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Cognitive Stimulation in a-MCI: An Experimental Study

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Abstract

Nowadays, preventing the effects of mental decline is an international priority, but there is little research into cognitive training in mild cognitive impairment (MCI). We present the results of a program aimed at teaching memory strategies and improving metacognitive abilities. This was associated with training to ameliorate caregivers' assistance. Two groups (A and B) were compared in a crossover design. After the first evaluation, group A (but not B) participated in a 6-month cognitive stimulation program. After a second assessment, only B received treatment and then a final evaluation was carried out on both the groups. The results show that (1) both the groups improved their performance as an effect of training; (2) improvements are specific to the functions trained; (3) in the interval without intervention, performance of group B worsened; and (4) group A has maintained their results over time. In conclusion, our results show that specific training may reduce memory impairment in MCI.

Keywords

mild cognitive impairment, cognitive stimulation, memory loss, strategy training, metacognition, individualized intervention

Introduction

It has been proposed that mild cognitive impairment (MCI) represents the clinical transition between normal age-associated cognitive changes and early dementia.[1] As the prodromal phase of Alzheimer's disease (AD) and as such the logical target for early intervention,[2] clinicians and researchers are paying more and more attention to the amnestic form of MCI (aMCI).

Primary prevention of MCI consists of all the factors related to a reduction in decline, for example, diet, education, physical exercise, mental activity, and the use of statins. Since drugs are of limited benefit, cognitive stimulation represents a significant opportunity for secondary prevention.

Nevertheless, a recent review[3] has shown that until now few studies concerning rehabilitative intervention have been published. Although not only randomized control studies but also nonrandomized and uncontrolled trails were considered, only 10 pertinent articles were identified. Of these, 6 concern cognitive exercise programs (ie, repeated practice of targeted cognitive abilities in a repetition-session format) and the other 4 use training in memory strategies (ie, the instruction and practice of techniques to minimize memory impairment and enhance performance).

In the abovementioned studies, with minor exceptions, cognitive amelioration due to intervention does not generalize into improvements in everyday life[2] and have not been checked over time. Here, we present data from a cognitive stimulation program based on 2 complementary methods: a metacognitive approach to rehabilitation and the training of strategies.

Metacognition is defined as thinking about one's own thinking,[4] a monitoring of our cognitive processes and setting goals for understanding and activating strategies. Initially created from a developmental perspective, it has also been progressively applied in the rehabilitation of adults.[5-7] Metacognition is made up of 2 components. Metacognitive knowledge implies the knowledge people have about their cognitive abilities (eg, memory, attention, etc), their cognitive strategies, and the cognitive-specific requests related to various typologies of cognitive tasks (eg, shopping lists, appointments, etc). Metacognitive regulation refers to cognitive monitoring (eg, error detection) and processes of cognitive control (eg, self-regulation strategies, conflict resolution, planning, error correction, etc).[8]

The training of strategies concerns learning, how to learn, and the acquisition of useful strategies.[9,10] Rather than teaching tasks, it involves techniques for remembering or retrieving information and consists of specific rules that are given to patients and discussed with them.

It appears evident that this approach is totally complementary to metacognitive rehabilitation. In reality, comprehension and acceptance of one's own deficits imply a process of introspection and self-reflection concerning one's own cognitive

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functioning. Moreover, the choice and use of different strategies presuppose the ability to drive, control, and monitor one's own mental processes.

An important element in our program is the presence of caregiver in all the phases of training. In this way, caregivers are able to give information concerning the patients' abilities in daily life activities in addition to explaining how they usually assist patients when they encounter difficulties. The therapist can then offer useful and practical suggestions and can recommended specific activities to do at home.

Thus, this study has more than one aim. First, we wanted to verify the efficacy of an individualized program of cognitive stimulation in participants diagnosed with MCI. The idea was to develop a training program resulting from the integration of 2 methodologies, metacognition and strategies training. This type of training has not been used before for memory disorders in MCI. In addition, we were interested in ascertaining the presence of any delayed effects of the training on memory performance.

This study also aims to confirm the hypothesis that the degree of decline over time is greater without any stimulation and to establish whether it is possible to reduce this decline. Finally, it will provide at least qualitative data concerning the changes in caregiver attitude. As the training was for memory abilities, we selected only participants with an aMCI on the basis of the Mayo criteria revised.[11]

Methods

A crossover design was used in the study. A total of 30 participants diagnosed with aMCI were divided into 2 groups of 15 people. Immediately after the first assessment, one of these 2 groups (group A), but not the other, underwent a rehabilitative training program that focused on enhancing memory strategies and metacognitive abilities. The other group (B) underwent the same program, but only after a second assessment, 6 months after the first. Neurological and neuropsychological initial assessment guaranteed that the 2 groups did not differ significantly in their abilities related to memory, attention, and executive functions.

In this way, the 2 groups served as reciprocal controls of each other. In fact, a second comparison of their performance allowed us to verify the efficacy of the treatment in group A and, at the same time, the decline that occurred in the second group (B). After the second phase, in which group B took part in a cognitive stimulation program, a further assessment permitted us to verify the degree of recovery of their previously recorded decline. This third assessment also enabled us to check whether the improvement in group A's performance had been maintained over time or had declined.

Study Participants

In 2008, a total of 408 new patients were admitted to the Unità Semplice Organizzativa, Centre for Alzheimer's and Cognitive Diseases at the University Hospital of Verona, and were subsequently assessed. They were of the most part physician referred, but a few of them were self-referred or referred by family or friends as the result of their memory problems. At the neuropsychological assessment (The Mental Deterioration Battery modified),[12] 20 of these patients showed no evidence of cognitive impairment and 253 were diagnosed as suffering from mental deterioration (185 with AD, 16 with AD with vascular dementia, 11 with lewy body dementia, 5 with frontotemporal dementia, 3 with vascular dementia, 8 with Parkinson's disease, and 25 with nonspecified dementia or dementia in psychiatric disorders). The other 135 (33.09%) showed signs of MCI; specifically, 66 participants presented with an aMCI and 69 with a multiple domain MCI.

Among the patients diagnosed as having aMCI, we identified 30 patients who agreed to participate in this study. They met the Mayo criteria for aMCI diagnosis proposed by Petersen and coworkers[1,11,13]: (1) memory impairment described by the patient, relatives, or both; (2) cognitive impairment objectified by means of a neuropsychological test battery (and interpreted in conjunction with the first criterion and the personal history of the patient); (3) no impairment of activities in day-to-day life; (4) absence of dementia as defined by the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition; *DSM-IV*) criteria.[14]

All patients underwent a comprehensive assessment of their symptoms, mood state, and performance before being included in the study. The Mini Mental State Examination,[15] the subtests of the Mental Deterioration Battery,[12] and a clinical interview with patients and informants were used to assess the general cognitive status. In particular, since recent studies have shown that word list learning is a better predictor of conversion in mental deterioration as compared to other neuropsychological tests,[16,17] the Auditory Verbal Learning Test (AVLT)[18] scores were considered as a main index of memory deficits. As suggested in the previous studies,[12] we considered not only the number of words correctly recalled on all 5 immediate recall trials but also the number of false responses and omissions. In this way, and referring also to Mayo criteria,[11,13] both pure aMCI and amnestic multi-domain MCI participants were included.

Impact on everyday activities was evaluated using the Clinical Dementia Rating (CDR) Scale.[19] The absence or the presence of minimal impairment in day-to-day life activities was determined in 2 clinical interviews, both with the patient and with the informant (Instrumental Activities of Daily Living and Basic Activities of Daily Living).[20,21] Depression was excluded using the Geriatric Depression Scale.[22]

Structural brain imaging (magnetic resonance imaging or computed tomography scans) enabled us to exclude the presence of relevant underlying cerebrovascular disease. In addition, standard laboratory blood tests (thyroid function, complete blood count, blood chemistry, folic acid and vitamin B12, homocysteine, and blood lipid profile) were performed to rule out potentially reversible causes of cognitive impairment.

Other exclusion criteria were: (1) current neurological and systemic diseases or a history of head injury with loss of consciousness; (2) history or symptoms of psychosis or

Table 1. Demographic data and T1 Baseline Test Results for Groups A and B[a]

	Group A				Group B				
	Mean	SD	Max	Min	Mean	SD	Max	Min	*P*
Age	73.27	6.91	84	57	68.53	8.74	81	50	ns
Education	8.93	4.4	18	3	11.07	2.79	16	5	ns
Attention									
Bell test	21.77	2.47	26.75	17	19.76	2.96	24.69	15.25	.053
Attentional matrices	44.93	9.61	56.5	23.75	48.93	5.4	57.5	40.25	.171
Trial-making test (A)	−81.6	57.21	−9	−195	−89.93	126.73	−15	−539	.818
Bourdon test (mean)	5.56	1.96	8.94	2.58	6.09	1.9	9.36	3.51	.456
Verbal span	4.75	0.88	6.5	3.75	4.57	0.88	5.75	2.5	.573
Memory									
AVLT (immediate recall)	41.02	10.41	59.9	20	33.88	9.31	51.5	18.3	.058
AVLT (delayed recall)	8.47	3.44	14.8	1.3	6.57	2.71	13	2.06	.103
Omissions	1.87	1.25	4	0	3.53	3.58	13	0	.100
False recognitions	3.33	5.34	19	0	2.2	2.31	6	0	.457
Listening span test	−1.45	2.34	2.55	−5.91	−0.61	1.68	2.37	−3.51	.264
Story recall	7.94	3.96	13.4	0	5.49	3.77	10.9	0	.094
Executive functions									
Verbal fluency (category)	33.33	6.54	43	23	35.6	6.37	48	25	.345
Tower of London	28.93	3.58	35	22	29.13	6.01	36	15	.913
Analogies	16.93	3.65	20	8	16.87	2.64	20	12	.955
Stroop test (seconds)	−38.02	23.17	−14.5	−100	−29.94	15.9	4.5	−56	.275
Trial-making test (B-A)	−146.8	100.62	−55	−420	−83.07	69.11	2	−228	.053

Abbreviations: SD, standard deviation; ns, not significant; min, minimum; max, maximum.
[a] *P* values of *t* test statistics.

major depression (*DSM-IV*); (3) alcoholism or other substance abuse.[23,24]

All the participants were native Italian speakers and gave their informed consent to participation in the study. The procedures were approved by the local ethics committee and the study was carried out in accordance with the guidelines of the Declaration of Helsinki.

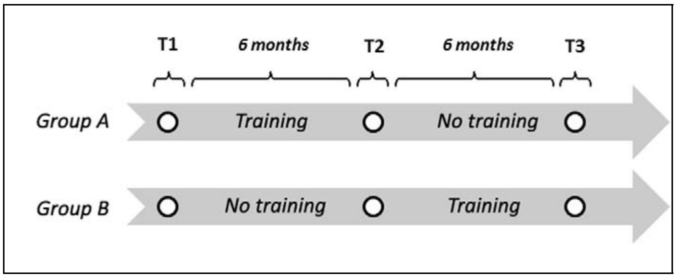

Figure 1. The time line of the crossover design utilized in the study. T1, T2, and T3 refer to the 3 consecutive assessment sessions.

Assessment Schedule

After the first screening, all the participants were given a further comprehensive battery of neuropsychological tests that assessed more deeply the domains of verbal memory, attention, language, processing speed, executive function, and visuospatial ability. Tests that are widely used in routine neuropsychological practice and are sensitive to early deficits in these cognitive domains were selected. These are shown in Table 1.

All the test scores were corrected for age, sex, and education and compared with the values available for the Italian population.[12,25-34] When these data were not available (Bourdon test),[7] the patients' scores were compared with those of a group of 20 neurologically healthy participants. The assessment (T1) was repeated 6 months and 12 months after the first examination.

Training Schedule

After the first assessment (T1), the participants were divided into 2 groups (A and B), according to a crossover design: group A received immediate training consisting of cognitive stimulation lasting 6 months, followed by a second assessment (T2). After this, a 6-month period without training followed and then these participants were retested (T3). On the contrary, group B did not receive any specific training between T1 and T2 but participated in the cognitive stimulation program for 6 months between T2 and T3. The time line is illustrated in Figure 1.

Participants were placed in one of the 2 groups as agreed with them and their caregivers in relation to individual requirements (eg, family organization, holidays, personal preferences, etc). Crucially, at T1, there were no statistical differences between the groups either for personal data or in the test scores concerning attention, memory, and executive functions (Table 1).

In this way, the same multiple measurements were collected for each participant and all of them followed the rehabilitation program. This allowed us to compare each group before and after training (A at T2 vs T1 and B at T3 vs T2) and also to evaluate the progression of symptoms in the absence of specific stimulation (B at T2 vs T1). Finally, T3 provided data on any delayed effects on group A.

The 6 months of training were organized as follows. In the first month (intensive treatment), 3 individual sessions per week took place. In this phase, strategies were explained and then tried out and practiced. A strong element of our program is that, despite the methodology which is common to all the patients, specific target training and activities are determined by each individual patient for themselves (ie, intervention focusing on problems). At the start of the training session, the patient, the caregiver, and the therapist indicate which memory problems are the most distressing in daily life and need treatment. The individual personal training program can then focus on these targets.

The program starts with a discussion regarding the patient's memory deficits and his or her acceptance of potential frustration due to failure to remember. This also implies acceptance of external memory aids. Thus, the importance of paying attention, taking time to learn, and making use of the various forms of repetition (simple, spaced, and varied repetition) was emphasized.[9] At this point, strategies such as verbal and visual association, organization of contents, categorization, visualization, anticipation and retrospection, and mental imagery were taught and tried out. They were subsequently practiced in tasks concerning memory for future events, remembering numbers and names, learning stories and texts, and remembering completed and intended actions. In effect, all these strategies need to be exercised over a period of time, and for this reason, patients were expressly invited to use them systematically. In addition, the use of spaced retrieval was applied.

From the first session and in all phases of training, caregiver accompanied patients participating in cognitive stimulation sessions. This permitted him or her to learn how and when to give assistance and what type of advice was more useful to the patient. When appropriate, patients were encouraged to use external memory aids and caregivers were trained to facilitate patients, utilizing the best cues from the environment. Regular training and monitoring ensured efficient use of these aids.

During the subsequent 5 months, patients participated in 1 session per week and did exercises at home with the support of the caregiver. This second training phase is absolutely necessary because it gives the patient the chance to use the strategies learned in everyday situations.

Data Analysis

For each test used, scores were analyzed by means of a repeated measure analysis of variance (ANOVA) 3 × 2, with the test session as a within-subject variable (3 levels: T1, T2, and T3) and group as a between-subject variable (2 levels: A and B). In the case of a significant main effect of the test session factor, or a significant interaction of the 2 ANOVA factors, we performed repeated contrasts or repeated interaction contrast, respectively, across the levels of the test session factor (group × T1 vs T2, group × T2 vs T3 or group × T1 vs T3). This permitted us to identify whether the differences were specifically linked to the cognitive stimulation training.

Thus, in order to explain significant 2-way contrasts (or interaction contrasts), the differences between the scores in the 2 assessment sessions for the same group were tested by means of *t* tests. In the same way, *t* tests were used to explain differences between the 2 groups' scores in the same assessment session.

Unfortunately, it was impossible to collect quantitative data concerning caregiver coaching, but their qualitative reports on the program are discussed in the results section.

Results

The mean scores and standard deviation for each group and test are shown in Tables 1 and 2. It is to be noted that no dropouts were recorded since all the participants completed the whole program and participated in all 3 assessments. Thus, all analyses refer to all the participants.

Memory

The results show a positive effect of cognitive stimulation on memory abilities, especially on short-term and working memory for group A and long-term memory for group B. The results of the individual tasks are as follows (Figure 2).

Auditory Verbal Learning Test (AVLT)[18]. In immediate recall, the ANOVA indicates an effect of interaction between test session and group ($F_{27,2} = 5.16$ $P = .009$), with a significant main effect both of group ($F_{27,1} = 5.63$, $P = .025$) and session ($F_{27,2} = 8.14$, $P = .001$; Figure 2A). In effect, the performance of the 2 groups across the test sessions is different. Interaction contrasts show that the 2 groups differ between T1 and T2 ($F_{27,2} = 10.6$, $P = .003$) and between T2 and T3 ($F_{27,2} = 6.24$, $P = .019$). Performance of group A improves after cognitive stimulation between T1 and T2 ($t_{14} = 2.37$, $P = .033$); however, this improvement is mostly lost between T2 and T3 ($t_{14} = 2.28$, $P = .039$). Overall, some degree of recovery is confirmed in a comparison of the mean scores between T1 and T3, although it does not reach a significant level ($t_{14} = 1.77$, $P = .099$).

Group B does not show any difference between T1 and T2 ($t_{14} = .159$, $P = .879$), while performance improves between T2 and T3 ($t_{14} = 3.60$, $P = .003$). This difference is confirmed in the comparison between T1 and T3 ($t_{14} = 2.86$, $P = .013$).

An effect of interaction also emerges in delayed recall between the testing sessions and group variables ($F_{27,2} = 4.19$, $P = .02$), with a significant main effect for session ($F_{27,2} = 5.59$, $P = .006$) and close to significant for group ($F_{27,1} = 3.9$, $P = .058$; Figure 2B). In effect, the interaction contrasts show that the performance of the 2 groups does not significantly differ between T1 and T2 ($F_{27,2} = 3.81$, $P = .061$) but is significantly different between T2 and T3 ($F_{27,2} = 18.85$, $P < .001$). These effects are due to the results of group B.

Table 2. The Results of Groups A and B in the T2 and T3 Assessment Session[a]

	T2					T3				
	Group A		Group B			Group A		Group B		
	Mean	SD	Mean	SD	P	Mean	SD	Mean	SD	P
Attention										
Bell test	22.16	4.2	20.19	3.41	.331	22.81	2.8	21.59	3.89	.331
Attentional matrices	52.2	6.84	46.9	4.96	.022	52	6.4	48.1	5.29	.079
Trial-making test (A)	−70.2	45.58	−86.8	112	.599	−71.47	44.27	−80.33	114.73	.782
Bourdon test (mean)	6.7	2.12	5.79	2.22	.260	6.2	1.71	5.6	1.84	.358
Verbal span	5.1	0.74	4.43	0.86	.031	5.1	0.74	4.57	0.88	.083
Memory										
AVLT (immediate recall)	46.52	11.2	33.8	8.65	.002	44.95	12.01	39.98	10.04	.229
AVLT (delayed recall)	9.14	3.87	5.79	3.05	.014	9.23	3.68	7.59	3.15	.200
Omissions	1.33	1.35	2.47	2.85	.175	1.4	1.5	1.67	2.85	.751
False recognitions	1.93	2.37	2.33	1.68	.598	1.13	1.55	1.2	1.32	.900
Listening span test	−1.02	1.43	−2.07	1.08	.031	−0.61	1.68	−1.38	1.17	.155
Story recall	9.22	4.4	5.5	3.1	.012	9.04	3.74	6.91	3.64	.126
Executive functions										
Verbal fluency (category)	35.33	8.01	33.6	7.22	.539	34.73	9.6	36.8	7.69	.520
Tower of London	29.53	4.5	29.53	6.19	1.000	28.93	5.08	30.47	6	.456
Analogies	17.13	3.44	16.87	2.67	.814	17.33	3.39	17.13	2.45	.854
Stroop test (seconds)	−31	25.6	−33.6	13.97	.733	−32.41	23.38	−26.15	13.83	.379
Trial making test (B-A)	−107.8	85.5	−87.93	70.72	.514	−106.8	66.85	−75	68.94	.235

Abbreviation: SD, standard deviation.
[a] *P* values of *t* test statistics.

Group A does not show any effect due to the stimulation or time either in T1 versus T2 ($t_{14} = 1.03$, $P = .32$) or T2 versus T3 ($t_{14} = .318$, $P = .755$). In contrast, for group B, there is a significant decline between T1 and T2 ($t_{14} = 2.137$, $P = .05$) which is recovered with cognitive stimulation between T2 and T3 ($t_{14} = 6.87$, $P = .000$).

The interaction between the testing session and group variables does not reach the significance for omissions (failure in word recognition; $F_{27,2} = 4.14$, $P = .052$), with a main effect for session ($F_{27,2} = 7.89$, $P = .001$) but not for group ($F_{27,1} = 1.61$, $P = .215$). Group A does not show any significant improvement or decline either in T1 versus T2 ($t_{14} = 1.196$, $P = .251$) or in T2 versus T3 ($t_{14} = 1.07$, $P = .301$).

For group B, there is a reduction in the number of omissions between T1 and T2 ($t_{14} = 4.00$, $P = .001$) but not for T2 versus T3 ($t_{14} = 1.67$, $P = .118$). For false recognition, there is no overall interaction between testing session and group ($F_{27,2} = .88$, $P = .357$). However, there is a significant main effect for session ($F_{27,2} = 4.37$, $P = .017$) but not for the group ($F_{27,1} = .078$, $P = .783$). In effect for both group A ($t_{14} = 2.175$, $P = .047$) and group B ($t_{14} = 2.43$, $P = .029$), there is a significant reduction in false recognition between T2 andT3 but not between T1 and T2 (A: $t_{14} = 1.157$, $P = .267$; B: $t_{14} = .414$, $P = .685$).

In the verbal working memory (listening span test)[31], the ANOVA indicates the interaction between testing session and group ($F_{27,2} = 4.93$, $P = .011$), without significant main effects either for group ($F_{27,1} = .513$, $P = .48$) or session ($F_{27,2} = 1.81$, $P = .174$; Figure 2C). In reality, the performance of the 2 groups is different. Interaction contrasts show that they differ between T1 and T2 ($F_{27,2} = 5.58$, $P = .025$) and between T1 and T3 ($F_{27,2} = 7.58$, $P = .010$), but not in T2 to T3 interval ($F_{27,2} = .273$, $P = .605$). Performance group A improves between T1 and T2 ($t_{14} = .636$, $P = .535$) and T2 and T3 ($t_{14} = .879$, $P = .394$) but this improvement only reaches a significant level in the comparison between T1 and T3 ($t_{14} = 2.48$, $P = .027$). Group B's performance declines between T1 and T2 ($t_{14} = 3.41$, $P = .004$), but partially recovers between T2 and T3 ($t_{14} = 2.76$, $P = .015$). The comparison between T1 and T3 for group B is not significant ($t_{14} = 1.61$, $P = .129$).

Story recall[25,28]: Session per group interaction is not significant ($F_{27,2} = 2.13$, $P = .156$), while the main effects for group and session are significant (group: $F_{27,1} = 4.39$, $P = .045$; session: $F_{27,2} = 6.08$, $P = .004$). The contrasts show an interaction in T2 to T3 interval ($F_{27,2} = 13.93$, $P = .001$). In reality, while performance of group A is stable and unaffected by the treatment (T1/T2 $t_{14} = 1.64$, $P = .124$; T2/T3 $t_{14} = .521$, $P = .610$; T1/T3: $t_{14} = 1.58$, $P = .136$), there is no difference in group B between T1 and T2 ($t_{14} = .023$ $P = .982$) but a significant improvement between T2 and T3 ($t_{14} = 5.42$, $P < .001$; Figure 2D).

Attention

Results from the attention tests show both the effects of cognitive stimulation and a decline over time in the absence of specific training. Training ameliorates attention abilities and compensates at least partially for any decline (Figure 3).

Indeed, the interaction between session × group is present in the T1 versus T2 interval in the attention matrices[28]

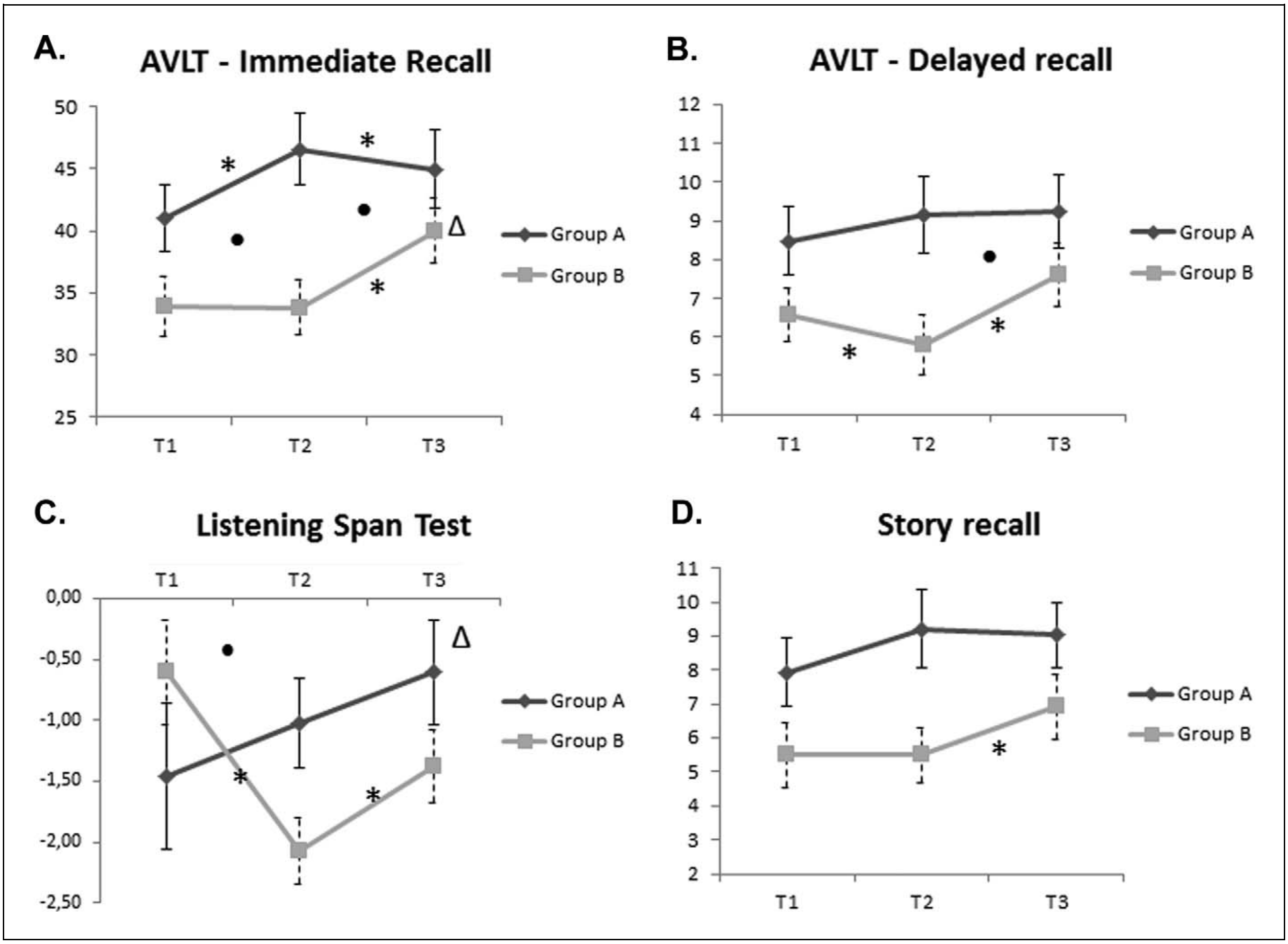

Figure 2. The performance in memory tasks (means and standard errors) of the 2 groups in the 3 assessment sessions: (A) immediate recall of AVLT; (B) Delayed recall of AVLT; (C), Listening span test; D, Story recall. •Contrasts <.05; *significant values of *t* test (*P* < .05) in within-group measurements (T1 versus T2 and T2 versus T3); Δ, significant value (*P* < .05) between T1 and T3.

($F_{27,2}$ = 18.52, P = .000), concentration,[7] (Bourdon test, $F_{27,2}$ = 5.56, P = .026), and verbal span tests[28] ($F_{27,2}$ = 8.99, P =.006). This is due to the fact that after training, performance of group A improves (attention matrices: $t_{14} = 3.69$, P = .002; Bourdon: $t_{14} = 2.16$, P = .049; verbal span: $t_{14} = 2.62$, P = .02).

Moreover, in the same interval, group B worsens in selective attention (attention matrices[28]: $t_{14} = 2.28$, P = .039) and concentration (Bourdon[7]: $t_{14} = 2.47$, P = .027).

However, the interaction between session × group is not significant in the T2 versus T3 interval. In fact, while the improvement of group A resists over time (all t tests P > .05), group performance of group B does not improve. Finally, in the Trail Making test[32] (part A) and Bell test,[33] no significant effect is recorded.

Executive Functions

No specific effects were found in executive functions. In the Tower of London test,[34] Trail Making Test (TMT) (B-A),[32] and the Test of Analogies,[27] no significant differences were found between the groups or assessment sessions. In the Verbal Fluency test,[26] a significant general interaction between group and session ($F_{27,2}$ = 4.19, P = .042) is present, without a main effect of group ($F_{27,1}$ = .11, P = .742) or session ($F_{27,2}$ = 1.48, P = .23). The interaction between T1 and T2 ($F_{27,2}$ = 6.72, P = .015) is fully explained by the decline of group B ($t_{14} = 2.93$, P = .011), and the interaction between T2 and T3 by the recovery of this decline ($t_{14} = 2.3$, P = .037). In the Stroop test,[29] (seconds) the group × session interaction is significant ($F_{27,2}$ = 5.33, P = .008) with a main effect for session ($F_{27,2}$ = 3.70, P = .031) but not for group ($F_{27,1}$ = .315, P = .579). Interaction is confirmed by the contrasts for T1/T2 ($F_{27,2}$ = 5.56, P = .026) and T2/T3 ($F_{27,2}$ = 38.29, P < .001) but not between T1 and T3 ($F_{27,2}$ = .234, P = .633). While group A improves in T2 with respect to T1 ($t_{14} = 3.24$, P = .006) but worsens between T2 and T3 (t_{14} = 2.36, P = .034), group B declines in the first interval ($t_{14} = 2.2$, P < .045), but recovers between T2 and T3 (t_{14} = 9.05, P < .001; Figure 4).

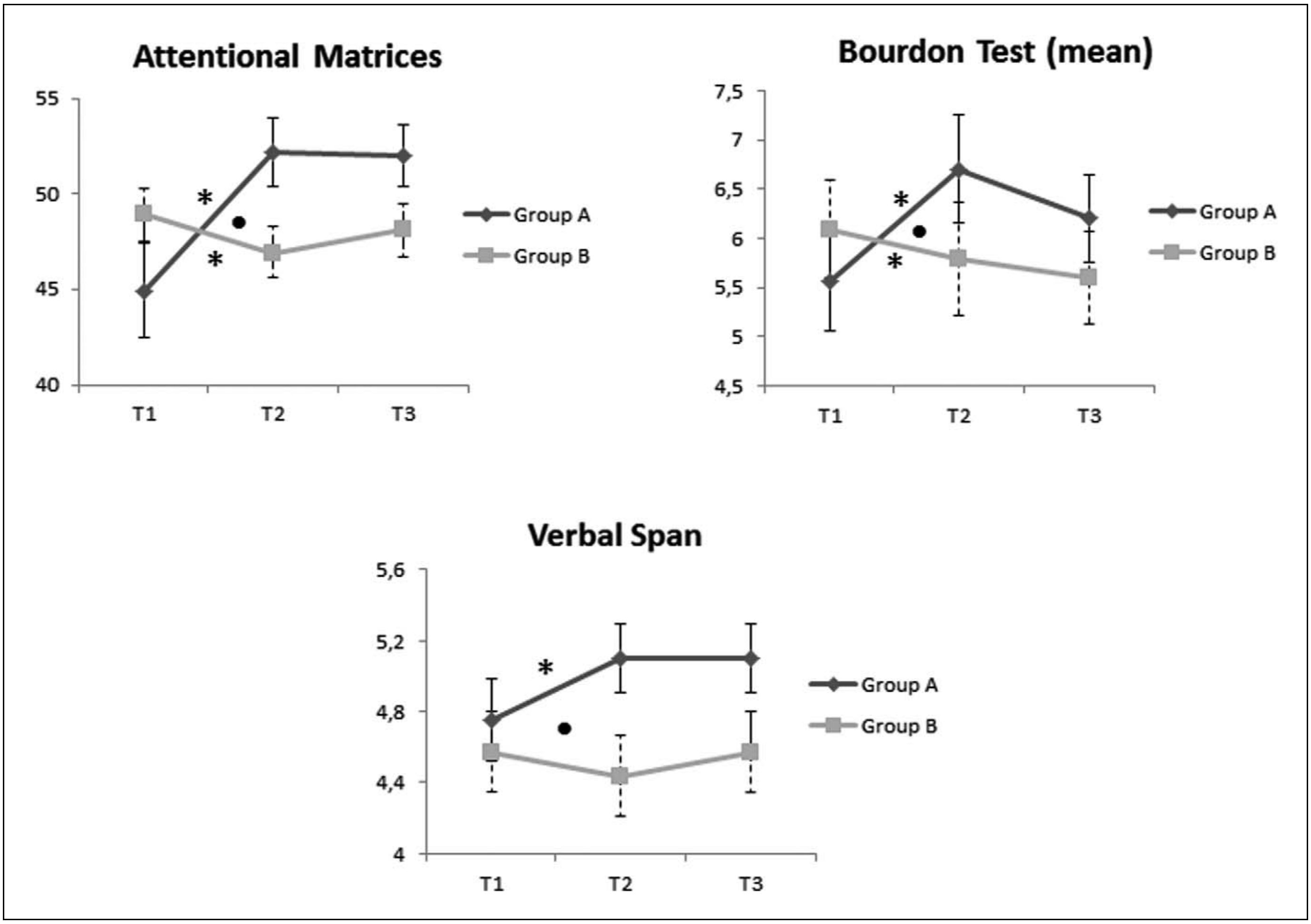

Figure 3. The performance in the attention test (means and standard errors) of both the groups in 3 assessment sessions. •Contrasts < .05; *significant values of *t* test ($P < .05$) in within-group measurements (T1 versus T2 and T2 versus T3).

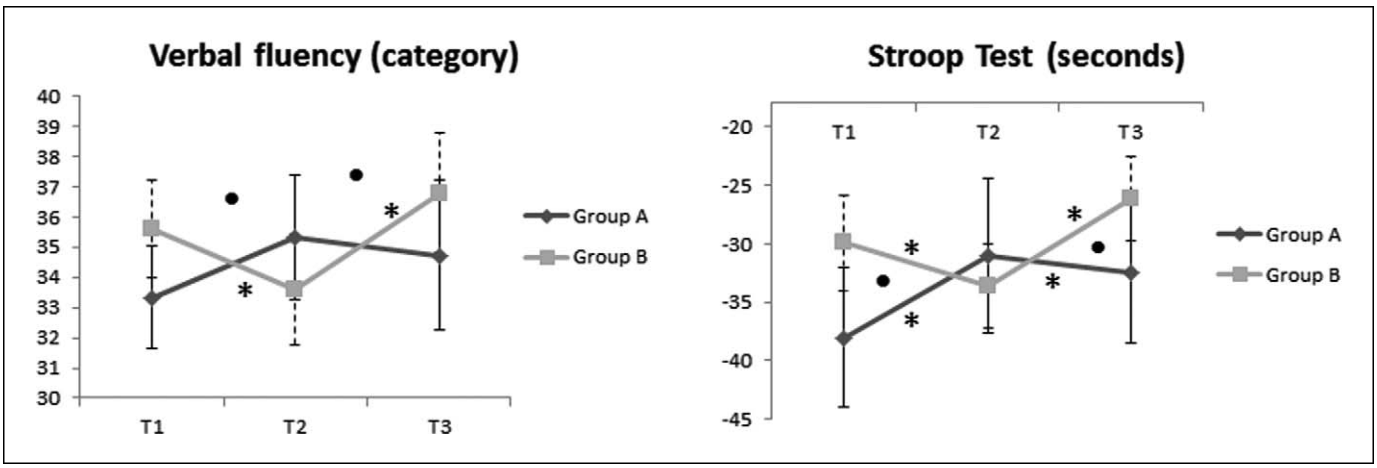

Figure 4. The performance in the verbal fluency and Stroop test (seconds; means and standard errors) in both groups. •Contrasts <.05; *significant values of *t* test ($P < .05$) in within-group measurements (T1 versus T2 and T2 versus T3).

Caregiver Report

Unfortunately, due to the lack of suitable instruments, we were unable to record any quantitative data concerning the effect of coaching on the caregiver. Nevertheless, clinical reports are extremely convincing and indicate the self-perception of improvement in assistance skills. Some of them reported that during training they learnt when they have to give help and when it is better not to intervene. Some state that before training, they had always had a tendency to do things for the patient not allowing him or her to act in autonomy. Two or three wives realized that before training, they had become a sort of teacher for their husbands and this had had a negative influence on the atmosphere in the family. During the program, a certain number of caregivers discovered their need to find moments in the week for their own interests, hobbies, and relationships, something which is fundamental to personal well-being.

Discussion

The main result of this study is a demonstration of the efficacy of a memory intervention program in participants with aMCI. Moreover, a comparison between groups A and B (with group B receiving training after a delay of 6 months) shows that without specific stimulation, the performance of these participants declines over time.

Finally, another important result of the study is the evidence that the benefits of the program are evident both immediately after the intervention and at a 6-month follow up check (group A). This is an important index of successful maintenance of newly learned behaviors, which has not been reported in previous research on MCI rehabilitation (but see Troyer et al[35]).

The extensive variability between MCI participants in terms of cognitive profiles and evolution is well known.[11] The rate of progression to dementia and the stability of MCI diagnosis vary widely depending on the study, the recruitment methods, and the operational criteria.[2] In our group, the pattern of performance is not homogeneous between patients. Globally, we found that 12 of 30 participants ameliorated their memory scores both in immediate and delayed recall, and another 4 improved their short-term but not long-term memory. This amelioration resisted over 6-month interval in group A. Mental abilities remained stable in 10 participants while 4 deteriorated. Globally, 6 participants subsequently showed an evolution in dementia in the checkup which followed: 1 with dementia Alzheimer's type, 4 with senile dementia Alzheimer's type, 1 with frontotemporal Dementia.

One result of our study that is worthy of attention concerns the decline that group B showed in the interval between the first and second assessments, relative to the period of time in which there was no cognitive stimulation. The literature indicates that the first phases of cognitive impairment are the most important for secondary prevention, that is, rehabilitative training aimed at preventing a further mental decline.[36,3] In fact, this is the moment when efficacious training may extend the possibilities of personal autonomy over time, favoring the preservation of employment, social activities, and a general sense of well-being. Our data confirm that a decline in MCI is possible and may also be rapid and as such early diagnosis and precocity in the intervention are essential.

Despite this decline, considering the pretraining and posttraining data (T1 versus T2 for group A and T2 versus T3 for group B), it is evident that the trend of recovery is analogous for the 2 groups (all the ANOVA $P > .05$) and thus directly related to intervention.

These data indicate some factors that are essential to the success of our program. First, in contrast with the previous strategy training programs,[35-38] our patients participated in individual and not in group sessions. This is noteworthy because individual training permits the focalization of intervention targets and the strategies relating to the needs and cognitive style of the individual patient. This leads to a greater likelihood of the strategies being used in everyday life.

A second factor of success is the presence of caregivers, which is very important since it means that they can be instructed on how to encourage and assist patients to use these strategies at home. Finally, the program lasts longer and the number of sessions is greater than previously proposed training programs.[3] In the first month, patients participated in 3 sessions per week. This allowed them to learn and apply the memory strategies in a large number of cognitive tasks. The next 5 months featured 1 session per week. Here, the aim was to monitor activity at home and address specific problems. The fact that the training given to both the patients and caregivers lasted for 6 months meant that it was possible to focus on day-to-day problems and give valid assistance.

Literature on the subject confirms the importance of the duration of the treatment, which is necessary for training in the use of cognitive strategies and gaining self-confidence in memory abilities.[37] In their program, Troyer and colleagues[35] report the best results in those patients who attended more sessions and completed more at-home assignments. It is clear that the individual motivation plays a crucial role in this as in every rehabilitative program.

Our study also revealed other unexpected evidence. The program is very demanding in terms of energy and time, not only for the operators but also for the patients and their caregivers. For this reason, a high degree of dropout was expected. However, all individuals completed their training and the follow-up assessment. Our hypothesis is that during the intensive phase of training, a very close relationship evolves between operator, patient, and caregiver, with a therapeutic form of alliance that helps to support patient motivation and effort.

This study has some limitations. The first is the lack of quantitative measurements of metamemory competences and the patient's sense of efficiency. Nevertheless, qualitative feedback from patients indicated an improved sense of control regarding memory and increased confidence in their ability to recall. This was confirmed by caregivers who also reported increased confidence in their assistance skills. However, in this case too, our results are limited by the lack of quantitative data.

Unfortunately, it was not possible to obtain data from neuroimaging in order to document pathological processes. Functional data concerning cerebral activation before and after training might offer information regarding the biological substrates correlated to recovery. Nevertheless, we can hypothesize that training of memory strategies utilizes and in some way reinforces the individual cognitive reserve.[39,40] This model suggests that when the brain attempts to cope with damage, it uses both preexisting cognitive processing and compensatory approaches. In other words, damage causes the brain to activate the networks or cognitive paradigms that are more efficient and less susceptible to disruption (neural reserve). At the same time, it also recruits networks and cognitive strategies that are not normally used or have not been previously used for that specific task (neural compensation).

The results of a recent functional magnetic resonance study[41] confirm this hypothesis. The authors investigated the neural correlates of a memory strategy program demonstrating "that the training-related brain changes involved the activation of new alternative brain areas in subjects with MCI, that is, areas that were not recruited during the memory task prior to the training."[p1632] In addition, they found a limited number of areas, already active prior to intervention, with accumulated activation. The authors conclude that "this finding agrees with models of brain compensation in ageing and suggests that maintaining optimal memory functions relies on both increased activation of specialized areas and recruitment of new alternative brain networks"[41(p1632)].

Further research will confirm and identify the neural correlates of recovery processes in order to establish the best strategies of rehabilitation. Another important objective of further research is to create better qualitative and quantitative instruments capable of measuring not only the skills but also the well-being of caregivers.

Conclusion

Teaching memory strategies and enhancing metacognitive competences may improve memory performance in participants affected by aMCI. This may prevent decline and will resist over time. We interpret these data as being the result of more than 1 factor. Memory strategies, unlike memory exercises, activate wide networks that involve not only the memory but also attention, reasoning, and planning functions. When these networks have not yet degenerated, they may be recruited and enhanced to ameliorate performance. Moreover, the extended duration of the intervention and the support of caregivers surely permit the consolidation of cerebral plasticity mechanisms, neither of that is possible in short-term programs.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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