baseline. Eta partial square (η_p^2) describes an effect size of 0.01 as small, 0.06 as medium, and 0.14 as large. Following previous studies[70–72] the 90% confidence interval (CI) was used to calculate the effect size. The ITT and PP analyses were corrected for multiple comparisons using the Benjamini-Hochberg method[73] to control for the false detection rate of $\alpha = 0.05$.

Additionally, in order to explore whether cognitive reserve moderates the effect of treatment arm on outcome measures, moderation analysis was carried out.[74] Linear regression analyses were performed on the ITT sample.

RESULTS

Sample Characteristics at Baseline

Of the 140 participants invited to take part, 7.14% were excluded by the inclusion criteria and 4.28% declined to participate. Of the 124 randomized participants, 101 completed the treatment. Five participants were excluded for protocol violation (incorrect or missing tests). The attrition rate after 3 months was 18.54% (Fig. 1). The sample analyzed consisted of 119 participants. There were no significant differences in the sociodemographic and neuropsychological basal variables (Mann-Whitney U and p values ranged from 424.00 to 1,153.50 and from 0.052 to 0.957, respectively), between the participants who completed the treatment and those who did not. ITT and PP analyses were used.

The sociodemographic and clinical variables of the RG and CG are shown in Table 1. No significant differences in sociodemographic variables, neurocognition, clinical variables, or QoL were found between the groups at baseline in the ITT sample, except for participants' subjective complaints ($t_{(117)} = -2.59$, $p = 0.011$). In the PP sample, the CG turned out to be significantly more apathetic ($U_{(101)} = 938.50$, $p = 0.023$).

Primary Outcome

After the intervention, the experimental group showed better performance in neurocognition in comparison with the CG (ANCOVA timexgroup interaction) with a small effect size ($\eta_p^2 = 0.05$, 90% CI = 0.00 −0.12; Table 3). The repeated measures ANCOVA timexgroup interaction for PP analyses showed very similar results ($F_{(1, 97)} = 17.17$, $p < 0.001$, $\eta_p^2 = 0.15$).

Secondary Outcome

Repeated measures ANCOVA timexgroup interaction showed significant differences between groups after the intervention, showing that the RG reduced apathy symptoms ($\eta_p^2 = 0.06$, 90% CI = 0.01−0.15) and participants' subjective complaints ($\eta_p^2 = 0.11$, 90% CI = 0.03−0.21), and improved QoL ($\eta_p^2 = 0.08$,

TABLE 1. Sociodemographic and Clinical Variables at T_0

		Control Group (n = 59) Mean (SD)	Rehacop Group (n = 60) Mean (SD)	t[a]/U[b]/χ^{2c}	*p*
Age		79.90 (9.05)	78.62 (8.43)	1,591.00	0.342
Years of education		8.31 (2.47)	8.28 (2.40)	1,598.50	0.712
TAP		17.44 (5.25)	18.73 (5.80)	−1.27	0.205
PROLEC		33.19 (5.03)	34.15 (5.14)	1,519.50	0.182
Sex	Male	17 (28.8%)	23 (38.3%)	1.208	0.272
	Female	42 (71.2%)	37 (61.7%)		
MMSE		25.90 (2.41)	26.37 (2.27)	1,598.50	0.356
Cognitive reserve		9.98 (3.23)	9.70 (3.44)	1,741.00	0.877
NPI-Q		0.86 (1.90)	0.70 (1.92)	1,662.00	0.436

Notes: n: sample; SD: standard deviation; t: paired t tests; U: Mann-Whitney U test; χ^2: chi-squared test; TAP: The Accentuation Reading Test; PROLEC: Assessment Battery of Reading Processes; MMSE: Mini-Mental State Examination; NPI-Q: Neuropsychiatric Inventory Questionnaire.
[a] $t_{(117)}$.
[b] $U_{(119)}$.
[c] $\chi^2_{(1)}$.

90% CI = 0.01−0.17) with a medium effect size (Table 3). The repeated measures ANCOVA time-xgroup interaction for PP analyses showed very similar results for apathy symptoms ($F_{(1,\ 99)} = 7.41$, $p = 0.008$, $\eta_p^2 = 0.07$), participants' subjective complaints ($F_{(1,\ 89)} = 8.69$, $p = 0.004$, $\eta_p^2 = 0.09$), and QoL ($F_{(1,\ 98)} = 10.80$, $p = 0.001$, $\eta_p^2 = 0.09$). Nevertheless, depressive symptoms ($F_{(1,\ 98)} = 0.47$, $p = 0.829$, $\eta_p^2 = 0.00$), fatigue ($F_{(1,\ 97)} = 0.91$, $p = 0.342$, $\eta_p^2 = 0.01$), neuropsychiatric behaviors ($F_{(1,\ 98)} = 0.19$, $p = 0.666$, $\eta_p^2 = 0.00$), and caregivers' subjective complaints ($F_{(1,\ 58)} = 0.00$, $p = 0.982$, $\eta_p^2 = 0.00$) showed no changes after treatment in any of the analyses performed (Table 3).

Linear regression analyses showed no cognitive reserve moderation effect on the intervention effects: neurocognition ($\beta = 0.02$; $p = 0.403$), apathy ($\beta = 0.05$; $p = 0.450$), fatigue ($\beta = 0.09$; $p = 0.326$), depressive

TABLE 2. Cognitive Performance Raw Scores in the Rehacop and Control Group at T_0

	Control Group (n = 59)			Rehacop Group (n = 60)		
	Mean	95% CI	SD	Mean	95% CI	SD
Digit forward	6.27	(5.95, 6.59)	1.21	6.27	(5.88, 6.65)	1.49
Digit backward	3.73	(3.37, 4.08)	1.36	3.62	(3.25, 3.98)	1.41
Salthouse	10.83	(9.23, 12.43)	6.13	11.75	(10.21, 13.29)	5.96
TMT-A	78.90	(74.80, 83.00)	15.74	76.67	(72.27, 81.07)	17.04
BTA	42.51	(38.70, 46.32)	14.62	11.48	(10.46, 12.50)	0.51
Stroop WC	10.31	(9.19, 11.41)	4.26	24.34	(19.21, 29.47)	2.56
CIFA animals	12.31	(11.22, 13.39)	4.17	12.67	(11.52, 13.81)	4.43
CIFA supermarket	13.39	(12.17, 14.61)	4.68	12.58	(11.45, 13.72)	4.38
CIFA "p" words	16.05	(13.66, 18.44)	9.01	17.18	(7.04, 9.09)	3.97
HVLT-R learning	15.37	(14.05, 16.70)	5.09	15.98	(14.98, 19.38)	8.51
HVLT-R recall	3.15	(2.39, 3.92)	2.93	3.00	(2.35, 3.65)	2.52
BVMT-R learning	10.32	(8.46, 12.19)	7.15	9.50	(8.12, 10.88)	5.33
BVMT-R recall	3.64	(2.78, 4.51)	3.30	3.28	(2.55, 4.01)	2.82
Clock-D	7.12	(6.50, 7.74)	2.38	7.83	(7.29, 8.36)	2.06
VOSP-L	16.85	(15.77, 17.93)	4.14	17.12	(16.15, 18.08)	3.74
VOSP-N	7.15	(6.53, 7.77)	2.38	7.55	(6.81, 8.29)	2.86

Notes: n: sample; CI: confidence interval; SD: standard deviation; MMSE: Mini-Mental State Examination; TMT-A: Trail Making Test-A; BTA: Brief Test of Attention; Stroop WC: Stroop Test Word-Color; CIFA: Calibrated Ideational Fluency Assessment; HVLT-R: Hopkins Verbal Learning Test-Revised; BVMT-R: Brief Visuospatial Memory Test-Revised; Clock-D: Clock Drawing Test-free drawing; VOSP-L: Visual Object and Space Perception Battery-Letters; VOSP-N: Visual Object and Space Perception Battery-Numbers.

TABLE 3. Repeated Measures ANCOVA for Primary and Secondary Outcome for the Rehacop and Control Group From T_0 to T_1

		Control Group (n = 59)		Rehacop Group (n = 60)		Time		Group		Timexgroup		Effect Size
		Mean 95% CI	SD	Mean 95% CI	SD	*F*	*p*	*F*	*p*	*F*[a]	*p*	η_p^2
Neurocognition	T_0	−0.04 (−0.21, 0.11)	0.67	0.04 (−0.11, 0.21)	0.55	0.00	0.984	2.00	0.159	5.57	0.020	0.05
	T_1	−0.10 (−0.27, 0.05)	0.65	0.09 (−0.05, 0.27)	0.57							
Subjective complaints-P	T_0	−0.17 (−0.37, 0.13)	0.59	0.17 (−0.16, 0.36)	0.86	0.00	0.974	0.83	0.364	15.03	<0.001	0.11
	T_1	0.07 (−0.09, 0.25)	0.70	−0.07 (−0.24, 0.09)	0.62							
Subjective complaints-C	T_0	0.04 (−0.16, 0.28)	0.86	−0.04 (−0.27, 0.16)	0.82	0.00	0.996	1.18	0.279	0.26	0.606	0.00
	T_1	0.06 (−0.12, 0.31)	0.88	−0.06 (−0.31, 0.12)	0.78							
GDS	T_0	2.08 (1.74, 2.79)	2.27	2.07 (−0.29, 0.21)	2.00	1.30	0.255	0.97	0.325	0.18	0.670	0.00
	T_1	1.94 (1.57, 2.50)	1.89	0.88 (1.32, 2.24)	1.71							
LARS	T_0	−20.49 (−22.54, −18.16)	8.38	−22.33 (−24.64, −20.29)	8.34	2.03	0.157	0.10	0.001	7.96	0.006	0.06
	T_1	−19.54 (−21.10, −17.58)	7.40	−25.24 (−27.17, −23.68)	6.03							
SWLS	T_0	27.31 (25.51, 28.53)	4.09	25.67 (24.44, 27.44)	6.64	2.10	0.149	0.67	0.415	10.46	0.002	0.08
	T_1	26.31 (24.30, 27.62)	7.88	28.31 (27.00, 30.29)	4.70							
MFI	T_0	15.22 (13.43, 16.90)	6.15	16.82 (15.15, 18.59)	7.00	0.50	0.480	1.14	0.287	0.61	0.436	0.01
	T_1	15.01 (13.41, 17.07)	5.83	15.88 (13.83, 17.46)	8.04							
NPI-Q	T_0	0.86 (0.47, 1.45)	1.90	0.70 (0.11, 1.08)	1.92	1.40	0.239	2.15	0.144	0.04	0.845	0.00
	T_1	0.64 (0.38, 1.02)	1.40	0.48 (0.95, 0.72)	1.08							

Notes: n: sample; *F*: repeated measures ANCOVA; CI: Confidence Interval; SD: Standard Deviation; η_p^2: partial eta squared; Subjective complaints-P: Cognitive and functional subjective complaints Participants' questionnaire; Subjective complaints-C: cognitive and functional subjective complaints Formal Caregivers' questionnaire; GDS: Geriatric Depression Scale-15; LARS: Lille Apathy Rating Scale; SWLS: Satisfaction With Life Scale; MFI: Multidimensional Fatigue Inventory; NPI-Q: Neuropsychiatric Inventory Questionnaire.

[a] $F_{(1,116)}$.

symptoms ($\beta = -0.05$; $p = 0.458$), quality of life ($\beta = 0.025$; $p = 0.594$), participants' subjective complaints ($\beta = -0.02$; $p = 0.683$), and caregivers' subjective complaints ($\beta = -0.09$; $p = 0.145$). However, the cognitive reserve showed a moderation effect on neuropsychiatric behaviors ($\beta = 0.27$; $p = 0.002$; $\Delta R^2 = 0.068$). Specifically, the experimental group with higher cognitive reserve showed fewer neuropsychiatric symptoms after the treatment in comparison with the CG. In contrast, the experimental group with lower cognitive reserve showed more neuropsychiatric symptoms after the treatment in comparison with the CG. Nevertheless, the group variable did not prove to be significant in the regression analysis, indicating a lack of significant improvement.

DISCUSSION

The primary aim of this study was to assess the efficacy of the Rehacop program in neurocognition, and the secondary aim was to determine its efficacy in clinical variables, QoL, and subjective complaints. The results showed direct effects as well as far-transfer effects after the intervention. Specifically, the RG showed direct effect on neurocognition in comparison with the CG. The RG also showed far-transfer effects on apathy, QoL, and subjective complaints. The effect size was small for neurocognition, medium for apathy and QoL, and large for participants' subjective complaints. This improvement is not due to the training in response to the neuropsychological assessment since, in general, the rehabilitation tasks differed sufficiently from the tests administered. Nor can it be attributed to the duration or the intervention's group format, as they were the same for both groups.

These results are in agreement with other studies[16,18,75–77] that found improvements in attention, verbal memory, phonological fluency, WM, PS, and reasoning with similar small effect sizes, which range from Cohen's d values 0.16 to 0.36.[19]

Along with the previous findings from different meta-analysis and systematic reviews,[21,26,27,78,79] our results support the idea that there is brain plasticity in the elderly and reveal that comprehensive CR could be effective in preventing ARCD, as suggested by other authors.[80] However, longitudinal follow-up of CR is needed to confirm that cognitive, clinical, and QoL gains are maintained over time.

The second aim was to evaluate whether rehabilitation would reduce apathy, depression, fatigue, neuropsychiatric behaviors, and improve QoL in comparison to the CG. Our results showed that the RG reduced apathy after rehabilitation with a medium effect size. Given the relationship between apathy, cognitive performance[10,81–83] and instrumental ADL,[6] we suggest applying CR from a holistic perspective. However, as far as we know, there are no published studies linking CR with improvement in apathy in older people without dementia. Future research is needed to determine whether CR could reduce severe apathy in elderly samples.

Contrary to our expectations, significant differences in depression, fatigue, and neuropsychiatric behaviors were not found. Actually, both groups showed fewer depressive symptoms, fatigue, and neuropsychiatric behaviors at post-treatment. Other studies have also shown a trend toward improvement in depression after CR.[30] A possible explanation could be that our sample did not show pathologic scores for depression, reaching the ceiling effect. Regarding fatigue, unlike apathy or depression, it is not as common in aging as in other pathologies such as Parkinson disease,[84] so it may not benefit from the intervention like other clinical variables. With regard to neuropsychiatric behaviors, they are not expected to improve greatly due to the established exclusion criteria. Nonetheless, the 2 groups show a slight improvement after the intervention. However, moderation analyses have revealed that the cognitive reserve moderates the presence of neuropsychiatric behaviors after receiving CR.

An additional finding was the improvement in QoL in the RG with a medium effect size. Only one study showed improvement in QoL after treatment[31] with a small effect size. However, the effect size obtained in our study may be a conjunction of the improvement obtained by the experimental group combined with the slight decrease in QoL in the CG.

A further finding was that the RG perceived significant differences in cognitive and functional complaints after rehabilitation. Similar results have been found in the review by Reijnders et al.,[79] showing that CR improves the subjective perception of memory.

Our study has some limitations that should be considered. First, in the ITT sample, the experimental group showed significantly more subjective complaints at baseline and the CG was significantly more apathetic at baseline in the PP sample. Second, only

the participants were blinded to treatment condition, and the authors cannot ensure that participants had not guessed which group they had been assigned to. Third, the groups' attendance rates were not systematically registered and, in consequence, the authors cannot determine whether the participants attending all the sessions performed better in the neuropsychological tests compared to the absentees, who carried out the tasks at home. In addition, the sample included in this study has a low educational level, which is representative of the Spanish population of such ages, but cannot be generalized across other populations.[43] Moreover, the verbal memory delayed recall score seems to be low for age and educational level, so participants may show long-term memory decline. Apart from that, other cognitive training studies on the elderly,[85] as well as studies with the Rehacop program on schizophrenia[38] and Parkinson's disease,[39] included specific tests in their protocol to evaluate functionality, which showed improvements after training. Future analysis of the relationship between cognitive training and the Rehacop program and functionality in the elderly is needed. Additionally, the results of this study show the benefits obtained after 3-month of CR. At present, we do not know the long-term effects of this intervention. Longitudinal studies are needed to determine to what extent the improvement obtained is maintained in the long term. In this regard, our group is currently working on the analysis of the results, after a 12-month follow-up, to investigate whether the changes post-CR are maintained in the long term.

DISCLOSURE

The authors would like to thank all of the different day centers for their contribution and the participants for their collaboration.

N.O. and J.P. are co-authors and copyright holders of the Rehacop cognitive rehabilitation program, published by Parima Digital, S.L. (Bilbao, Spain). G.M.M. and N.I.B. have no conflicts of interest to report. N.I.B, J.P., and N.O. received funds from the Education Department of the Basque Government (Equipo A) (IT946-16). G.M.M. received a collaborative predoctoral grant from the University of Deusto.

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