CLINICAL SCIENCE

Effects of a multidisciplinary 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.

INTRODUCTION

Given the progressive, irreversible nature of Alzheimer’s disease (AD) and the limited symptomatic benefits delivered by pharmacotherapy, 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. Cognitive
rehabilitation refers to the use of techniques to improve performance for specific mental functions, 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. Several methods targeting cognition and functionality have been proposed for patients with AD dementia. 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. 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.

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. Loewenstein et al. 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. 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 multimodal cognitive rehabilitation program in older adults. Spector and colleagues published a multicare center, 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. 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-ADRSA) 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) and a score of 16 or more in the Mini-Mental State Examination (MMSE), 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, which is a brief cognitive screening test that evaluates temporal and spatial orientation, memory, attention, calculation, language, and visuocognitive capacity; the Short Cognitive Test (SKT), which is a broad cognitive screening battery that addresses attention, processing speed, and memory; the Neuropsychiatric Inventory (NPI), 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), and the Quality of Life in Alzheimer’s Disease Evaluation Scale (QoL-AD). 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
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.\(^27\)

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

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

| Variable                  | Group | Baseline | Endpoint | p-value |
|---------------------------|-------|----------|----------|---------|
| **Mini-Mental State Examination** |       |          |          |         |
| EG  | 23.3 (3.9) | 22.4 (2.8) | 0.1      |
| CG  | 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 and differences (baseline vs. endpoint) in test scores (significant differences are shown in bold).

\(^1\)Independent-sample t-tests comparing mean scores at baseline yielded nonsignificant differences between EG and CG.
was also conducted in Brazil, Camara et al.\textsuperscript{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.\textsuperscript{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\textsuperscript{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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