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Comparing two programs of cognitive training in Alzheimer's disease: a pilot study

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Objectives – To evaluate the efficacy of two different procedures of individual cognitive training in mild to moderate Alzheimer's Disease (AD). *Material and methods* – Twenty-two AD patients entered the study. We compared stimulation of procedural memory (group 1) with training of partially spared cognitive functions (group 2). Assessment included: neuropsychological tests, scales, and the Functional Living Skills Assessment (FLSA), a standardized battery built to directly evaluate patients' performance in everyday life. *Results* – We observed a significant improvement for both groups after training in FLSA total score ($P = 0.005$) and subscales. For group 1, we also found a slightly improved performance in two tests: Attentional Matrices ($P = 0.041$), and Verbal Fluency for Letters ($P = 0.059$). After 3 months, patients' results showed a tendency to regress to the pre-training level. *Conclusion* – Both AD groups showed a substantial improvement after training in a direct performance measure of everyday functioning. However, results at neuropsychological tests suggest that training activities of daily living (supported by procedural memory) may be more effective than stimulating 'residual' cognitive functions.

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Key words: Alzheimer's disease; cognitive rehabilitation; non-pharmacological treatment; procedural memory; functional measures

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Introduction

Alzheimer's disease (AD), the most common form of dementia, implies an impairment of cognitive functions and functional abilities progressively declining until death. Despite that, literature data have provided positive support to the notion that AD patients show some sort of cognitive reserve capacity. Different neuropsychological functions are not equally affected in AD: in most cases, episodic memory is first affected, followed only later by semantic memory and instrumental functions, and later on by executive functions (1, 2). Data also demonstrate a relative sparing of procedural memory and perceptive priming in contrast with declarative memory (3, 4). Moreover, several manipulations aimed to structure the acquisition and retrieval of memory traces have shown to improve learning in AD (5–7).

Based on these data, non-pharmacological interventions have been attempted in AD patients to improve their performance and behavior in everyday life.

Reality Orientation Therapy (ROT), first described by Taulbee & Folsom (8), aims to re-orientate demented patient by means of repetitive stimulation. According to a recent review of the Cochrane Collaboration, ROT has clear benefits to dementia sufferers, and it should be considered as part of dementia care (9). However, even if it has been found to improve orientation and memory for personal facts (10, 11), it is less certain whether it produces changes in other cognitive functions (12, 13), or in behavior (11, 14), and only some studies have analyzed the persistence of ROT effects (15, 16).

Less evidence of efficacy can be found in the literature for techniques of cognitive remediation and training (17–19). A group program based on stimulation of attention, semantic memory, and language has been found to improve performance at Mini Mental State Examination (MMSE) and a

word list memory test, without any effect on activities of daily living (ADL) score (20).

Recently, a rehabilitative program based on procedural learning has been developed (21). The authors selected 20 basic and instrumental activities of daily living (IADL), and included 10 mild to moderate AD patients in the study. Five of the patients were trained during 3 weeks on half of the activities, and the other five patients were trained on the remainder. A significant reduction of time spent to perform both the trained and untrained procedures was noted. Other authors have also reported positive results for training of basic ADL (22).

Recreational activities (e.g. crafts, games, pets) and art therapies (e.g. music, dance, art) have been also proposed as non-pharmacological treatments in demented patients. There is some evidence that these interventions can decrease behavioral problems and improve mood (23–27). However, research into this field has lacked methodological design rigor, thus the evidence of efficacy is not firm (28, 29).

Emotion-oriented approaches represent another type of non-pharmacological intervention employed in dementia. Reminiscence therapy (RT) aims to bring into consciousness past experiences and unresolved conflicts, thus helping elderly people prepare for death (30). According to a recent review (31), in the only randomized controlled trial, results were not significant, with a trend favoring treatment in the behavioral outcome (14). Validation Therapy (VT), another emotion-oriented technique, was developed by Naomi Feil between 1963 and 1980 (32). It is based on eye and physical contact, and empathic listening. Various observational studies have indicated that there are positive effects in using VT with regard to patients' social interactions (33, 34). However, once again, randomized controlled trials are scanty (35, 36), and conclusions regarding the efficacy of VT are not reliable (37).

In summary, even if preliminary findings suggest that AD patients can somehow benefit from non-pharmacological interventions aimed to improve cognitive functioning and/or behavior, there is a clear need for further research. More detailed studies comparing different techniques in well-defined AD populations are lacking: the definition of the target population is important, because each technique could be suitable only for a subgroup of AD patients.

The aim of our work was to evaluate the efficacy of two different individual cognitive training procedures in mild to moderate Alzheimer's Disease (AD). We compared stimulation of procedural memory with training of partially spared cognitive functions.

Patients and methods

The study was conducted in the Day-Hospital of the Neurorehabilitation Unit at Don Gnocchi Foundation, Milan. Selection criteria were: i) diagnosis of probable or possible AD according to NINCDS–ADRDA criteria (38), ii) mild or moderate cognitive impairment as defined by Clinical Dementia Rating (CDR) comprised between 0.5 and 2 (39).

Patients with MMSE score (40) less than 15, severe aphasia (Token test score less than 20) (41), severe auditory and/or visual loss or overt behavioral disturbances were excluded.

Twenty-two consecutive outpatients entered the study. We obtained informed consent by patients and their leading caregivers. Following the order of entry in the study, patients were sequentially attributed to the first (group 1) or the second (group 2) treatment program. Each program consisted of a 5-week individual training; patients were treated 3 days a week, two sessions a day. Each session lasted 45 min and was conducted by a physical therapist with experience in cognitive rehabilitation.

Patients attributed to group 1 received a 'procedural memory training' based on 24 ADL (six for each session). Twelve activities were trained in a kitchen, e.g. washing hands, setting and unsetting the table, preparing tea or coffee, etc. The remaining 12 activities were trained in a room, e.g. writing and sending a letter to himself/herself, opening and closing a door-lock, identifying currency, making a phone call to his/her relatives, etc.

Program for patients attributed to group 2 was based on 'training of residual cognitive functions'. Activities aimed to stimulate attention comprised of different types of attentional matrices and researching specific words in a list or in an array. Short-term memory was trained by asking the patient to immediately recall digits, pictures, etc., and to reproduce block-tapping sequences. Language was trained by the several tasks, e.g. comprehension of phrases, semantic and phonemic verbal fluency, naming pictures, ranging in alphabetical order words from a list, etc. Visuospatial tasks included identifying specific visuospatial stimuli in an array, matching similar figures of different size, identifying visuospatial relationships, drawing figures on a point matrix, puzzles, mazes, etc. Categorization of items belonging to different semantic categories was also proposed.

Patients were evaluated at the beginning and at the end of training, and 3 months later. Assessment was conceived in order to evaluate training efficacy on different parameters: cognitive

performance, independence in ADL, behavioral disturbances, and caregiver burden.

Neuropsychological tests were administered by a psychologist blinded to the treatment. The following tests were used: 1) Mini Mental State Examination (40). 2) Rivermead Behavioral Memory Test (42): an 'ecological' memory test being a good predictor of real life behavior. 3) Attentional matrices (41): a digit cancellation task measuring selective attention and psychomotor speed. 4) Verbal fluency for letters and categories (43): assessing the timed production of words after phonemic and semantic cues.

Tools specifically aimed to assess independence in everyday life were the following: 1) Functional Living Skills Assessment (FLSA) (44): an ecological tool [similar to other instruments conceived to directly assess functional ability of demented patients, such as the Direct Assessment of Functional Status (45), and the Structured Assessment of Independent Living Skills (46)] which explores patients' abilities in eight relevant areas of everyday functioning, both by verbal questioning and practical tasks (see Table 1 for details). Material, procedures and scoring have been standardized for the Italian population. Score is based on the level of performance and need of aid by the examiner (range: 27–135). FLSA was administered by a physical therapist different from the one treating the patient. 2) ADL (47), IADL (48), and the Nurses' Observation Scale for Geriatric Patients (NOSGER) (49), which were scored by caregivers.

Assessment also included the Revised Memory and Behavior Problems Checklist (RMBPC) (50) a caregiver-report measure, which provides a score for patients' behavioral problems, and a parallel score for caregiver reaction. The impact of providing care to AD patients on family members' life was assessed by means of a disease specific health related quality of life (DSQoL) questionnaire (51).

Care was assured to avoid any change in pharmacological treatment throughout the study, even if minor changes in neuroleptic therapy were made in two patients.

Table 1 Functional Living Skills Assessment (FLSA)

Area	Tasks
Resources	Describing town utilities
	Remembering emergency telephone numbers
	Describing public transports
	Selecting TV programs
Consumer skills	Food categorization
	Filling a check
	Comparing prices
Public transportation	Consulting a train time-table
	Consulting a city map
	Selecting city transports
Time management	Leisure scheduling
	Filling a daily diary
	Filling a monthly diary
	Managing a rendezvous planning
Money management	Profit calculation
	Consulting a restaurant menu
	Food price appraising
	Doing a payment by mail
Leisure	Describing leisure resources
	Describing procedure for theatre subscription
Telephone skills	Calling a restaurant
	Consulting telephone directories
	Number dialing
Self-care and health	Understanding a recipe
	Describing health resources

Statistical analysis

T-tests (and chi-square tests when appropriate) were employed to compare demographic data and pharmacological variables between the two groups. *T*-tests were also used to compare scores of neuropsychological tests, FLSA, and scales at baseline.

Two-way repeated measures ANOVAs with contrast analyses were employed to evaluate efficacy measures, with pre-treatment, post-treatment, and follow-up as within-group factors and treatment 1 and 2 as between-groups factors.

Results

No significant difference in clinical and demographic characteristics was detected between the two groups at baseline (see Table 2). The same was true for the pharmacological treatment.

Baseline scores at neuropsychological tests, FLSA and scales/questionnaires were not significantly different between groups 1 and 2, with the exception of Verbal Fluency for Letters (group 2 scored better, $P = 0.015$).

Table 2 Demographic and clinical data

	Group 1	Group 2
Age (years, mean ± SD)	73.2 ± 6.8	74.5 ± 8.4
Education (years, mean ± SD)	8.8 ± 4.6	10.5 ± 5.0
Sex		
M	3	7
F	8	4
MMSE	19.3 ± 3.3	20.1 ± 3.1
CDR		
0.5		3
1	8	6
2	3	2

MMSE: Mini Mental State Examination; CDR: Clinical Dementia Rating Scale.

Two patients (one for each group) dropped out: one patient was excluded already in the initial testing phase for severe behavioral problems during the baseline evaluation; the other one requested to terminate the program after some sessions because of excessive anxiety. Efficacy analysis on neuropsychological tests, FLSA and scales/questionnaires were therefore conducted on 20 patients (10 for each treatment group).

A significant improvement for both groups after training was observed in FLSA total score and several subscales (see Table 3).

Group 1 (but not group 2) obtained better scores after training in Attentional Matrices [$F(2, 18) = 4.900$, $P = 0.041$], also showing a trend to higher performance in Verbal Fluency for Letters [$F(2, 18) = 4.098$, $P = 0.059$; see Table 4].

Scales and questionnaires detected no significant difference between the two groups' performance. In particular, we did not find any significant effect on family burden (see Table 5). No correlation was found between improvement at FLSA or at neuropsychological tests and age, education, or dementia severity.

A follow-up assessment was performed 3 months after the end of the training: patients' performances in both neuropsychological tests and FLSA showed a tendency to regress to the pre-training level. Moreover, both groups scored significantly worse than in baseline evaluation at NOSGER [$F(2, 18) = 8.413$, $P = 0.010$) (see Tables 3–5).

Discussion

In this pilot study, we compared two different rehabilitation techniques in a homogeneous and well-characterized group of mild to moderate AD patients. Both treatments induced a substantial improvement after training in FLSA, a direct performance measure of everyday functioning that focuses in complex and intermediate ADL, being therefore most appropriate for patients affected by a mild to moderate form of dementia. In this type of demented population, we have recently demonstrated relatively high correlations between total FLSA score and both MMSE and IADL and CDR, with no floor effect (44).

In spite of the positive results at FLSA, we did not find significant changes in ADL and IADL scores. This is not surprising, however, because these scales have a low sensitivity to mild functional changes, and they do not adequately reflect the kind of help that is needed for cognitively impaired persons (52).

Even if both AD training groups improved at FLSA, without detection of a specific technique effect, it seems unlikely that the improvement at this measure would be interpreted as a generic effect of 'taking care' of patients and their caregivers: in this case, we would expect a 'general' improvement in efficacy measures.

On the other hand, some data of the present study suggest that the rehabilitation of ADL (supported by procedural memory) may be more effective than a cognitive training aimed to stimulate 'residual' cognitive functions in AD patients. In fact, group 1 (but not group 2) obtained better results in a task of selective attention after training, and showed a tendency to better performance in a test of verbal fluency. It is noteworthy that the improvement was evident for patients of group 1, who did not receive a direct training of selective attention and verbal fluency, as it was the case for patients of group 2. We can hypothesize that training procedural memory allows to re-automatize motor and cognitive procedures involved in performing ADL, thus disengaging attentional resources which can be employed in other tasks (53).

Table 3 Functional Living Skills Assessment (FLSA)

	Group 1			Group 2		
	Pre-training (mean ± SD)	Post-training (mean ± SD)	Follow-up (mean ± SD)	Pre-training (mean ± SD)	Post-training (mean ± SD)	Follow-up (mean ± SD)
Resources	14.4 ± 4.2	15.3 ± 2.9	13.2 ± 3.3	14.6 ± 2.4	15.7 ± 2.3	14.5 ± 3.2
Consumer skills*	11.0 ± 3.1	12.4 ± 1.7	10.6 ± 2.9	10.6 ± 2.9	12.3 ± 1.2	10.3 ± 3.0
Public transportation§	12.1 ± 3.7	14.2 ± 2.6	12.4 ± 3.2	12.7 ± 5.0	14.1 ± 3.4	12.3 ± 5.1
Time management*	14.0 ± 3.6	15.6 ± 3.0	13.7 ± 3.8	13.5 ± 4.9	15.1 ± 3.2	12.0 ± 5.5
Money management*	13.0 ± 4.9	14.3 ± 4.4	12.2 ± 5.5	14.1 ± 4.3	15.5 ± 3.6	11.8 ± 6.0
Leisure	7.7 ± 2.1	7.7 ± 1.6	7.6 ± 2.0	7.7 ± 2.5	8.4 ± 1.3	7.2 ± 2.0
Telephone skills	15.4 ± 3.3	16.7 ± 2.6	13.8 ± 5.1	15.7 ± 3.3	16.2 ± 4.3	13.1 ± 4.7
Self-care and health	8.3 ± 2.5	9.7 ± 0.9	8.6 ± 2.3	9.1 ± 2.2	9.6 ± 1.0	8.7 ± 2.1
Total score§	94.5 ± 20.6	105.0 ± 14.5	92.0 ± 24.0	97.9 ± 22.4	106.9 ± 14.2	92.6 ± 25.6

* Difference between pre- and post-training score for both groups, $P < 0.05$.
§ Difference between pre- and post-training score for both groups, $P < 0.005$.

Table 4 Neuropsychological tests

	Group 1			Group 2		
	Pre-training (mean ± SD)	Post-training (mean ± SD)	Follow-up (mean ± SD)	Pre-training (mean ± SD)	Post-training (mean ± SD)	Follow-up (mean ± SD)
MMSE	19.4 ± 3.4	21.1 ± 4.4	20.3 ± 4.7	20.3 ± 3.2	20.9 ± 4.5	20.5 ± 4.4
RBMT – profile	19.8 ± 10.8	22.1 ± 9.2	22.2 ± 13.0	25.5 ± 12.9	28.9 ± 9.6	27.7 ± 10.0
RBMT – screening	0.8 ± 1.8	1.3 ± 2.5	0.9 ± 1.8	1.2 ± 1.5	1.9 ± 2.0	1.3 ± 1.3
Attentional matrices	28.3 ± 9.6	31.6 ± 8.1*	31.0 ± 11.3	31.6 ± 12.7	31.1 ± 10.6	31.2 ± 13.4
VF for letters	16.3 ± 7.2	18.6 ± 8.5†	16.7 ± 10.4	25.2 ± 7.6	22.5 ± 10.0	20.7 ± 8.7
VF for categories	13.8 ± 3.2	14.0 ± 4.9	11.8 ± 5.0	16.1 ± 4.2	18.0 ± 7.9	16.5 ± 8.5

* Difference between pre- and post-training score for Group 1, $P < 0.05$.

† Difference between pre- and post-training score for Group 1, $1 < P < 0.05$.

MMSE: Mini Mental State Examination; RBMT: Rivermead Behavioral and Memory Test; VF: verbal fluency.

Table 5 Scales and questionnaires

	Group 1			Group 2		
	Pre-training (mean ± SD)	Post-training (mean ± SD)	Follow-up (mean ± SD)	Pre-training (mean ± SD)	Post-training (mean ± SD)	Follow-up (mean ± SD)
ADL (KI)	7.2 ± 1.2	6.9 ± 1.4	6.9 ± 1.7	7.2 ± 1.5	7.2 ± 1.8	7.4 ± 2.1
IADL	5.0 ± 1.8	5.2 ± 1.2	5.6 ± 1.2	4.9 ± 0.9	4.8 ± 1.4	5.3 ± 1.5
RMBPC – total^F	34.3 ± 10.4	31.2 ± 10.3	37.3 ± 10.4	32.8 ± 11.1	32.3 ± 13.5	35.4 ± 14.4
RMBPC – total^R	17.0 ± 13.5	17.4 ± 14.1	23.9 ± 14.3	17.0 ± 12.5	18.3 ± 14.6	17.9 ± 13.8
NOSGER*	77.5 ± 15.4	78.1 ± 17.2	83.9 ± 16.8	70.2 ± 12.7	69.5 ± 14.5	73.1 ± 18.1
DSQoL	11.5 ± 7.0	12.6 ± 9.5	11.6 ± 5.4	7.2 ± 6.4	7.0 ± 4.8	8.9 ± 5.9

*Difference between pre- and follow-up score for both groups, $P < 0.05$.

ADL: activities of daily living; KI: Katz index; DSQoL: disease specific health related quality of life; IADL: instrumental activities of daily living; NOSGER: Nurses' Observation Scale for Geriatric Patients; RMBPC: Revised Memory and Behavior Problems Checklist; ^{F}frequency; ^{R}reaction.

We must recognize that the improvement in functional and cognitive performances obtained by cognitive training appears to be lost in a relatively short period. Both AD groups returned to baseline levels of performance at follow-up examination, 3 months after the end of the training. We must carefully consider these data, to make a correct balance between cost and efficacy of non-pharmacological intervention in dementia. As already suggested in literature (16), a long-term program might allow more lasting effects: such a program, however, could be too expensive in terms of public health resources. On the other hand, relatively simple techniques that appear to show some positive effect on demented patients, such as the procedural training of ADL, could be administered by non-professional trainers allowing a continuous stimulation with lower costs.

A limit of our actual study is the lack of efficacy of both techniques to reduce behavioral disturbances and depression of AD patients, and to lessen caregiver burden. In fact, the improvement in cognitive and/or functional performance obtained by cognitive-oriented techniques might not be mirrored by a parallel improvement in patient behavior and caregiver distress (11, 14): one can wonder whether these techniques should be associated with other approaches (e.g. psychotherapy, emotion oriented techniques or recreational activities) for this purpose. Our next step will be to compare the effect of a cognitive-oriented training versus a recreational approach, and to test the efficacy of associating support psychotherapy for patients' and caregivers to the cognitive training.

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