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Cognitive stimulation in moderate Alzheimer's disease

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Abstract

Cognitive stimulation is one of the non-pharmacological therapies recommended for dementia intervention. The present study evaluated the efficacy of an intervention based on cognitive stimulation in people with moderate Alzheimer's disease.

Fifty-nine subjects with moderate dementia were randomly assigned to the stimulation group (*N* = 36) and the control group (*N* = 35). The treatment group received 16 intervention sessions cognitive tasks. All participants were evaluated with a battery of neuropsychological tests at three time points (pre, post, and follow-up).

The treatment group showed significant increases in the three domains studied (memory, attention, and executive functions), although some of these effects were not maintained at follow-up. The control group progressively worsened.

Cognitive stimulation was found to be an effective intervention for people with moderate Alzheimer's disease because it helped to maintain memory function, executive functions, and attention. However, the effects were minimized at the three-month follow-up.

Keywords: dementia, cognition, intervention, memory

Based on the projections for the aging of the population worldwide, Alzheimer's disease (AD) is going to acquire considerable importance in the care of the elderly. AD is a disease that produces a slow, very disabling, general deterioration, with cognitive and functional deficits and behavioral changes (Zvěřová, 2019). It is necessary to develop effective interventions that focus on the cognitive aspect of the disease in an attempt to prevent or reduce cognitive impairment.

At the cognitive level, memory is one of the main cognitive functions affected from the early stages of the disease, due to an altered medial temporal/hippocampal component, which causes deficits in coding, loss of information after a short time, low influence of help cues, a high number of intrusions, and false recognitions (Dubois, 2018; Pitarque et al., 2016).

Another cognitive domain that is affected in Alzheimer's disease is executive functions, a set of competencies related to inhibitory control, self-control, selective attention, working memory, cognitive flexibility, planning, and organization (Diamond, 2013). Deficits in executive functions occur quite frequently, even in the early stages of AD. They are usually evident in moderate stages and become the key to predicting the evolution of the severity of the disease (Lacerda et al., 2021).

Finally, a cognitive domain whose role has not been given much importance in this disease is attention. Recent studies (Siéroff et al., 2020) highlight its importance from early stages of the disease, especially because it is a key factor in other cognitive functions, such as executive functions or memory. Specifically, deficits in divided attention, selective attention, sustained attention, spatial-visual processing, and attentional focus have been found in AD (Huntley et al., 2017).

Treatments designed to slow down cognitive deterioration in dementia have followed two main lines of intervention, pharmacological and non-pharmacological. Pharmacological treatments, although showing interesting results, are currently being criticized because there is a stagnation in their results, given that there are no significant advances that manage to minimize the deterioration in the cognitive abilities of patients with dementia (Fink et al., 2018). Among the non-pharmacological treatments, a series of cognitive interventions (reality orientation therapy, cognitive stimulation, rehabilitation, cognitive training, reminiscence and other therapies) have been applied with different objectives and results, although all of them seek the activation of cognitive abilities (Meléndez et al., 2017; Roswiyani et al., 2019). In addition, this type of therapy stands out for its low cost and lack of side effects (Dyer et al., 2018).

One of the non-pharmacological interventions that has had the best results is cognitive stimulation (CS), which has the capacity to maintain cognition (Meyer & O'Keefe, 2020). The NICE guidelines for Dementia: assessment, management and support for people living with dementia and their caregivers (NICE, 2018) recommend offering group cognitive stimulation therapy to people living with mild to moderate dementia, recognizing the need for people with moderate cognitive impairment to participate in cognitive stimulation programs. CS can be defined as a set of cognitive activities designed to capitalize on the use of preserved cognitive functions to slow cognitive decline (Spector et al., 2008). CS involves performing a series of group activities, preferably pleasant ones, that stimulate thinking, attention, and memory (Woods et al., 2012).

There is a large body of literature on programs based on CS for dementia that have obtained good results in terms of maintaining cognitive capacity and improvement of quality of life (Dyer et al., 2018). For example, Tsantali et al. (2017) used a cognitive stimulation program for memory consisting of 32 group sessions over a period of four months for people with moderate AD and found a slower progression of deterioration. Piras et al. (2017) administered an intervention consisting of 14 structured group sessions to people with vascular dementia. The treatment group, compared to the active control group, showed an improvement in their cognition on measures of general and specific cognitive outcomes (short-term memory and executive function). Tarraga et al. (2016) concluded that CS improves cognition in people with Alzheimer's dementia after a 24-week program with five weekly sessions, although this effect is attenuated over time.

Other authors have used specific cognitive stimulation therapy (CST) programs and found improvements in various cognitive domains in people with dementia (Capotosto et al., 2017; Djabelkhir-Jemmi et al., 2018). In a recent review, Cafferata et al. (2021) found a mean effect of CS on global cognition that was slightly larger than those reported in previous meta-analyses (Aguirre et al., 2013); they also found substantial evidence for the benefits of CS on memory.

However, there is a need for further evidence in this field, mainly due to methodological problems in many studies that keep these results from being consistent (Lobbia et al., 2019; Woods et al., 2012). Validated intervention programs should be developed through rigorous studies, including the assessment of different cognitive functions to evaluate the effects of these interventions on specific cognitive domains and determinants of AD. There is a need to develop an intervention program based on cognitive stimulation for people with AD, in order to offer a therapeutic tool that corrects some of the errors of previous work and contributes more scientific evidence to the field.

The present study aimed to evaluate the efficacy of cognitive stimulation for maintaining functionality in specific areas of cognition: memory, executive function, and attention, in people with moderate AD, in a multi-center controlled trial. In agreement with previous studies, we expected to find positive outcomes on the cognition measures in the treatment group, observing a maintenance of their scores at the end of the intervention, whereas the control group would obtain significantly worse scores. Furthermore, although there is little evidence about the extent to which the potential benefits of cognitive stimulation can continue after the sessions end, we expected that, even if the significant improvements in the treatment group were not maintained at follow-up, their scores would not be equal to the scores of the control group.

Methods

Participants

Fifty-nine subjects with moderate dementia participated in a cognitive stimulation program. Participants were between 69 and 97 years old and had a mean age of 81.22 (*SD* = 6.7); 67.8% were women, 39% were married, 5.1% were single, and 55.9% were widowed. The mean number of years of schooling was 7.3 (*SD* = 1.3). The subjects belonged to four different care centers for people with dementia pertaining to the *Federación Valenciana de Familiares y Amigos de Personas con Alzheimer* (FEVAFA) in Spain. The design included pretest, posttest, and a follow-up evaluation after three months, and members of the control group were on a waiting list for intervention. The inclusion criteria were age > 65 years; score > 13 on the Mini-Mental State Examination (MMSE; Folstein et al., 1975); score between 3 and 4 on the Global Deterioration Scale (GDS; Reisberg et al., 1982); attendance at the center for more than two months; clinical diagnosis of Alzheimer-type dementia by the neurologist; not presenting depressed mood; completing 80% of the cognitive stimulation program. Exclusion criteria were illiteracy, severe behavioral problems, sensory deficits that prevented the delivery of the intervention, communication problems, as well as any serious medical or psychological condition.

Initially, 71 subjects were randomly assigned to the treatment group ($N = 36$) and the control group ($N = 35$). In the treatment group, six subjects dropped out of the study, five because they did not complete the required percentage of sessions and one due to a loss of diagnosis. Thus, 30 participants completed the study. In the control group, six subjects dropped out of the study, four due to illness at the time of the evaluation (after the intervention or during follow-up) and one due to death. Thus, 29 participants finished the study. All the participants met the inclusion/exclusion criteria and gave their informed consent. Table 1 shows sociodemographic data and tests for homogeneity between groups at pre-treatment.

The average number of sessions attended by participants in the treatment group was 15.93 ($SD = 0.31$). This represents a 99.5% participation rate.

INSERT TABLE 1

2.2. Instruments

Mini Mental State Examination (MMSE; Folstein et al., 1975). Is a screening test that quantitatively estimates the existence and severity of cognitive impairment. The maximum score is 30 points, which is obtained by adding together the scores on all the items.

The Spain-Complutense Verbal Learning Test (TAVEC; Benedet & Alejandre, 1998) was used to evaluate short-term recall, total learning, and delayed recall. This test consists of a list of 16 words from four different categories that are presented orally in five trials. After each trial, subjects have to repeat the words they remember, scoring between 0 and 16 on each trial and between 0 and 80 on all five trials (TAVEC total). In addition, after 20 minutes, they are asked to say the words they remember again to evaluate delayed memory (TAVEC delayed).

The Digit Span Forward and Backward subtest of the WAIS-III (Wechsler, 2001) was used. The Digit Span Forward assesses immediate recall; the subject has to repeat the sequence of numbers in the same order in which they are read. On the Digit Span Backward, the subject has to say the numbers in reverse order to the order read, thus requiring further processing of working memory. This test measures processes such as operative memory and mental flexibility. Both subtests have eight elements containing two items each, and so it is possible to obtain a maximum score of 16 on each subtest.

The semantic verbal fluency (name animals for one minute) and phonological fluency (words that begin with the letter "p" for three minutes) subtests of the Barcelona Test Revised (TBR; Peña-Casanova, 2005) were administered to assess language ability and observe the capacity for accessing and evoking elements from the lexical and semantic warehouse.

The clock drawing and copying test (CDCT) has been shown to be a very sensitive instrument for cognitive screening. It focuses on several cognitive domains, including verbal comprehension, perceptual and executive function (abstract thinking and planning), motor coordination, concentration, spatial knowledge visuospatial ability, and verbal and semantic memory. Based on Rouleau et al. (1992), the maximum score is 10 points on each of the three subscales: (1) representation of the clock face (maximum of 2 points); (2) number design (maximum of 4 points); and (3) position of the hands (maximum of 4 points). Lower scores indicate greater deterioration.

The Golden Stroop Test (Golden, 2001) is subdivided into three subtests. The first had the words "RED", "BLUE", and "GREEN" printed in black ink; in this subtest the task consisted of reading the words out loud as fast as they could. The second subtest consisted of 100 items written as "XXX", printed in blue, red, and green; subjects were asked to name out loud the color of the printed XXX as fast as they could. In the third subtest, the words "RED", "BLUE", and "GREEN" appeared in different color inks than the word. Participants were instructed to ignore the written words and name out loud the color of the ink as fast as they could.

Procedure

Care centers for people with dementia in the province of Valencia (Spain) that belong to the *Federación Valenciana de Familiares de Personas con Alzheimer* (FEVAFA) were contacted by email. After the centers agreed to participate in the project, a letter was sent to the relatives of people who met the inclusion criteria to explain the intervention to be performed in detail and obtain their informed consent. At the same time, an evaluation protocol manual was prepared, and four collaborators were trained to ensure that they understood the procedure and evaluated in the same way. A manual for the intervention program was also prepared, and the collaborators who would perform the intervention received training, these collaborators had to be psychology professionals with training in aging care. In the case of the evaluators (psychology professionals), the group to which the evaluated subjects belonged was masked to ensure the independence of the evaluations. A pilot test of the evaluation protocol and the intervention was carried out in a small group to adjust the times and make small corrections to aid comprehension (these data are not included).

The intervention lasted two months and consisted of two 50-minute group sessions per week, for a total of 16 sessions. Attention, executive functions, and memory tasks were worked on for a similar amount of time in each session. The specific activities carried out were categorization (three related words were indicated and they had to indicate to which category they belonged), answering previously presented short story questions, stimulus selection (a table with numbers was given to them and they had to indicate how many times a specific number was repeated), social problem solving, recalling biographical moments, planning simple tasks (they were asked about two steps they would perform in a daily task), and analyzing schedules they were given a person's weekly timetable and had to answer questions about this timetable). The intervention was carried out in groups of eight people guided by a professional. At the beginning of the session, the instructions were explained, then the activity sheets were handed out (first the memory activities, then the executive function activities and finally the attention activities), and at the end there was a farewell. The important thing was not the result, but the cognitive activation process. Routines were created to guide the participants: the same time, same day of the week, same place of work.

The control group on the waiting list came to the centers to do different entertainment activities (drawing, board games, etc.). They performed the activities also in groups, and for a total time similar to that of the experimental participants.

A committee of the participating centers formed by managers, relatives of the participants and the participants themselves, authorized the research. informed consent was obtained and the ethical principles of the Helsinki declaration were followed.

Results

The interaction effects were significant for MMSE, TAVEC1, TAVEC-TOT, TAVEC-DLY, TBR-SEM, TBR-PHON, CLOCK-D and STROOP-W, but not for CLOCK-C, DIG-DIR, DIG-INV, STROOP-C, STROOP-W/C and STROOP-I (see Table 2).

INSERT TABLE 2

The study of simple effects confirmed that there were no between-group differences in any of the scores at pre-treatment. Significant differences between groups were obtained at post-treatment in all the variables studied, with the treatment group obtaining higher scores in all cases. Finally, in the follow-up, no significant differences were observed between the groups in any of the variables (see Table 3).

INSERT TABLE 3

The results of the evolution of the groups over time in each of the cognitive measures whose interaction was significant are presented below.

Mini Mental State Examination

Regarding the MMSE significant changes were observed in the treatment group ($F2$, 56 = 14.45; $p < .001$; $\eta^2 = .340$). Bonferroni post-hoc comparisons showed that there was a significant increase in scores from pre-treatment to post-treatment (mean difference = -0.83, SE = 0.31, $p = .029$, $d = -0.29$), with a small effect size, but a significant decrease from post-treatment to follow-up (mean difference = 1.90, SE = 0.39, $p < .001$, $d = 0.62$), with a medium effect size. In the control group, significant changes were observed ($F2$, 56 = 15.75; $p < .001$; $\eta^2 = .360$). Bonferroni post-hoc comparisons showed that there was a significant decrease in scores from pre-treatment to post-treatment (mean difference = 1.62, SE = 0.32, $p < .001$, $d = 0.47$) and a significant decrease from pre-treatment to follow-up (mean difference = 2.45, SE = 0.49, $p < .001$, $d = 0.57$). The effect sizes observed were small and medium, respectively.

Spain-Complutense Verbal Learning Test

For the TAVEC-1, significant changes were observed in the treatment group ($F2$, 56 = 9.49; $p <.001$; $\eta^2 = .253$). Bonferroni post-hoc comparisons showed that there was a significant increase in scores from pre-treatment to post-treatment (mean difference = -1.07, SE = 0.27, $p = .001$, $d = 0.86$) and a significant decrease from post-treatment to follow-up (mean difference = 0.87, SE = 0.23, $p = .001$, $d = 0.75$). The effect sizes were large and medium, respectively. In the control group, significant changes were observed ($F2$, 56 = 4.30; $p = .018$; $\eta^2 = .133$). Bonferroni post-hoc comparisons showed that there was a significant decrease in scores from pre-treatment to follow-up (mean difference = 0.59, SE = 0.23, p = .035, d = 0.50). The effect size observed was medium.

Regarding the TAVEC total significant changes were observed in the treatment group ($F2$, 56 = 13.95; $p < .001$; $\eta^2 = .333$). Bonferroni post-hoc comparisons showed that there was a significant increase in scores from pre-treatment to post-treatment (mean difference = -2.83, SE = 0.85, p = .005, d = 0.52) and a significant decrease from post-treatment to follow-up (mean difference = 3.07, SE = 0.69, $p < .001$, d = 0.49). The effect sizes were medium and small, respectively. In the control group, significant changes were observed ($F2$, 56 = 12.09; $p < .001$; $\eta^2 = .302$). Bonferroni post-hoc comparisons showed that there was a significant decrease in scores from pre-treatment to post-treatment (mean difference = 4.10, SE = 0.87, $p < .001$, d = 0.48) and from pre-treatment to follow-up (mean difference = 4.86, SE = 0.87, $p < .001$, d = 0.55). The effect sizes were small and medium, respectively.

For the TAVEC delayed, significant changes were observed in the treatment group ($F2$, 56 = 6.55; p = .003; $\eta^2 = .190$). Bonferroni post-hoc comparisons showed that there was a significant increase in scores from pre-treatment to post-treatment (mean difference = 1.00, SE = 0.28, p = .002, d = 0.89), with a large effect size. In the control group, no significant changes were observed ($F2$, 56 = 1.55; p = .220; η^2 = .053).

Barcelona Test Revised

On semantic verbal fluency, significant changes were observed in the treatment group ($F2$, 56 = 20.07; $p < .001$; $\eta^2 = .417$). Bonferroni post-hoc comparisons showed that there was a significant increase in scores from pre-treatment to post-treatment (mean difference = -2.20, SE = 0.39, $p < .001$, d = 0.73) and a significant decrease from post-treatment to follow-up (mean difference = 1.87, SE = 0.37, $p < .001$, d = 0.56). The effect sizes were medium in both cases. In the control group, no significant changes were observed ($F2$, 56 = 3.13; p = .051; $\eta^2 = .101$).

For phonological verbal fluency, significant changes were observed in the treatment group ($F2$, 56 = 9.23; $p < .001$; $\eta^2 = .248$). Bonferroni post-hoc comparisons showed that there was a significant increase in scores from pre-treatment to post-treatment (mean difference = -3.20, SE = 0.79, p = .001, d = 0.45) and a significant decrease from post-treatment to follow-up (mean difference = 2.50, SE = 0.73, p = .004, d = 0.35). The effect sizes observed were small in both cases. In the control group, significant changes were observed ($F2, 56 = 11.59$; $p < .001$; $\eta^2 = .293$). Bonferroni post-hoc comparisons showed that there was a significant decrease in scores from pre-treatment to post-treatment (mean difference = -2.29, $SE = 0.81$, $p = .019$, $d = 0.40$) and from pre-treatment to follow-up (mean difference = 3.79, $SE = 0.78$, $p <.001$, $d = 0.70$). The effect sizes were small and medium, respectively.

Clock drawing and copying test

Regarding the direct drawing Clock Test, no significant changes were observed in the treatment group ($F2, 56 = 1.79$; $p = .192$; $\eta^2 = .057$). In the control group, significant changes were observed ($F2, 56 = 10.59$; $p < .001$; $\eta^2 = .274$). Bonferroni post-hoc comparisons showed that there was a significant decrease in scores from pre-treatment to post-treatment (mean difference = 1.09, $SE = 0.31$, $p = .003$, $d = 0.51$) and from pre-treatment to follow-up (mean difference = 1.48, $SE = 0.39$, $p = .001$, $d = 0.63$). The effect sizes observed were medium.

Golden Stroop Test

Finally, for the Stroop words test significant changes were observed in the treatment group ($F2, 56 = 3.38$; $p = .041$; $\eta^2 = .108$). Bonferroni post-hoc comparisons showed that there was a significant increase in scores from pre-treatment to post-treatment (mean difference = -4.40, $SE = 1.68$, $p = .034$, $d = 0.24$). The effect size observed was small.

Discussion

Due to the increase in the older adult population, there are more people with AD who require effective treatments. Although CS is one of the most widely used non-pharmacological treatments, evidence of its efficacy still needs to be strengthened. This study demonstrated the efficacy of a cognitive stimulation intervention for older adult patients with AD. However, the same results were not obtained for all the cognitive domains and variables studied.

Taking the MMSE as a measure of general cognitive functioning, in the treatment group, no modifications in the baseline scores were observed after treatment, which means that they were maintained, whereas in the control group, a significant decrease was observed. This result is similar to those obtained in other investigations that indicate that CS is beneficial for general cognitive functioning in people with dementia (Djabelkhir-Jemmi et al., 2018; Tarraga et al., 2006; Tsantali et al., 2017). Spector et al. (2008) and

Dyer et al. (2018) point out that CS has a protective effect on the progression of deterioration, which in this research was observed in the maintenance of the scores in the treatment group, slowing down their possible reduction.

The cognitive domain of memory showed significant effects after the intervention in the treatment group, with an increase in immediate memory, learning, and delayed memory scores; however, this effect was not maintained at follow-up, when the participants obtained scores similar to baseline. The control group showed a significant decrease in their scores from baseline to follow-up. The initial mitigating effect of cognitive stimulation in the treatment group could be explained by a constant cortical reorganization caused by repeated stimulation and activation, favoring synaptic plasticity and strengthening cortical connections (Yeung et al., 2015). However, it is important to point out that, after the end of the treatment, the effects were lost, which reinforces the importance of maintaining this type of treatment over time. On variables related to working memory, such as direct and inverse digits, where there is involvement with other cognitive domains such as executive functions and attention, no benefits were found. Huntley and Howard (2010) point out that, in the progression of AD deterioration, digit span tests are significantly affected by an impairment in the central executive (which involves coordination with other domains, focusing, division of attention, inhibition, and updating and manipulation of information).

Regarding executive functions, similar to the effects on memory, a significant increase is observed from baseline to the end of the intervention, but once the intervention is over, patients return to their initial scores. In the control group, a continuous decrease in scores was observed, indicating a progressive worsening in this domain. These results are similar to those found by Moro et al., (2015) with MCI. In addition, Moro et al. (2015) observed an improvement in EF that positively influences the results of memory and general cognition tests. Therefore, EF seems to be an important aspect to consider in interventions with people with Alzheimer's disease and moderate cognitive impairment. Specifically, this study shows that variables such as verbal fluency (TBR-SEM, TBR-PHON) or spatial planning (CLOCK-D) benefitted from the application of CS, at least immediately after receiving the intervention.

Finally, regarding attention, a significant effect was only found after the intervention in the basic ability to maintain the focus of attention (STROOP-W). The ability to maintain attentional focus involves fewer cognitive resources and can be dissociated from other cognitive processes (McAvinue et al., 2012), which could explain the results obtained. CS could provide short-term benefits in a basic aspect of attention, such as maintaining focus, without benefiting other components of attention. It should be kept in mind that attentional processes are severely affected in dementias with moderate cognitive impairment (Huntley et al., 2017), and so it might be advisable to intervene in the attentional variables in the early stages of dementia. However, even though attentional deficits in dementias, and specifically in AD, are important, there is very limited literature on the effects of CS on this cognitive domain, and mixed conclusions have been reached (Tsantali et al., 2017). There is a need for further research on this domain.

In summary, CS has been shown to be an interesting intervention for people with moderate AD in order to maintain memory and some aspects of executive functions and attention. The main contributions of this study, unlike previous ones, is the group nature of the intervention, as opposed to individual interventions, which is in moderate dementia versus early dementia and, finally, highlights the assessment of specific cognitive domains. However, there is still a need for further studies in the field, specifically about the effects on specific domains and on attention, as well as the effects of maintaining CS over time.

Limitations

One of the main limitations of the present study is that there was no control over the pharmacological treatments that may have been administered to the participants in both groups. In addition, it would be interesting to apply maintenance CS during the months after the intervention by holding similar sessions to work on the three large domains addressed in this study.

Conclusions

Cognitive stimulation has proven to be an effective intervention for people with moderate dementia. The proposed group intervention program has been shown to be useful in maintaining some aspects of attention, executive functions and memory in people with moderate dementia. The results are diluted without the implementation of the intervention. In general, it is necessary to continue working on the development of non-pharmacological intervention programs for people with dementia, providing more and more evidence in this regard, combining the importance of research and applied work.

Declaration of Conflicting Interests

The Authors declares that there is no conflict of interest.

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Table 1. Sociodemographic data and tests for homogeneity of groups.

		Treatment ($N = 30$)	Control ($N = 29$)	p
Age		82.17 (6.59)	80.30 (6.97)	.294
Gender	Man	30%	34.5%	.715
	Women	70%	65.5%	
Marital status	Married	36.7%	41.4%	.626
	Single	6.7%	3.4	
	Widow	56.6%	55.2	
Years of education		7.71 (1.36)	7.41 (1.22)	.502

Table 2. Effects of interaction and group means on time.

	Interaction effects			Treatment Group			Control Group		
	F	p	η^2	T1	T2	T3	T1	T2	T3
MMSE	16.32	<.001	.368	19.30	20,13	18.23	19.93	18.31	17.48
TAVEC-1	5.04	.010	.152	1.87	2.93	2.07	2.38	2.28	1.79
TAVEC-TOT	17.68	<.001	.387	15.73	18.57	15.50	18.62	14.52	13.76
TAVEC-DLY	6.76	.002	.194	.77	1.77	1.30	1.38	.93	.93
DIG-DIR	1.88	.161	.061	4.60	4.57	4.03	4.48	3.93	3.72
DIG-INV	1.58	.215	.053	2.20	2.23	2.00	2.48	2.07	1.86
TBR-SEM	9.58	<.001	.255	6.53	8.73	6.87	7.10	6.86	6.10
TBR-PHON	12.88	<.001	.315	8.83	12.03	9.53	10.59	8.29	6.79
CLOCK-D	9.51	<.001	.254	3.73	4.30	3.93	4.22	3.14	2.74
CLOCK-C	2.97	.059	.096	5.22	5.50	4.73	6.14	4.72	4.60
STROOP-W	5.68	.006	.169	42.23	46.63	44.13	41.45	38.03	38.31
STROOP-C	.911	.408	.032	27.13	28.87	27.23	26.00	27.38	28.24
STROOP-W/C	.508	.604	.018	23.40	24.17	22.67	26.34	25.34	25.48
STROOP-I	.543	.584	.019	7.17	6.98	6.08	10.77	8.24	8.35

Note: MMSE: Mini Mental States Examination; TAVEC-1: TAVEC trial 1; TAVEC-TOT: Total words TAVEC; TAVEC-DLY: TAVEC delayed; DIG-DIR: Direct digits; DIG-INV: Inverse digits; TBR-SEM: Barcelona semantic verbal fluency; TBR-PHON: Barcelona phonological verbal fluency; CLOCK-D: direct drawing Clock Test: CLOCK-C: Copy Clock Test; STROOP-W: Stroop words; STROOP-C: Stroop color; STROOP-W/C: Stroop word/color; STROOP-I: Stroop interference

Table 3. Simple effects between groups in pre-intervention, post-intervention, and follow-up scores.

	Pre-treatment			Post-treatment			Follow-up		
	F	p	η^2	F	p	η^2	F	p	η^2
MMSE	.76	.387	.013	4.21	.045	.069	.47	.497	.008
TAVEC-1	2.25	.139	.038	4.15	.046	.068	.84	.362	.015
TAVEC-TOT	2.79	.100	.047	4.17	.046	.068	.71	.402	.012
TAVEC-DLY	3.35	.072	.055	6.58	.013	.103	1.22	.275	.021
TBR-SEM	.59	.445	.010	4.74	.034	.077	.77	.383	.013
TBR-PHON	1.11	.297	.019	4.81	.032	.078	3.65	.061	.060
CLOCK-D	.87	.353	.015	4.35	.042	.071	3.48	.067	.058
STROOP-W	.03	.860	.001	4.08	.048	.067	1.59	.213	.027

Note: MMSE: Mini Mental States Examination; TAVEC-1: TAVEC trial 1; TAVEC-TOT: Total words TAVEC; TAVEC-DLY: TAVEC delayed; TBR-SEM: Barcelona semantic verbal fluency; TBR-PHON: Barcelona phonological verbal fluency; CLOCK-D: direct drawing Clock Test; STROOP-W: Stroop words