

AIMS Medical Science, Volume 3(1): 1–14.

DOI: 10.3934/medsci.2016.1.1 Received 29 September 2015,

Accepted 2 December 2015, Published 10 December 2015

http://www.aimspress.com/journal/medicalScience

Research article

The Efficacy of Cognitive Stimulation on Depression and Cognition in Elderly Patients with Cognitive Impairment: A Retrospective Cohort Study

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Abstract: Cognitive decline due to neurodegenerative diseases is a prevalent worldwide problem. Both pharmacological and non-pharmacological treatments to improve, delay or stop disease progression are of vital importance. Cognitive stimulation is frequently used in clinical practice; however, there are few studies that demonstrate its efficacy. Aim: To evaluate the efficacy of cognitive stimulation in patients with mild cognitive impairment (CDR = 0.5) and dementia (CDR = 1). Methods: A retrospective cohort study was performed. Patients with cognitive impairment receiving weekly cognitive stimulation (16 or 24 sessions) were evaluated with a complete neuropsychological battery before and after the stimulation program. Each stimulation session was carried out by a trained neuropsychologist. Results: Forty two patients receiving cognitive stimulation were evaluated over a period of 12.53 months (SD 5.5). Patients were grouped as 11 amnesic mild cognitive impairment (aMCI), 23 multi domain mild cognitive impairment (mMCI) and 8 Mild Alzheimer's Dementia (CDR 1). None of the groups improved their cognitive functions after the cognitive stimulation program. MCI group was also divided according to their global intelligence quotient (IQ) into two groups: low (IQ < 98.5) and high (IQ > 98.5). Each group was compared before and after the stimulation program and no significant difference was found ($p \ge 0.05$). Moreover, MCI group was also analyzed according to the duration of the stimulation program: less than 9, between 9 and 13 and more than 13 months. Different duration groups were compared before and after the cognitive stimulation program and no significant differences were found. Depression, anxiety and subjective memory symptoms were also analysed and neither improvement nor worsening could be demonstrated. Conclusions: Patients remained stable, both in cognitive and behavioural domains, for more than 18 months. However, no significant cognitive or behavioural improvement can be reported in these patients after the stimulation program (duration time: 12.53 months SD 5.5).

Keywords: mild cognitive impairment; Alzheimer Disease; dementia; cognitive stimulation; cognitive reserve

1. **Introduction**

Cognitive decline due to neurodegenerative diseases is a prevalent worldwide problem affecting more than 400.000 people in Argentine [1]. Both pharmacological and non-pharmacological treatment to improve, delay or stop the disease progression is of vital importance. Pharmacological therapy already approved for patients with dementia, such as cholinesterase inhibitors (CheIs), have been tested in individuals with amnesic mild cognitive impairment (aMCI) in randomized clinical trials. However, a systematic review did not show any delay in the progression to Dementia in the CheIs patient groups compared to placebo groups [2]. In this context, health care professionals should be aware of other available therapies for these populations such as cognitive interventions.

There are three categories of cognitive intervention to improve memory and other cognitive functions: stimulation, training and rehabilitation.

Cognitive stimulation (CS) is based on patient engagement in a range of activities and discussions, usually in groups, which aims to stimulate general enhancement of cognition and functioning [3]. Cognitive stimulation involves a general approach whereby cognitive functions, such as memory, are not used in isolation but in an integrated manner with other domains such as language, attention and executive functions [4].

Cognitive training involves the guided practise of a set of standard tasks designed to enhance a particular cognitive function such as attention, memory or executive function. The general concept is that continuous practise can improve or at least maintain a particular cognitive domain [5,6].

Cognitive rehabilitation is a more individualized approach to help people with cognitive impairment. In cognitive rehabilitation, patients and their family work together with the health care professionals in order to identify personal relevant goals and device strategies for addressing these. The principal aim of cognitive rehabilitation is to enhance functioning in everyday context [7].

In a systematic review, where randomized controlled trials (RCT) of CS for dementia were included, Woods et al. concluded that CS enhances cognitive functions in people with mild and moderate dementia [8]. Although a benefit was found in cognitive functions (specially memory), the

main improvement was demonstrated in quality of life and well being, with no improvement in everyday functioning [8].

However, there are few reports and research studies about the effects of cognitive stimulation therapy in people with MCI. Moreover, follow up time of many studies are only of a few months.

It is well known that the results of randomized controlled clinical trials (RCT) are not always seen in clinical practise where patient and doctor behaviours are very different from that in an RCT context [9].

The objective of this research was to study the efficacy of CS therapy for delaying, stopping or improving cognitive decline.

2. **Methods**

2.1. Study

A longitudinal, retrospective, no controlled observational study was performed with patients attending to the memory clinic of the CEMIC University Hospital between 2012 and 2015.

2.2. Study population

Patients who consulted for memory problems at the CEMIC University Hospital were recruited. Patients were assessed with at least two cognitive evaluations, one before and the other after the cognitive stimulation program. Patients, who participated in the study, attended to at least 16 stimulations sessions each year.

2.2.1. Inclusion criteria

Patients over 65 years old at the moment of the first cognitive evaluation

Patients who accepted to participate in this research project and signed an informed consent

Patients with aMCI, mMCI or Mild Alzheimer's Dementia (CDR1) [10]

2.2.2. Exclusion criteria

Patients with a psychotic disorder

Patients who did not accept to participated in this research

Alcohol o substance disorders

Patients with severe communications skills

All patients underwent neurological and psychiatric evaluation, laboratory tests to exclude reversal dementia aetiologies (vitamin B12 or folic acid deficiencies, venereal disease research laboratory, thyroid function) and magnetic resonance imaging of the brain.

Patients were diagnosed with mild cognitive impairment according to Petersen et al. [11,12] and classified as follows:

aMCI (n = 11): patients having low performance only on memory tests, less than 1.5 standard deviations below mean values, according to age and education. Immediate memory recall, delay memory recall and recognition were considered to evaluate memory domain.

mMCI (n = 23): patients with low performance in several cognitive domains: e.g. attention, memory, language, executive functions and visuospatial ability, less than 1.5 standard deviations below the mean values, according to age and level of education. Immediate memory recall, delay memory recall and recognition were used to evaluate memory; trail making A (TMA) and digit number (WAIS) were considered to assess attention; trail making B (TMB) and phonological fluency were used to evaluate executive function; Boston Naming Test (BNT) and semantic fluency were the parameters to assess language and Rey Complex Figure was used to assess visuospatial abilities.

Mild Alzheimer's Dementia (n = 8): patients who met the Diagnostic and Statistical Manual for Mental Disorders IV edition (DMS IV) criteria for dementia [13] and the National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association (NINDS-ADRA) criteria [14] the lower repercussion in their everyday life activities according to the Cognitive Dementia Rating Scale (CDR 1).

Both aMCI and mMCI patients (n = 34) were grouped according to their Global IQ and classified as above and below the median IQ value (98.5), since higher IQ is one of the hallmarks of cognitive reserve [15].

Patients received between 16 and 24 CS sessions. All MCI patients (n = 34) were divided in three groups: less than 9 months, between 9 and 13 months and more than 13 months of stimulation.

3. Neuropsychological Test Battery

All patients were evaluated with a complete test battery to assess the following cognitive domains:

Memory: Rey Auditory Verbal Learning Test [16]

Attention: Digit span forward and reverse and TMA [17]

Executive and Visuospatial functions: TMB [17] and Rey Complex Figure [18]

Language: Boston Naming Test [19], semantic fluency and phonological fluency [20]

Language and Executive Intelligence Quotient: Wechsler Abbreviated Scale of Intelligence (WASI) that consists of four items: matrix reasoning and block design for executive functions, vocabulary and similarities for language [21,22].

The Mini Mental State Examination (MMSE) was not included in this battery since Global Intelligence Quotient was used as a measure of Global Cognition [11].

All patients were also evaluated with the Hospital Anxiety Depression Scale (HAD) and the subjective memory scale of McNair [23,24].

4. Cognitive Stimulation Program

CS was based in patient's involvement in group activities which aimed to enhance cognitive and functional activities with no specific patterns. It included various topics such as word association, object categorization, visual imaging, discussion of current affairs, orientation and executive control training techniques. The program was built on person-centred care principles, emphasizing the importance of treating people with dementia as adult individuals.

The CEMIC health system covers up to 24 sessions each year that are automatically renewed. The sessions were carried out by trained neuropsychologists, lasted one hour, and patients were grouped (two to four patients of similar clinical characteristics).

During sessions, three of the following domains were at least stimulated: language, attention, executive functions and memory. For example, to stimulate episodic memory, patients were asked to read or hear to a story, or watch a video. Spatial memory was trained by learning places and object locations. Patients were encouraged to use association strategies, categorization, visual imaging and to write down notes as a way of consolidating learned issues. Attention was stimulated through visual exercises designed to search and identify numbers, letters and images, asking the patient to avoid omissions. Distracting complex graphic exercises were also provided to stimulate attention. Language was stimulated by object denomination, word categorization, concept association, word definition, among others. Finally, executive functions were stimulated by the organization of lists of words, pathway planning and daily living activities organization.

5. Statistical Analyses

The statistical analysis was performed with SPSS 15.0 software. The mean and standard deviations for quantitative variables and the distribution and frequency for qualitative variables were obtained. The analysis of variance was used to compare variables between groups. When normal distribution was not assumed a Kruskal Wallis test was performed. Groups were compared before and after the stimulation program intervention using a t-test for related groups (different time between evaluations). A gain score [(post-score – pre-score)/pre-score] was calculated for each variable. Comparison of gain scores between groups were made with ANOVA using a non parametric test. The value of p < 0.05 was considered as statistically significant.

6. **Results**

Forty two patients attending to the memory clinic of the CEMIC University Hospital were included, Demographical variables are depicted in Table 1. There were no statistically significant differences in the demographic variables between groups.

Table 1. Demographics variables at baseline.

	aMCI	mMCI	Dementia (CDR 1)	n volue
	(n = 11)	(n = 23)	(n = 8)	<i>p</i> -value
Age (Mean and SD)	70.9 (+/-24.29)	77.19 (+/-5.06)	78.4 (+/-3.24)	0.78
Gender (F/M)	7/11	14/23	6/8	0.38
HAD depression (Mean and SD)	3.66 (+/-2.26)	6.71 (+/-4.26)	3.38 (+/-3.85)	0.05
HAD anxiety (Mean and SD)	4.88 (+/-3.14)	7.14 (+/-4.39)	4.38 (+/-3.02)	0.40
Cholinesterase inhibitors (yes/ no)	4/11	9/23	5/8	0.38
Antidepressants (yes/ no)	9/11	14/23	5/8	0.38
Time between evaluations in months	11.58 (+/-4.68)	12.39 (+/-6.6)	13.18 (+/-3.24)	0.83
Baseline Global IQ	104 (+/-15.15)	105,41 (+/-17.44)	97 (+/-10.39)	0.44

References: aMCI: Amnestic Mild Cognitive Impairment; mMCI: Multidomain Mild Cognitive Impairment; HAD: Hospital Anxiety Depression Scale; CDR: Cognitive Dementia Rating Scale; SD: standard deviation. IQ: intelligence quotient.

Table 2 shows the mean and standard deviation at baseline and during follow up of the different neuropsychological variables in each group of patients, significant differences between pre and post intervention were not found in any of the groups.

Table 2. Mean and Standard Deviations of Neuropsychological tests in aMCI. mMCI and Dementia patients group at baseline and follow up.

	al	MCI (n = 11)		mM	mMCI (n = 23)			Dementia (DCR 1) (n = 8)		
	BS	AS	<i>p</i> -value	BS	AS p	-value	BS	AS	<i>p</i> -value	
RVLT-	27.64	27.45		29.04	31		20.38	22.88		
Inmediate list recall	(+/-8.37)	(+/-9.15)	0.68	(+/-8.4)	(+/-9.79)	0.31	(+/-8.38)	(+/-6.06)	0.31	
RVLT-Delayed	3.55	4.18		5.48	4.47		1.75	1.88		
list recall	(+/-1.97)	(+/-3.25)	0.21	(+/-3.45)	(+/-3.2)	0.21	(+/-2.38)	(+/-3.23)	0.76	
Boston	51.9 (+/-4.8)	51.9 (+/-6.15)	1	46.7 (+/ - 6.1)	45.65 (+/-8.79)	0.53	43.13 (+/-8.34)	40.38 (+/-10.01)	0.11	
TMA	60.5 (+/ - 40.94)	61.9 (+/-38.22)	0.6	52.45 (+/-13)	55.54 (+/-14.52)	0.28	63.13 (+/ - 24.67)	59 (+/-16.2)	0.43	
TMB	124.14 (+/ - 74.68)	126.5 (+/ - 73.39)	0.61	179.35 (+/-100.16)	186.47 (+/ - 112)	0.32	245.67 (+/-119.4)	280 (+/ - 65.32)	0.52	
Complex figure of Rey	34.45 (+/-1.86)	33.7 (+/-1.26)	0.37	26.71 (+/-6.65)	25.12 (+/-10.75)	0.35	27.38 (+/-10.64)	26.56 (+/-10.69)	0.37	
Phonological Fluency	12 (+/-5.08)	14.91 (+/-4.72)	0.1	13.7 (+/-4.56)	12.57 (+/-4.87)	0.33	13 (+/-5.21)	11.5 (+/-3.93)	0.52	
Semantic fluency	16.26 (+/ - 4.79)	14.82 (+/-5.85)	0.56	14.52 (+/ - 4.29)	14.91 (+/-5.62)	0.85	11.75 (+/-3.73)	10.75 (+/-3.24)	0.60	

Digit number Wais	11.27 (+/ - 2)	11 (+/ - 2.65)	0.81	9.13 (+/-3.18)	9.65 (+/-2.95)	0.38	11.5 (+/-2.2)	10.13 (+/-1.36)	0.11
Global IQ	104 (+/-15.15)	103.8 (+/-15.22)	0.97	105.41 (+/-17.34)	103 (+/-12.76)	0.27	97 (+/-10.39)	97.13 (+/ - 7.77)	0.97

References: aMCI: Amnestic Mild Cognitive Impairment; mMCI: Multidomain Mild Cognitive Impairment; HAD: Hospital Anxiety Depression Scale; RVLT: Rey Verbal Learning Test; TMA: Trail Making A; TMB: Trail Making B; CDR: Cognitive Dementia Rating Scale; Gender (F/M) (Female/Male); BS (before stimulation); AS (After stimulation); IQ: Intelligence Quotient.

Cognitive stimulation sessions were the same for all patients (between 16 and 24). However, time between neuropsychological pre and post intervention evaluations differ. So grouped aMCI and mMCI patients (n = 34) were divided in three groups, according to time elapsed between evaluations: less than 9 months, between 9 and 13 months and more than 13 months. Groups were compared before and after the stimulation program intervention using a t-test for related groups. No statistically differences were found between them (Table 3).

Table 3. Mean and Standard Deviations of Neuropsychological test at baseline and follow up according to the time of the second evaluation in MCI patients.

		< 9 months (N = 12)		9–1	9-13 months (N = 11)			> 13 months (N = 11)		
	BS	AS	<i>p</i> -value	BS	AS	<i>p</i> -value	BS	AS	<i>p</i> -value	
RVLT-	26.67	30.08	0.76	29.91	30.45	0.8	29.36	29	0.87	
Inmediate list recall	(+/-7.68)	(10.95)		(+/-8.3)	(+/-8.88)		(+/-9.29)	(+/-9.58)		
RVLT-	3.17	3.92	0.25	4.45	4.09	0.65	4.82	4 (+/-3.16)	0.53	
Delayed list recall	(+/-2.86)	(+/-3.63)		(+/-3.67)	(+/-3.53)		(+/-3.76)			
Boston	48.92	49.75	0.43	44.91	46.73	0.24	51.2	45.8	0.10	
	(+/-5.18)	(4.58)		(+/-7.13)	(+/-8.83)		(+/-4.05)	(+/-11.58)		
TMA	57.67 (+/-28.88)	62.75 (+/-31.86)	0.23	56.5 (+/-26.86)	52.1 (+/-21.5)	0.2	50.2 (+/-18.48)	58.8 (+/-14.5)	0.10	
TMB	173 (+/92.64)	128 (+/ - 88.14)	0.18	128 (+/-84.29)	131.71 (+/-74.37)	0.83	166.43 (+/-107.6)	165.86 (+/-95.42)	0.98	
Complex figure of	28.42 (+/ - 7.67)	27.42 (+/-9.62)	0.48	30.78 (+/-6.44)	28.11 (+/-11)	0.18	29 (+/-5.89)	28.3 (+/-9.19)	0.83	
Rey Phonologi cal	12.67 (+/ - 4.76)	12.58 (+/-4.5)	0.14	12.82 (+/-5.69)	12.73 (+/-4.41)	0.94	14 (+/-3.9)	12.55 (+/-5.82)	0.44	
Fluency Semantic	13.75	14.83	0.52	14.36	14.73	0.67	17.27	15.09	0.14	

fluency	(+/-4.41)	(+/-6.45)		(+/-4.55)	(+/-5.08)		(+/-3.98)	(+/-5.65)	
Digit	10.08	10.75	0.38	8.45	9.45	0.033	10.91	10	0.36
number	(+/-2.97)	(+/-3.39)		(+/-2.91)	(+/-3.36)		(+/-2.84)	(+/-1.61)	
Wais									

References: aMCI: Amnestic Mild Cognitive Impairment; mMCI: Multidomain Mild Cognitive Impairment; NS: Not significant; HAD: Hospital Anxiety Depression Scale; RVLT: Rey Verbal Learning Test; TMA: Trail Making A; TMB: Trail Making B; BS (before stimulation); AS (After stimulation)

HAD depression and anxiety scores were compared before and after the stimulation program in all the patient groups (n = 42). It also was tested if cognitive stimulation could improve Subjective Memory, comparing pre and post intervention scores. Trends towards enhancement can be described for anxiety and subjective memory scores after the stimulation program but no statistically significant differences were found (Table 4).

Table 4. Anxiety, Depression and Subjective Memory Scores pre and post intervention.

	BS (N = 42)	AS $(N = 42)$	<i>p</i> -value
HAD Anxiety	6.15 (+/-4.11)	5.5 (+/-3.56)	0.31
HAD Depression	5.41 (4.21)	5.53 (+/-4.33)	0.83
Subjective Memory	5.26 (+/-2.85)	4.47 (+/-2.86)	0.11

References: NS: Not significant; HAD: Hospital Anxiety Depression Scale; BS (before stimulation); AS (after stimulation).

It was also compared if cognitive stimulation had a greater efficacy in any of the groups using a gain score. The gain score was calculated as explained in methods section, and after that, the three groups were compared between each other. There were no statistically significant differences between groups. Although no statically differences were found, a trend to improvement was seen in delay recall and TMB in aMCI group and in digit WAIS in mMCI (Table 5).

Table 5. Mean (DS) Gain Scores and significance between group comparisons.

	aMCI	mMCI	Dementia (CDR 1)	<i>p</i> -value
RVLT-Inmediate list recall	-2.15 (+/-12.92)	2.93 (+/-21.16)	42.77 (+/-58.36)	0.28
RVLT-Delayed list recall	35.83 (+/-74.70)	-1.40 (+/-51.14)	-23.81 (+/-67.51)	0.10
Boston	-1.67 (+/-5.58)	-4.01 (+/-18.01)	-3.73 (+/-14.13)	0.55
TMA	22.09 (+/-18.87)	6.45 (+/-20.79)	-7.80 (+/-13.76)	0.65
TMB	9.96 (+/-48.34)	-2.17 (+/-25.17)	2.28 (+/-39.21)	0.13
Complex figure of Rey	-6.03 (+/-2.46)	-11.74 (+/-37.19)	-3.16 (+/-11.70)	0.73
Phonological Fluency	64.58 (+/-158.17)	0.19 (+/-30.07)	74.87 (+/-111.01)	0.13
Semantic fluency	-12.35 (+/-35.50)	4.02 (+/-36.02)	6.19 (+/-33.88)	0.81

Digit number Wais	-2.68 (+/-28.78)	5.40 (+/-23.66)	-12.96 (+/-20.85)	0.15
HAD anxiety	15.71 (+/-84.16)	40.67 (+/-142.00)	-30.00 (+/-38.44)	0.31
HAD depression	40.00 (+/-95.22)	25.19 (+/-59.22)	-13.89 (+/-70.87)	0.26

References: aMCI: Amnestic Mild Cognitive Impairment; mMCI: Multidomain Mild Cognitive Impairment; NS: Not significant; HAD: Hospital Anxiety Depression Scale; RVLT: Rey Verbal Learning Test; TMA: Trail Making A; TMB: Trail Making B; CDR: Cognitive Dementia Rating Scale.

Grouped aMCI and mMCI patients (n = 34) were divided according to their Global IQ on above and below the median value (98.5). No statistically significant differences were found between baseline and follow up results after cognitive stimulation. The Dementia group was excluded from this analysis. All patients in the MCI group remained stable. Neither group of MCI patients enhanced their post intervention performance in a statistically significant way (Table 6).

Table 6. Mean and Standard Deviation of Neuropsychological tests, pre and post intervention in MCI patients with low and High IQ.

	Lo	w global IQ (N	I = 17)	Hig	High global IQ (N =17)			
	BS	AS	<i>p</i> -value	BS	AS	<i>p</i> -value		
RVLT-Immediate list recall	26.06 (+/ - 7.7)	27.72 (+/ - 9.61)	0.36	31.44 (+/-7.01)	32.25 (+/-9.29)	0.54		
RVLT-Delayed list recall	3.56 (+/-2.46)	3.33 (+/-3.16)	0.87	6.31 (+/-3.28)	5.69 (+/-2.77)	0.64		
Boston	46.53 (+/-7.03)	47.59 (+/ - 6.77)	0.28	50.13 (+/-4.24)	47.5 (+/-10.26)	0.24		
TMA	65.63 (+/-30.42)	68.31 (+/-28.74)	0.46	44.31 (+/10.22)	46.81 (+/-10.85)	0.39		
TMB	211 (+/-113.01)	163.13 (99.5)	0.18	128.67 (+/ - 68)	128.67 (+/ - 76)	0.56		
Complex figure of Rey	28.88 (+/ - 7.97)	27.06 (+/-10.69)	0.58	29.73 (+/-5.31)	28.8 (+/-8.51)	0.32		
Phonological Fluency	13.17 (+/-5.14)	13.06 (+/-4.93)	0.97	13.13 (+/-4.38)	13.63 (+/-4.97)	0.66		
Semantic fluency	14.67 (+/-4.26)	14 (+/-5.21)	0.21	15.56 (+/-4.79)	15.88 (+/-6.02)	0.52		
Digit number Wais	8.33 (+/-2.99)	8.61 (+/-2.68)	0.71	11.5 (+/ - 2)	11.75 (+/-2.15)	0.63		

References: aMCI: Amnestic Mild Cognitive Impairment; mMCI: Multidomain Mild Cognitive Impairment; HAD: Hospital Anxiety Depression Scale; RVLT: Rey Verbal Learning Test; TMA: Trail Making A; TMB: Trail Making B; IQ: Intelligence Quotient; BS (before stimulation), AS (After stimulation)

7. **Discussion**

The objective of this research was to study the efficacy of CS therapy for delaying, stopping or improving cognitive decline. After the analyses, we observed that the cohort of patients studied in the present research did not enhance cognitive functions with the cognitive stimulation program. However, patients remained stable, both in cognitive and behavioural domains, without decline in their cognitive functions or progress to dementia, for more than 18 months.

This information is important because in a previous research, Serrano et al, reported that of 20 patients with aMCI, seven (35%) converted to Alzheimer's Dementia (AD): four (20%) after 6 months and three (15%) after 12 month follow up [25]. Also, it was found that 31 (31.6%) mMCI rotated to AD: 15 (15.3%) at 6 months and 16 (16.3%) at 12 months. Patients included in Serrano's study did not receive any type of cognitive stimulation. In contrast, the MCI patients of the present study, receiving cognitive stimulation, did not progress to dementia and remained without significant changes in the neuropsychological test and global Intelligence Quotient during 18 months. Global IQ usually declines when patients with MCI convert to dementia [26].

Huntley et al., in a recent meta-analysis in Alzheimer Disease patients reported that CS improved scores on MMSE and ADASCog in dementia, but the benefits on the ADAS-Cog were generally not clinically significant [27]. In contrast, Spector et al. in a randomized controlled trial demonstrated that a 14 sessions CS program was as effective as medication in cognition [28]. After that, this intervention was recommended in the 2006 NICE guides for treating cognitive symptoms of dementia [29]. In other paper, Rojas et al. studied the effect of early CS and cognitive training in patients with MCI and reported that these training programs can improve patient performance on cognitive and functional measures [30]. Finally, two systematic reviews demonstrated significant improvement with all intervention programs in MCI patients, one of them only included papers referring to aMCI patients [31] and the other studies with cognitive training and computerized exercises [32].

In relation to anxiety and depression scores, our patient's cohort did not improve after CS therapy. Several research papers reported that CS could improve anxiety and depression scores [33–35]. Talassi et al, in a case controlled study found significant differences with CS intervention in anxiety and depression scores [36]. However, different scales for measuring depression and anxiety symptoms and different cognitive intervention programs were used. Rozzini et al. found significant improvements in depressive symptoms in patients with MCI. However, in this study all patients were treated with ChEIs, were assessed with Geriatric Depression Scale (GDS) and received cognitive training program [35]. On the other hand, in a systematic review, Woods et al. reported five studies

involving 201 participants with dementia that used a self-report measure of mood, the GDS or the Mongomery Asberg Depression Rating Scale (MADRS). Cognitive stimulation was not associated with a clear improvement in mood across these studies [8].

We also measured subjective memory, comparing baseline and post-intervention scores but not significant improvement was seen. In contrast, Jean et al., in a systematic review, reported significant improvement in subjective memory in patients with aMCI [31].

Finally, we studied if patients with higher IQ could have better results with CS than patients with lower IQ. We found that none of them made a better use of CS sessions. It was expected that patients with higher IQ, as a measure of cognitive reserve [37,38], would have more improvement with CS than patients with low IQ [38]. Belleville et al. found a positive correlation between higher education level and efficacy of cognitive training [33]. Although we used IQ to measure cognitive reserve and Belleville used educational level, there seems to be a strong correlation between educational level and intelligence, as reported by Deary and Johnson [39].

The strengths of this study were the use of an extensive neuropsychological evaluation that assessed the principal cognitive domains such as attention, episodic memory, semantic memory, language, visuospatial skills, and executive functions. Other strength was that the time of follow up of most patients was more than 12 months. Finally, the neurophysiologists conducting cognitive evaluations and stimulation were blind about the results of this study, avoiding possible bias.

The study limitations were that activities of daily living were not measured because data was incomplete; CS effect in the quality of life was not assessed and no control group was included.

Future research should include bigger sample size, randomized MCI controlled trials, comparison of different cognitive interventions. Moreover, it would be of interest to study brain changes produced by the cognitive interventions through functional imaging.

8. **Conclusion**

No significant cognitive or behavioural improvement was observed in these patients after the CS program. However, patients remained stable, both in cognitive and behavioural domains for more than 18 months. Furthermore, the aMCI and mMCI patients remained independent in their everyday activities and Mild Dementia patients did not get worse. Cognitive stimulation programs could be considered as a possible non pharmacological treatment in MCI and mild dementia patients.

Conflict of Interest

All authors declare no conflicts of interest in this paper.

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