CLINICAL SCIENCE

Effects of a multidisciplinar cognitive rehabilitation program for patients with mild Alzheimer's disease

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OBJECTIVE: To evaluate the effects of a multidisciplinary rehabilitation program on cognition, quality of life, and neuropsychiatric symptoms in patients with mild Alzheimer's disease.

METHOD: The present study was a single-blind, controlled study that was conducted at a university-based day-hospital memory facility. The study included 25 Alzheimer's patients and their caregivers and involved a 12-week stimulation and psychoeducational program. The comparison group consisted of 16 Alzheimer's patients in waiting lists for future intervention.

INTERVENTION: Group sessions were provided by a multiprofessional team and included memory training, computer-assisted cognitive stimulation, expressive activities (painting, verbal expression, writing), physiotherapy, and physical training. Treatment was administered twice a week during 6.5-h gatherings.

MEASUREMENTS: The assessment battery comprised the following tests: Mini-Mental State Examination, Short Cognitive Test, Quality of Life in Alzheimer's disease, Neuropsychiatric Inventory, and Geriatric Depression Scale. Test scores were evaluated at baseline and the end of the study by raters who were blinded to the group assignments.

RESULTS: Measurements of global cognitive function and performance on attention tasks indicated that patients in the experimental group remained stable, whereas controls displayed mild but significant worsening. The intervention was associated with reduced depression symptoms for patients and caregivers and decreased neuropsychiatric symptoms in Alzheimer's subjects. The treatment was also beneficial for the patients' quality of life.

CONCLUSION: This multimodal rehabilitation program was associated with cognitive stability and significant improvements in the quality of life for Alzheimer's patients. We also observed a significant decrease in depressive symptoms and caregiver burden. These results support the notion that structured nonpharmacological interventions can yield adjunct and clinically relevant benefits in dementia treatment.

KEYWORDS: Alzheimer's disease; Treatment; Rehabilitation; Cognition; Quality of life.

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INTRODUCTION

Given the progressive, irreversible nature of Alzheimer's disease (AD) and the limited symptomatic benefits delivered by pharmacotherapy,[1,2] the provision of nonpharmacological treatment in addition to standard outpatient care is an asset of good clinical practice. The clinical perception supports that nonpharmacological interventions of various kinds may be helpful in the long-term global management of the disease. More controlled studies are required, however, to yield evidence-based information on the effectiveness of cognitive rehabilitation.

Rehabilitation is a process of active change that allows disabled people to reach an ideal level of physical, psychological, and social functioning in the presence of ongoing or previous disease or impairment.[3,4] Cognitive

rehabilitation refers to the use of techniques to improve performance for specific mental functions,[5] whereas neuropsychological rehabilitation, in a broader sense, aims to help patients and their family members deal with the cognitive, emotional, and social burden of the disease, thereby ultimately improving the quality of life.[6,7] Several methods targeting cognition and functionality have been proposed for patients with AD dementia.[8-11] Most of these techniques involve multiprofessional teamwork and include restructuring of the home environment, nutritional advice, physical activities, psychological counseling, support for family members and caregivers, and neuropsychological rehabilitation.[12] Because AD is a progressive neurodegenerative disorder, cognitive stimulation rather than rehabilitation *per se* may be a more appropriate term to refer to the possible interventions within the context of this disease.[13]

The comparison among distinct studies using cognitive stimulation techniques is sometimes difficult because of a wide variability in the type, complexity, and duration of interventions; lack of uniformity in target cognitive functions and training protocols; small sample sizes in the majority of studies; unavailability of comparison groups; and other methodological constraints. As a whole, however, physicians generally accept that cognitive stimulation can improve cognition and behavioral symptoms of patients with dementia.[1] Loewenstein et al.[14] showed that a combination of cognitive and functional rehabilitation with pharmacological treatment with cholinesterase inhibitors promoted cognitive and functional stability for patients with mild AD. Similarly, Talassi et al.[15] recently found that systematic cognitive training may optimize the benefits of pharmacological treatment in patients with early-stage AD. Interestingly, no training-related improvement in memory was obtained from a 12-week multimodular cognitive rehabilitation program in older adults.[16] Spector and colleagues[17] published a multicenter, randomized, placebo-controlled study on psychosocial interventions in AD showing that patients who received a 14-session reality orientation and cognitive stimulation schedule had significant benefits in cognition and quality of life. In another study, Raggi et al.[10] administered a multidisciplinary rehabilitation program to AD patients in a hospital setting that used reality orientation and computerized cognitive training to stimulate attention, language, numerical and spatial skills, psychomotor speed, and memory. The intervention yielded significant improvements in activities of daily living, neuropsychiatric symptoms, and cognition.

The objective of the present study was to evaluate the effect of a multifunctional stimulation program on cognition, neuropsychiatric symptoms, and quality of life in patients with mild AD in a controlled, single-blind design. We also addressed the benefits of this intervention for the mental health parameters of caregivers.

METHODS

Participants and setting

Forty-one AD patients, who were diagnosed according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA)[18] criteria, and their respective caregivers were recruited at the memory clinic of the Psychogeriatric Unit of the Institute of Psychiatry between August 2007 and June 2009. The study was approved by the local ethics committee, and informed consent was obtained from patients and/or caregivers. Participants were referred from outpatient units dedicated to psychogeriatric care at the same institution. In addition, some patients were referred from other sources in the local community. Inclusion criteria were mild dementia, which was indicated by a score of 0.5 or 1.0 in the Clinical Dementia Rating Scale (CDR)[19] and a score of 16 or more in the Mini-mental State Examination (MMSE),[20] and concomitant standard pharmacological treatment for AD (i.e., use of cholinesterase inhibitors and/or memantine in stable therapeutic doses for at least three months).

Measurements

All patients and controls were submitted to clinical, cognitive, and quality of life assessments by two independent raters who were blinded to the group assignments. The same instruments were used at the baseline and the endpoint. The assessment battery included the MMSE,[20] which is a brief cognitive screening test that evaluates temporal and spatial orientation, memory, attention, calculation, language, and visuoconstructive capacity; the Short Cognitive Test (SKT),[21] which is a broad cognitive screening battery that addresses attention, processing speed, and memory; the Neuropsychiatric Inventory (NPI),[22] which evaluates the presence of 10 psychiatric symptoms (i.e., delusions, hallucinations, irritability, disinhibition, agitation, anxiety, depression, euphoria, apathy, and psychomotor abnormalities); the Geriatric Depression Scale (GDS),[23] and the Quality of Life in Alzheimer's Disease Evaluation Scale (QoL-AD).[24] The caregivers were assessed with the GDS and the caregiver's protocol of the QoL-AD, which assessed the caregivers' perceptions of their patient's quality of life.

Although the rehabilitation program included physical training, and physiotherapy (as detailed below), the assessment protocol did not include direct measures of these intervention components because the primary goal of the study was to investigate the effects of multiprofessional intervention on cognitive, functional, psychiatric, and quality of life outcome variables. The lack of direct measures, however, can be regarded as a limitation of the study.

Intervention

Four distinct intervention groups were formed (one per semester), and each group contained a maximum of 12 patients plus their respective caregivers. The first 12 patients to be referred to the service were assigned to the experimental group, and the following 12 patients were assigned to the waiting-list control group. In the second wave of intervention, subjects in the first control group were assigned to the second experimental group, and the next referrals constituted the second control group. This procedure was repeated for the subsequent waves of intervention. This recruitment strategy was chosen to avoid delays in treatment to patients formerly allocated in the control group (i.e., intervention was provided within a maximum time-lag of 6 months from referral).

The final sample consisted of 25 patients in the experimental group and 16 patients in the control group. Five patients with moderate dementia (CDR = 2) were referred to our service during the recruitment phase. Although these patients did not meet inclusion criteria (their data were not

included in the analysis), participation in all treatment sessions was granted for ethical reasons. From the total sample of 41 patients, five subjects failed to reach the experimental endpoint: one died, two were unable to comply with all sessions because of limited accessibility, and two dropped out for personal reasons. Compliant patients were able to attend at least 90% of the treatment sessions (i.e., 22 from a total of 24 treatment days). Caregivers were mostly represented by family members (90.2%) of AD patients. Professional caregivers were expected to spend at least 12 h a day with their patients.

The intervention was administered in group sessions offered twice a week at the day-hospital facilities for 12 consecutive weeks. Sessions lasted from 9:00 AM to 3:30 PM (lunch and refreshments were provided and lasted 90 minutes), and the 24 sessions resulted in a total of 120 h of intervention (5 h daily). The program consisted of the following activities: cognitive rehabilitation, computer-assisted cognitive training, speech therapy, occupational therapy, art therapy, physical training, physiotherapy, and cognitive stimulation with reading and logic games. Each activity lasted for 60-90 minutes and was offered once a week (Table 1). Psychoeducation and psychological counseling were provided in group sessions for caregivers twice a week. The purpose of these meetings was to explain the clinical aspects of the disease by focusing on its progressive course and the expected loss of autonomy of the patient. The exchange of personal accounts and experiences among participants was also encouraged. Patients on the waiting list for forthcoming intervention groups (control group) received standard outpatient care, including monthly follow-up visits to the memory clinic.

The rehabilitation sessions contained a variety of components. Cognitive rehabilitation was delivered through exercises to improve attention, memory, spatial and temporal orientation, and self-adaptations to cognitive impairment. Computer-assisted cognitive training consisted of a preparatory session (in which participants were made familiar with the use of the computer) followed by the engagement in different tasks that primarily consisted of memory and attention games (user-friendly and adjustable for complexity). Art therapy aimed at stimulating cognitive, emotional, and interpersonal skills through expressive and artistic techniques, and a special emphasis was placed on nonverbal expression that was devoid of any critical judgment of the actual quality of the artistic work. Occupational therapy was intended to develop resources and strategies to improve the completion of functional goals, including training in basic (hygiene, feeding, getting dressed) and instrumental activities of daily living (paying bills, shopping, leisure, and social activities). In addition, patients and caregivers were instructed about the need of household adaptations to enhance orientation and autonomy. Physiotherapy was aimed at improving balance and preventing falls through exercises administered to patients. In addition, caregivers were also coached to reinforce exercises and habits at home. Physical training was offered as a complementary program for physically able patients to improve physical conditioning. Special emphasis was placed on motor, emotional, social, and cognitive aspects. In addition to strength and balance exercises, patients were invited to group walks and stretching sessions. Speech therapy was also provided to enhance general communication and communication strategies in specific daily-life situations. The sessions also involved cognitive stimulation through logic games (e.g., simplified chess and related games), which consisted of preliminary lessons on the rules and objectives of the games and was designed to improve concentration, logical-mathematical reasoning, rapid thinking, and decision making.

Statistical analysis

The Kolmogorov-Smirnov test was used to determine whether study variables followed a normal distribution, which supported the use of parametric tests (t test for two independent samples) in the analysis of outcomes. Chi-square (when necessary, adjusted by the Monte Carlo method) and independent-sample t tests were used to assess the similarity between experimental and control groups at baseline. Paired-sample t tests were used to address changes from the baseline within each group.

RESULTS

No significant differences were observed in the mean age and education level between patients in the experimental and control groups. The average age of the patients was 75 years, and the patients had an average of 10 years of schooling. In addition, there were slightly more females in each group (experimental group, 64%; control group, 62%, $p = 0.9$). All patients were either married or widowed, and more patients in the experimental group group were married (56%, N.S.). At baseline, no significant differences between experimental and control groups were found with respect to mean scores in the various psychometric tests pertaining to the assessment battery. Nine patients in the experimental group and 7 in the control group had CDR = 0.5, whereas 16 patients in the experimental group and 9 in the control group had CDR = 1. Fisher's exact test did not indicate any significant difference between the CDR scores of experimental and control groups.

Most caregivers were family members (34.1% spouses, 56.1% children, 9.8% formal caregivers). The mean age of the caregivers was 51.6 years (15.3 SD), and the mean educational level was 9.1 years (4.1 SD). There were no significant differences for age and education between caregivers in the experimental and control groups ($p = 0.996$ and $p = 0.423$, respectively).

Table 1 - Schedule of activities (experimental group).

Time	Tuesdays	Time	Thursdays
9:00-10:30 AM	Cognitive rehabilitation (computer-assisted)	9:00-10:30 AM	Cognitive rehabilitation
10:30-12:00 AM	Art therapy	10:30-12:00 AM	Physical training
12:00-1:00 PM	Lunch	12:00-1:00 PM	Lunch
1:00-2:00 PM	Occupational therapy	1:00-2:00 PM	Logic games
2:00-2:30 PM	Rest	2:00-2:30 PM	Rest
2:30-3:30 PM	Physiotherapy	2:30-3:30 PM	Speech therapy

Table 2 displays the mean values and standard deviations for psychometric test scores at baseline and at the end of the study. Paired-sample *t* tests addressing within-group differences (baseline *vs.* endpoint) in test scores showed that patients in the control group had a tendency for cognitive decline, which was indicated by a slight, but significant, increase in total SKT scores and in the attention SKT subscore (i.e., higher scores in the SKT mean worse performance). Conversely, patients in the experimental group remained stable with respect to the aforementioned variables. Although the MMSE scores remained unchanged in both groups (irrespective of treatment), the intervention was associated with a significant reduction in GDS scores, which indicated improvement in depressive symptoms from both the patients' and caregivers' perspectives. In addition, there was a significant decrease in caregiver distress, which was indicated by a reduction in the NPI distress subscore. Interestingly, patients and caregivers in the experimental group also reported an improvement in their quality of life according to the QoL-AD.

DISCUSSION

This was a single-blind, controlled study addressing the effects of a nonpharmacological treatment program in AD patients with mild dementia. The intervention consisted of an extensive, multimodal stimulation program that primarily focused on the rehabilitation of cognitive abilities; however, the ultimate goal was to promote well being and improve quality of life. In regards to cognition, patients in the experimental group remained stable, whereas those in the comparison group had a mild but significant worsening in attention and global performance. We understand that this effect is plausible given the progressive nature of the disease, which can render untreated patients prone to cognitive deterioration over time. Although some cognitive changes may not have been detected by the MMSE in the relatively short duration of this study (i.e., three months), cognitive changes were seen in the SKT. Indeed, there were significant changes in the total score and the attention subscore, which indicated subtle worsening of patients in the control group. Studies involving combined pharmacological and nonpharmacological treatment with multimodal stimulation programs reported slight improvements in MMSE scores.[8,10] Most studies that have evaluated the effect of nonpharmacological interventions in AD observed stabilization or, at most, modest improvement of cognitive functions.[1] Conversely, untreated patients may show cognitive decline. Our results are in agreement with the findings of previous studies, which have suggested that robust changes in cognition are unlikely to occur as a consequence of cognitive training in patients with AD. Gains tend to be modest and may be best documented as a slight improvement in certain cognitive domains.[16,25] Compared with the MMSE, the SKT may be more sensitive to subtle changes because it is a more comprehensive cognitive assessment battery and takes into account processing speed and response accuracy.[21,26] In addition, the availability of five parallel versions of the test makes it less prone to learning effects upon retesting, which is an important issue in longitudinal studies.[27]

Table 2 - Psychometric test scores at baseline and after intervention (endpoint).

Variable	Group	Baseline[#]	Endpoint	*p*-value*
Mini-Mental State Examination	CG	23.3 (3.9)	22.4 (2.8)	0.1
	EG	22.6 (2.9)	22.5 (3.8)	0.9
Short Cognitive Test (SKT)				
Total SKT score	**CG**	**12.6 (5.4)**	**13.8 (5.5)**	**0.05**
	EG	14.5 (5.4)	14.6 (6.1)	0.9
Memory subscore	CG	5.5 (1.9)	5.2 (2.2)	0.4
	EG	5.2 (2.2)	4.9 (2.6)	0.5
Attention subscore	**CG**	**7.1 (5.0)**	**8.6 (4.8)**	**0.01**
	EG	9.3 (4.3)	9.6 (4.7)	0.5
Neuropsychiatric Inventory				
Total score	CG	36.5 (23.9)	28.7 (18.5)	0.1
	EG	27.5 (22.4)	25.9 (20.8)	0.4
Distress subscore	CG	13.5 (9.1)	13.6 (9.2)	0.9
	EG	**11.7 (8.9)**	**9.9 (7.9)**	**0.02**
Geriatric Depression Scale (GDS)				
Patient	CG	4.3 (3.2)	4.7 (3.4)	0.7
	EG	**4.7 (3.1)**	**3.4 (3.0)**	**0.001**
Caregiver	CG	4.0 (3.2)	3.9 (3.3)	0.9
	EG	**3.9 (3.5)**	**3.1 (2.9)**	**0.02**
Quality of Life in AD Scale				
Patient	CG	36.1 (5.8)	35.4 (6.1)	0.5
	EG	**35.2 (5.0)**	**37.3 (4.4)**	**0.004**
Caregiver	CG	31.1 (7.4)	32.7 (6.6)	0.3
	EG	**30.8 (5.2)**	**33.0 (6.0)**	**0.04**

EG, experimental group; CG, control group. Values represent means and standard deviations (SD) of test scores;

**p*-values in the right column: paired-sample *t* tests addressing within-group differences (baseline *vs.* endpoint) in test scores (significant differences are shown in bold).

[#]Independent-sample *t* tests comparing mean scores at baseline yielded nonsignificant differences between EG and CG.

Although well-established outcome measures have become available in pharmaceutical trials in recent years, the effects of nonpharmacological interventions may not be properly identified by commonly used psychometric tests. Interestingly, functional or quality-of-life outcome measures may be better tools to measure nonpharmacological effects. Thus, negative data based on quantitative testing must be interpreted with caution, particularly in light of the clinical experience, which suggests that qualitative benefits to global function are observed in the close, continuous management of AD patients. Benefits associated to nonpharmacological interventions may encompass minor, nonsignificant changes in test scores, and we understand that the modification of noncognitive functions may partially explain the clinical perception of change. In a recent study conducted by our group, Machado et al.[28] suggested that the impressions of changes in the quality of life in patients with AD can be better depicted by a qualitative analysis of patients' reports than by objective test scores.

Accordingly, a relevant outcome of the present study was the reduction of depressive symptoms in patients who received the intervention along with their caregivers. This finding is clinically relevant and is in line with similar studies in the literature[1,10,29] (i.e., there is a high rate of depression in caregivers of AD patients).[30-32] In addition, the incidence of neuropsychiatric symptoms was low in both groups (there was no significant difference between the groups), which seemed to be because our sample only contained patients with mild dementia (i.e., those who were less likely to present with important behavioral manifestations). Interestingly, participation in the program resulted in a mild reduction in caregiver distress. In a recent study that

was also conducted in Brazil, Camara et al.[33] reported decreases in caregiver distress as an indirect benefit of the rehabilitation of patients with AD. Caring for patients with dementia is highly stressful because of the progressive loss of autonomy and the presence of behavioral symptoms associated with AD. Thus, psychoeducation and psychological counseling, which was offered biweekly in the present study, may have contributed to the reported benefits, even in the absence of significant changes in the presentation of the disease.[34,35] Moreover, we found significant improvements in the quality of life for both patients and caregivers after the intervention. This outcome corroborated earlier studies[10,28,29,36] suggesting that improvements in quality of life can be demonstrated by objective measures (to a certain extent).

The relatively small sample of patients, especially in the control group, was a limitation of the present study. In addition, the current intervention program required a significant investment of time and human resources to deliver the therapeutic sessions that may not be available in most settings because of the requirement for specialized training. Future studies should investigate the contribution of individual rehabilitation components to the outcome measures because the present investigation only assessed the impact of the global rehabilitation protocol. In addition, there may have been some training redundancies in the format of the present study (e.g., in the computer assisted training and cognitive rehabilitation components and in the physical training and physiotherapy components). In future protocols, these rehabilitation modalities might be merged to guarantee the best use of financial and human resources.

CONCLUSION

The current multimodal stimulation program was beneficial for patients with mild AD. Future studies that are based on larger, more homogeneous samples and use more rigorous randomization methods should be pursued in this field of research.

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