NEUROPSYCHOLOGICAL REHABILITATION
2006, 16 (1), 96–109

Psychology Press
Taylor & Francis Group

Long-term cognitive treatment of Alzheimer's disease: A single case study

Alberto Luis Fernández, Laura M. V. Manoiloff, and Angel A. Monti

Private Institute of Neurosciences, National University of Córdoba, Córdoba, Argentina

The effects of long-term treatment in a demented patient were evaluated in this study. One individual diagnosed with Alzheimer's dementia (AD) was treated with neuropsychological rehabilitation techniques as well as drugs for a period of 2 years and 10 months. An A–B–A–B design was performed for the cognitive treatment. Neuropsychological treatment consisted of a combination of direct re-training and training in activities of daily living. Cognitive performance was monitored with the Mattis Dementia Rating Scale. Results showed improvement and a slower decline during the treatment phases (A) as compared to the no-treatment phases (B). The Conceptualisation and Attention subscales benefited most followed by the Memory subscale. Long-term treatment was shown to be effective in AD. Although cognitive drugs may have been beneficial neuropsychological rehabilitation played an important role in the success of this treatment, appearing as a necessary condition.

Treatment of Alzheimer's dementia (AD) has proven to be a difficult enterprise. Different therapeutic approaches have provided evidence of their capacity to ameliorate AD symptoms but not to stop their progression. Usually, pharmacology has been the first choice. Positive effects with drugs have been found to last up to one year (Winblad et al., 2001). Research performed with donepezil, for instance, has shown that there was improvement in cognitive functioning as measured by the cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-cog), Mini-Mental State Examination and Clinical

Correspondence should be sent to Alberto Fernández, Instituto de Neurosciencias, Arquitecto thays 60, Nueva Córdoba, Córdoba, CP 5000, Argentina. Tel: 54 351 4649283, Fax: 54 351 4697914/460 8869. Email: neurorehab@onenet.com.ar *or* albertolfernandez@hotmail.com

http://www.psypress.com/neurorehab DOI:10.1080/09602010443000164

Interview Based Assessment of Change-Plus (CIBIC-plus) at 12, 18 and 24 weeks (Rogers et al., 1998). At follow-up, after a washout period, scores regressed to the baseline level. Another study with the same drug found an advantage in global dementia symptoms, cognition and activities of daily living in patients treated with donepezil over those treated with placebo 52 weeks after starting treatment (Winblad et al., 2001).

Other research using a different drug—galantamine—showed improvement on ADAS-cog, CIBIC-plus, activities of daily living and behavioural symptoms after five months of treatment (Tariot et al., 2000).

Studies with memantine, an NMDA-receptor antagonist, also showed some efficacy in the treatment of AD. In a study by Reisberg et al. (2003) results demonstrated a reduction in clinical deterioration in moderate-to-severe patients with AD.

Moreover, evidence has been provided that cholinesterase inhibitors (CEIs), such as donepezil and rivastigmine, change the natural history of AD. López et al. (2002) found that CEIs decreased the risk of nursing home admission in AD patients as compared to those who did not take these drugs. Nonetheless, they failed to find an association between CEI use and time to cognitive and functional end points, or to death.

However, pharmacology is not the only approach that has shown effectiveness in the treatment of this dementia. Several neuropsychological rehabilitation (NR) techniques have been successfully implemented. Camp, Foss, O'Hanlon, and Stevens (1996), for instance, demonstrated the utility of spaced retrieval—a cognitive rehabilitation technique—in the training of patients with AD who were taught to look at the calendar in order to orient themselves in time. In addition, they were also trained to complete some tasks that were written on each page of the daily calendar. Arkin (2001) also showed positive results in the administration of NR to demented patients. She trained 11 patients with a diagnosis of moderate to very mild AD to improve their biographical memory. These individuals were repeatedly exposed to a tape containing factual statements about their life history. Using spaced retrieval as well as errorless learning techniques, she found that after 20 sessions patients retained between 83% and 100% of the information they were given. Another more complex study yielded successful results in the treatment of AD (Farina et al., 2002). In this case, two neuropsychological methodologies were compared. Individuals were assigned to two groups where they were administered either stimulation of procedural memory or training of partially spared cognitive functions. They observed a significant improvement for both groups on the Functional Living Skills Assessment scale. Nevertheless, three months after the end of the training patients' results showed a tendency to regress to the pre-training level.

A single case study showed long-term maintenance of results in a patient who was trained to learn the names of 10 members of his social club using a mnemonic strategy (face–name association) (Clare et al., 2001). During the two

years following training the patient had practice in the real-life setting. The positive effects of this training were maintained after two years of follow-up.

To sum up, as these studies and others have shown, NR has demonstrated efficacy in the treatment of AD (Arkin, 2001; Camp et al., 1996; Clare et al., 2001; Clare, Wilson, Carter & Hodges, 2003; Farina et al., 2002). However, these studies have not addressed two important issues: (1) In many cases patients who underwent NR were also receiving drug treatment and it is not clear what the contribution of NR is in a patient already receiving drug treatment. (2) Since all of the investigations involved only a few weeks of training, it has not been demonstrated whether long-term cognitive treatment is worthwhile.

This article describes a single case study of a patient diagnosed with probable AD treated with drugs for three years prior to entering into NR for a further three years. The objective of this study was to address the issues raised in the two questions above, i.e., how does the addition of neuropsychological rehabilitation change the cognitive performance of a demented patient who is under drug treatment; and what is the efficacy of long-term treatment?

METHODOLOGY

Subject

In April 1997 EI, a male retired physician aged 67 years, was diagnosed with probable AD at the Private Institute of Neurosciences according to the NINCS-ARDRA criteria. The patient underwent a clinical neurological evaluation, neuropsychological test battery, magnetic resonance imaging, laboratory studies and a psychiatric interview. The diagnosis was made by consensus between a neuropsychologist, neurologist and psychiatrist (Becker et al., 1994). The patient was married, right-handed, and lived with his wife and a domestic. His wife died some time after the diagnosis.

During the neuropsychological evaluation the following tests were administered: Mini-Mental State Examination (MMSE); Mattis Dementia Rating Scale (MDRS); Modified Rey's Complex Figure (Becker, Boller, Saxton, & McGonigle, 1987); Memory and Naming subscales of ADAS (Rosen, Mohs, & Davis, 1984); Digit Span (Weschler, 1955); and Verbal Fluency (animals) (Newcombe, 1969). The ADAS Memory Subscale was modified by the addition of a 15-minute delayed free recall trial. Positive answers were scored at this trial. The ADAS Inmediate Recall and Naming scores are error scores, i.e., number of words not recalled, and incorrectly named items. Therefore, the best score in these tasks is zero. Table 1 shows the scores obtained by EI on these tests.

The administration of this battery was decided upon on the basis of its high accuracy in the identification of demented and control patients. Becker et al. (1994) demonstrated a classification accuracy of 97.5% with this battery.

TABLE 1
Neuropsychological tests scores of EI on his first assessment (April 1997)

Tests	*Scores*
MMSE (maximum 30)	21
MRDS (maximum 144)	
Total Score (maximum 144)	122
Attention (maximum 37)	36
Initiation/Perseveration (maximum 37)	26
Construction (maximum 6)	6
Conceptualisation (maximum 39)	36
Memory (maximum 25)	18
ADAS	
Immediate recall (maximum 0)	5, 33
Delayed recall (maximum 10)	5
Naming (maximum 0)	0
Modified Rey's Complex Figure Test (maximum 24)	
Copy	23
Recall	5
Verbal Fluency Test (animals)	13
Digit span:	
Forward	4
Backwards	4

EI obtained a score of 21 out of 30 on the MMSE and 122 out of 144 on the MDRS. Noticeable was his impairment in memory, time orientation and semantic verbal fluency in that assessment.

The ability of EI to live independently was difficult to assess since he has always been cared for by his wife or domestic. He never cooked and he did very few household activities. However, he was able to manage money with some problems and to move independently.

After diagnosis EI was prescribed memantine, a drug that he took until December 1998. Doses were variable but were in a daily range of 10–15 mg.

In December 1998 pharmacological treatment was modified. The patient was prescribed donepezil in doses ranging from 5–10 mg daily. At this point, memantine was stopped.

In May 1999, in addition to donepezil, he was prescribed paroxetine. These two drugs were maintained until the last assessment in 2003 except for a period of approximately one month in June–July 2002 when the family decided to stop the anti-depressant.

The patient was also taking benzodiazepine for symptoms of anxiety and a sleeping disorder. During the first phase the doses and frequency of taking benzodiazepine were highly variable because EI was reluctant to take it.

Usually, doses were not higher than 2 mg, but occasionally he took up to 6 mg. However, from February 1999 to February 2003 he was put on lorazepam. Doses varied between 1 mg and 3.75 mg. This medication was also stopped by the family between June and July 2002.

EI returned for annual assessment in April 1998 and February 1999. No neuropsychological rehabilitation was administered during this period.

Treatment

In March 2000 EI entered cognitive rehabilitation treatment. Treatment consisted of a combination of direct re-training and training in activities of daily living. Overall, the patient was corrected when he made mistakes and he was provided with the correct answers in order to make him monitor his task performance and to prevent him from learning incorrect information.

Direct re-training consisted of engaging the patient in several types of exercise. On the whole the exercises were quite different to the tasks required in the MDRS. For instance, he was never trained on alternating movements, supermarket items, or discriminating similar/distinct drawings in a set of three drawings. Occasionally, he was trained on related tasks such as copying pictures (the exercise pictures were complex: flag designs, geographical pictures, etc.), naming animal pictures or recognising similar pictures in an array of several pictures. However, although some exercises were similar, they were never the same as the tasks required in the MDRS.

Attentional exercises involved searching for a specific letter in an array of letters, cancellation tasks, card sorting, etc. Language was trained with phonetic and semantic fluency exercises where the patient was asked to name items from semantic categories such as tools, fruits, names, countries, etc.; or phonemic categories such as words beginning with “a”, “p”, or other letters. Visuospatial ability exercises comprised drawing designs to copy, searching for a hidden object in an array of objects, estimating distances, and similar tasks. Executive functioning was trained with the completion of mazes, sorting objects or words, alphabetical classification, planning activities, etc. Memory was trained with short-term memory tasks such as remembering a string of letters or numbers, and prospective memory exercises. Semantic memory was also trained by asking the patient to retrieve geographical and historical information. For instance, he was given the name of a country and subsequently asked to produce the name of its capital city. Conceptualisation was trained by using analogies, discussing the content of a paragraph where current facts were described, and so forth.

Among the activities of daily living, he was asked to count money, look for a name in the telephone directory, write a paragraph, read an article, interpret a newspaper or magazine article, perform additions and subtractions, and similar tasks.

The sessions did not have a structured schedule. Exercises used and functions targeted in every session were variable in order to keep the patient motivated. When the exercises were repeated over several sessions the patient became bored and asked for different activities.

However, on the whole, the sessions started with attentional exercises followed by exercises targeting a different cognitive function or daily living activity. The therapists included rest periods within the sessions, every time they noticed the patient was fatigued. The patient worked with one therapist but sometimes there were up to two therapists present in the session. The second therapist was frequently a non-active observer undergoing training.

Treatment was delivered in three one-hour sessions a week. Up to the last assessment he had completed 336 sessions in a period of 2 years, 10 months.

Experimental design

Experimental design consisted of an A–B–A–B model. The baseline phase (A1) lasted 3 years from April 1997 to March 2000. During this phase EI was evaluated once a year in April 1997, April 1998, and February 1999. Neuropsychological rehabilitation was not administered during this phase because it was not available either in our institution or other local institutions. This treatment began in March 2000. This phase (B1), lasted until September 2002—a total of 30 months. During the next phase (A2) the patient was not administered NR. Treatment was interrupted because the patient and his companion went on a trip for two weeks. After the trip the patient decided not to attend for treatment for two more weeks. Thus, this phase lasted one month. During the last phase (B2) the patient re-entered treatment and attended for approximately four more months.

Cognitive performance was measured with the Mattis Dementia Rating Scale (MDRS) (Mattis, 1988). This scale consists of five subscales measuring attention, memory, initiation/perseveration, conceptualisation, and construction. The total score ranges from 0 to 144. Previous local research has shown that patients with a score below 123 can be considered as demented (Fernández & Scheffel, 2003).

RESULTS

Figure 1 shows the scores obtained on the MDRS by the patient over the whole observation period. During the first phase (A1) the patient shows a consistent decline in the scores in the annual assessments. In the first assessment he obtained a score of 122. In the next assessment, one year later he obtained 119 points. Ten months later, he scored 110 points. Thus, EI declined 3 points during the first year and 9 points during the second year in his performance on this test. It can be observed that during the second phase (B1)

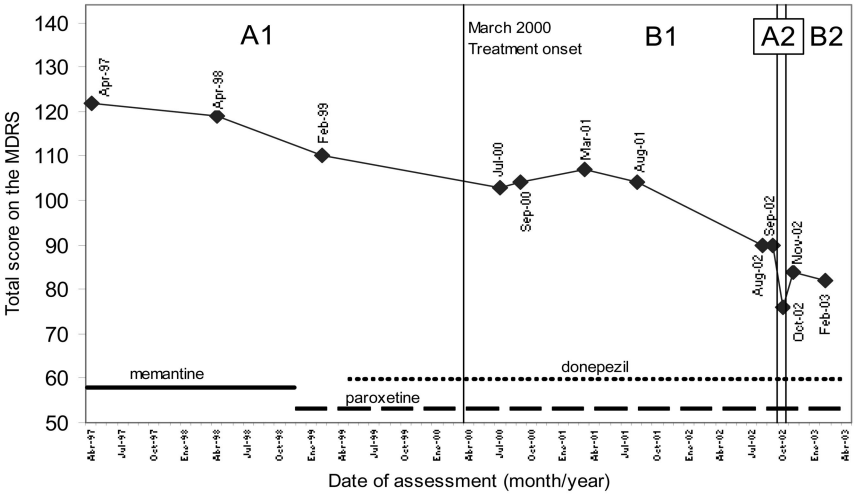

Figure 1. Scores of the patient EI on the MDRS.

the scores remained stable for approximately 13 months. In July 2000 EI obtained a score of 103 and in August 2001 his score was 104. Unfortunately, the data from one assessment performed in March 2002 were lost; therefore there is no record of the cognitive status of EI during one entire year. Besides, as stated previously, during June–July, 2002 the family stopped EI's antidepressant and benzodiazepine medication. This medication was re-started in August 2002. Following interruption of the medication EI exhibited several behavioural and neurological symptoms that were absent previous to this withdrawal. Behaviourally he showed psycho-motor excitability and hypomanic mood. He slowly developed the following neurological symptoms: cogwheel rigidity, dizziness, visual illusions, adiadochokinesia, resting tremor and plantar reflex. These symptoms disappeared after the medication was re-started. By then his performance had declined abruptly: EI scored 14 points lower on the MDRS. Because of the medication withdrawal during this period of phase B1, only the scores obtained during the first 13 months of phase B1 will be considered in this analysis.

In September 2002, in the last assessment before treatment was stopped, he again scored 90 on the MDRS. When EI first re-entered treatment he was evaluated and obtained a score of 76. Thus, he fell 14 points from the last evaluation. After one month of treatment his score rose to 84 and remained stable for three more months. In February 2003 he scored 82.

In summary, for three years (April 1997–July 2000) EI showed a continued decline in the pre-treatment phase. After entering NR the decline stopped and EI remained stable for 13 months. After suffering another decline during

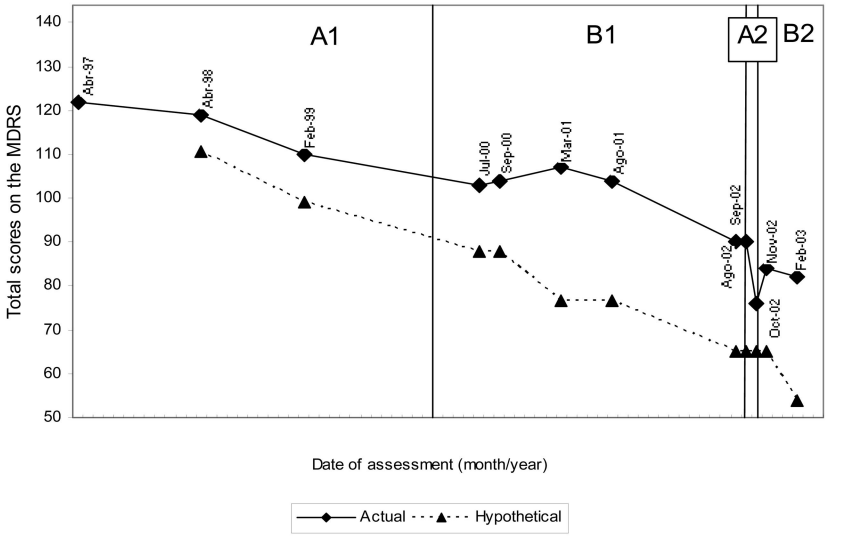

Figure 2. Actual and hypothetical scores of EI on the MDRS.

phase B1, EI stabilised his scores at a lower level. After the interruption of treatment (phase A2) he declined 14 points from his last assessment but his cognitive performance improved when he re-entered treatment (phase B2).

In Figure 2, the dotted line depicts the hypothetical cognitive decline of EI according to Salmon, Thal, Butters, and Heindel (1990) who estimated the annual rate of cognitive decline in AD patients on the MDRS. According to their results patients are expected to decline 11.38 points per year. Unfortunately, there is no information about the drug treatment of the patients included in their research. Thus, the dotted line in Figure 2 shows the expected rate of decline for EI should he have not had NR. It clearly demonstrates a more abrupt cognitive decline. At the second annual assessment in phase A1, EI should have scored 110.62 but he scored 119, a difference of 8.38 points. At the last assessment in February 2003 EI should have scored 53.72, but he scored 82, a difference of 28.28 points.

During phase B1 differences between the expected and the actual performance of EI on the MDRS are smaller at the beginning than at the end. At the beginning the difference is 15.14 whereas at the end this difference rises to 24.9. At the beginning of phase B2, when the patient was assessed after one month without training, this difference of 24.9 dropped to 10.9. Thus EI was performing closer to the level expected in a patient receiving no treatment.

An analysis of the MDRS subscales was performed. Figure 3 shows the subscales scores obtained by EI in every assessment. An individualised analysis of each subscale across the phases yields the following results. First, the

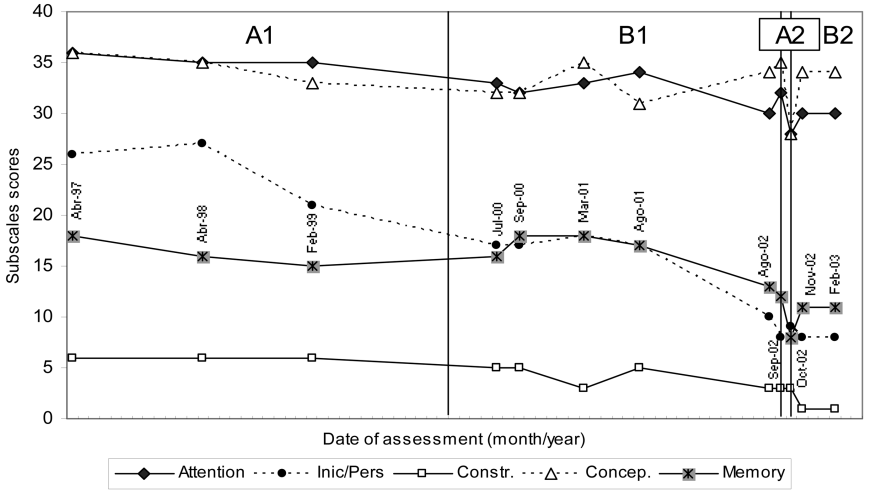

Figure 3. Scores of EI on the MDRS subscales.

most noticeable effects can be observed in two out of the five subscales, namely, Conceptualisation and Memory. As shown in the graph, EI's scores on these scales were declining during phase A1 and stabilised in phase B1. Likewise, these scores dropped markedly during phase A2 and improved during phase B2, remaining stable until the last evaluation.

Second, a partial effect can be observed on the Attention and Initiation/Perseveration subscales. In the first case the effect can be observed in phase B2. EI's scores declined markedly after phase A2, but improved during phase B2. This effect is not visible when considering the differences in the scores between phases A1 and B1. In the second case, the effect can be observed when phases A1 and B1 are compared. EI's scores were declining during phase A1 and they stabilised during phase B1. This effect was not visible when phases A2 and B2 were compared.

Third, there is no visible effect on the Construction subscale in any phase.

An analysis of the total loss in points in each subscale was also carried out. Since the subscales have different ranges we computed the total loss in points from the first evaluation (April 1997) to the last one (February 2003) as a percentage. The resulting rank is: Conceptualisation 5%, Attention 17%, Memory 39%, Initiation/Perseveration 59%, and Construction 83%.

DISCUSSION

Several conclusions can be drawn from the results of this study. First, these results confirm the positive effects of NR on AD patients (Arkin, 2001;

Camp et al., 1996; Clare et al., 2001; 2003; Farina et al., 2002). As shown, with the A–B–A–B design used in this study an AD patient demonstrated both stabilisation (first 13 months of phase B1) and improvement (phase B2) in the scores obtained on a cognitive scale.

Second, and probably most importantly, these results demonstrate that long-term treatment was effective in a patient with AD. This kind of treatment delayed the progress of dementia in EI over the first 13 months of treatment (July 2000–August 2001) as shown by his MDRS scores. Moreover, if the hypothetical progression of cognitive decline based on the Salmon et al. study is taken into account, it might be considered that NR delayed the progression of the disease in EI for a period of 2 years and 10 months. During his first year within phase A1, EI lost 3 points on the MDRS, while he lost 9 points during the second year within the same phase. In contrast, during 13 months of treatment within phase B1 he not only stopped his loss of points on this scale, but he gained 1 point. Moreover, it is likely that his score at the very beginning of phase B1 (March 2000), when no MDRS was administered, was lower. Therefore, it may be hypothesised that his gain was even more than 1 point.

Unfortunately, no definitive statements can be made about the progress of his disease and the effect of NR during the period September 2001–August 2002. During this period there was only one MDRS administration and these scores were lost. In addition, the withdrawal of his medication by the family caused a myriad of behavioural and neurological symptoms, and was also probably the cause of his abrupt cognitive decline since the last assessment. It is tempting to hypothesise that these drugs were providing EI with behavioural, emotional and brain functioning stability that prepared the basis for the development of NR. When these medications were withdrawn his fragile equilibrium broke down and an abrupt cognitive decline arose.

An accepted method to demonstrate the effect of a treatment in single case studies is the comparison of the actual performance of the patient with the hypothetical progress of the disease, based on previous information about its course (Kazdin, 2001). As shown in the comparison with the hypothetical decline on the MDRS, EI obtained 28.28 more points than expected at his last assessment. Taking into account that it has been estimated that 11.38 points is the annual rate of decline in the scores on this scale (Salmon et al., 1990), it may be alleged that the progression of the dementia in EI was delayed for more than two years, thus, increasing the time the patient remained relatively integrated into the social environment. While EI was under treatment, he was, for example, capable of having a clear and meaningful conversation on several topics (politics, present events, etc.), using money, and moving around in a relatively independent way (he was able to take a taxi on his own and make everyday payments). However, it must be stated that as the disease progressed EI's participation in these activities decreased.

Third, although the effect of the drug treatment might have played a role in EI's cognitive performance, the NR was a necessary condition. During the baseline phase (A1) the patient was under drug treatment but the scores continued declining. In contrast, when he started the cognitive treatment (B1) his scores stabilised. This stabilising effect was never seen during the baseline phase. When the patient entered into the NR (B1) he had been taking donepezil for 1 year and 4 months. Unfortunately, there is no MDRS score available at treatment onset (March 2000). But even if NR had had a null effect on cognition in EI during the first three months of treatment (phase B1) the patient still lost 7 points on the MDRS after 19 months of treatment with donepezil (December 1998–July 2000). It is clear, then, that cognitive decline continued after 19 months of treatment with donepezil. Previously, EI had been administered memantine for 20 months. Consequently, he had been receiving drug treatment to prevent cognitive decline for a period of 36 months previous to the onset of NR. Despite this, decline was observed year by year. There is no empirical data showing a stabilising effect on cognition in AD patients after three years of pharmacological therapy. Thus, the stabilisation of the scores cannot be attributed solely to the drug. Moreover, during phase A2 EI continued to receive drug treatment but not NR. At the end of this phase EI's scores had declined significantly, but they increased again after re-starting treatment (B2). Hence, the drug by itself was not enough to stop the cognitive decline. In contrast, after the re-administration of NR EI's scores stopped declining and even improved. Furthermore, although EI lost only 3 points in the first year during phase A1, he lost 9 points in the second year, probably reflecting the fact that the effects of the drug in delaying cognitive decline had decreased or ended. When he was first assessed after three months of treatment he had lost 7 points compared to the last assessment in the pre-treatment phase, which supports this conjecture.

Two hypotheses might be formulated to explain these results: (1) the drug was potentiated by the NR, or (2) the effect was produced by the NR independently of the drug effect. In any case, the NR was a necessary condition. Further research is needed to investigate the specific effects of every variable in the final result.

One other interesting funding is EI's performance on each MDRS subscale. According to our results the Conceptualisation, Attention and Memory subscales benefited most in this case. During the three years, EI only lost 5% of the points on the Conceptualisation subscale, which means that he was almost intact on this domain.

Attention and Memory were also relatively preserved with less than 50% of points lost. Moreover, the effect on the Memory subscale, the a domain thought not to benefit from direct retraining, was remarkable. Initiation/Perseveration and Construction lost the largest number of points, appearing as the least amenable domains to this treatment. Nevertheless, the Construction

subscale, for example, has a very restricted score range (0–6), which means that the loss of three points represents 50% of the total score on this subscale. This might suggest a larger loss than in other subscales, when actually the absolute loss of points is the same or fewer.

Taking all this into consideration, conceptualisation and attention seem to be the domains most amenable to treatment. However, this conclusion should be interpreted with caution. In the first place, the analysis of these results is limited by the poor item sampling of the cognitive functions that each subscale represents, and the narrow score range of some of them. The administration system of the MDRS, in which some items are not administered if the patient passes the screening items, is another confounding factor in this analysis. Consequently, further research is needed to confirm these results.

Although the phases were not the same length in this study, this does not affect the results because within the phases there are periods that can be compared. For example, the results obtained after the first year within phase B1 can be compared to the annual evaluations of phase A1. Similarly, results of the last month of phase B1 can be compared to the results of phase A2—which lasted one month—or the results after the first month of treatment within phase B2.

Single case studies, nevertheless, have some drawbacks. First, in this study the patient has always been under treatment, either pharmacological or a combination of pharmacology and NR. As a consequence, the specific contribution of NR to the maintenance of the cognitive performance in EI cannot be determined. In order to establish the specific contribution of NR it would have been necessary to set a washout phase where no pharmacological treatment was administered, while NR was maintained. Ethical reasons precluded the interruption of any of the treatments. It would not be ethically correct to withdraw any treatment to a patient who has already been diagnosed with a disease.

Second, it may be argued that the delay in the progress of the cognitive decline in phase B1 might be produced by a natural delay in the progression of the disease and not by the effect of the NR. However, when considering phase B2 it is very clear that the patient increased his scores after re-entering treatment, thus supporting the fact that the introduction of NR was responsible for the improvement of EI's performance. But this effect, nonetheless, is not visible after the introduction of phase B1. This is probably due to a methodological limitation produced by the fact that the first assessment during phase B1 was made after three months of treatment. Unfortunately, there is no evidence of the actual performance of EI on the MDRS at the very beginning of phase B1. Thus, it is possible that in March 2000 EI was performing below 103 points (which is the score obtained in July 2000). Therefore, this may explain why the improvement observed in phase B2 is not visible in phase B1.

Third, it may be argued that there is a learning effect and that the patient was learning to respond to the test, i.e., his scores were not reflecting his actual cognitive performance but his ability to respond to this specific test. However, there is evidence that contradicts this argument. First, the performances on different subscales varied between each test suggesting that there is no learning effect. As can be seen in Figure 3 the scores of each scale were neither constant nor did they increase progressively in every assessment, thus, not supporting the idea of a learning effect. If these had been a learning effect the performance on the subscales would have remained stable across the different assessments. During phase B1, for example, except for the last assessment, which was performed one month after the previous one, the interval varied between 3 and 12 months. Thus, considering the large number of trials it takes to teach specific information to a demented person (Camp et al., 1996) it is not likely that EI was showing a learning effect across these assessments.

Another limitation of this study is that it has been very difficult to assess the impact of these results on EI's activities of daily living. It is a very common picture in our society that once patients are diagnosed with AD their family progressively withdraws them from responsibilities and activities. As a result, patients end up doing very few or no activities other than walking or watching television. This scenario was even worse in the case of EI who never had done much at home, and specially after his retirement. Therefore, little can be said about how much of the test score benefits were transferred to his daily living activities. However, within his limited range of activities the family judged the effects of NR positively, since they observed improved personal interaction.

One more limitation of this study should be highlighted. Because both treatments, training of activities of daily living and direct re-training, were administered simultaneously it is not possible to evaluate the specific effect of either one. Nevertheless, the aim of this study was not to demonstrate the effect of each one of these techniques, which has been already done by other researchers (Farina et al., 2002), but to show the utility of a long-term treatment.

As a conclusion, the issue of the utility of long-term treatment should be addressed. Considering the results of this study and those obtained by Farina et al. (2002), it seems very clear that long-term treatments are commendable. In the first place, this study showed a meaningful delay of disease progression not only at a mild stage (phase B1) but also at a moderate stage (phase B2). Furthermore, interruption of treatment in both studies resulted in a regression to the previous or even lower level of performance. The benefits are the extension of patients' independence and the maintenance of their ability to function in their natural environment. Therefore, in our opinion, NR in demented patients should be conceived as a long-term treatment. However, it remains questionable how far to continue with the treatment. It is reasonable to think that treatment should stop once patients enter a severe stage because they would neither understand the commands nor obtain any benefit from it.

REFERENCES

Arkin, S. M. (2001). Alzheimer rehabilitation by students: Interventions and outcomes. *Neuropsychological Rehabilitation*, *11*(3–4), 273–318.

Barlow, D. H., & Hersen, M. (1988). Diseños experimentales de caso único. [*Single case experimental designs*]. Barcelona: Martínez Roca.

Becker, J. T., Boller, F., López, O. L., Saxton, J., & McGonigle, K. L. (1994). The natural history of Alzheimer's disease. Description of study cohort and accuracy of diagnosis. *Archives of Neurology*, *51*, 585–594.

Becker, J. T., Boller, F., Saxton, J., & McGonigle, K. L. (1987). Normal rates of forgetting of verbal and non-verbal material in Alzheimer's disease. *Cortex*, *23*, 59–72.

Camp, C. J., Foss, J. W., O'Hanlon, A. M., & Stevens, A. B. (1996). Memory interventions for persons with dementia. *Applied Cognitive Psychology*, *10*, 193–210.

Clare, L., Wilson, B. A., Carter, G., & Hodges, J. R. (2003). Cognitive rehabilitation as a component of early intervention in Alzheimer's disease: A single case study. *Aging and Mental Health*, *7*(1), 15–21.

Clare, L., Wilson, B. A., Carter, G., Hodges, J. R., & Adams M. (2001). Long-term maintenance of treatment gains following a cognitive rehabilitation intervention in early dementia of Alzheimer type: A single case study. *Neuropsychological Rehabilitation*, *11*(3/4), 477–494.

Farina, E., Fioravanti, R., Chiavari, L., Imbornone, E., Alberoni, M., Pomati, S., Pinardi, G., Pignatti, R., & Mariani, C. (2002). Comparing two programs of cognitive training in Alzheimer's disease: A pilot study. *Acta Neurologica Scandinavica*, *105*(5), 365–371.

Fernández, A. L., & Scheffel, D. L. (2003). A study of the criterion validity of the Mattis Dementia Rating Scale. *International Journal of Testing*, *3*, 49–58.

Kazdin, A. E. (2001). Métodos de investigación en psicología clínica. [*Research design in clinical psychology*]. México: Pearson Educación.

Lopez, O. L.; Becker, J. T.; Wisniewski, S., Saxton, J., Kaufer, D. I., & DeKosky, S. T. (2002). Cholinesterase inhibitor treatment alters the natural history of Alzheimer's disease. *Journal of Neurology, Neurosurgery and Psychiatry*, *72*(3), 310–316.

Mattis, S. (1988). *Dementia rating scale.* Odessa, FL: Psychological Assessment Resources.

Newcombe, F. (1969). *Missile wounds of the brain*. New York, NY: Oxford University Press.

Reisberg, B., Doody, R., Stoffler, A., Schmitt, F., Ferris, S., Mobius, Hans, J. et al. (2003). Memantine in Moderate-to-severe Alzheimer's disease. *New England Journal of Medicine*, *348*(14), 1333–1341.

Rogers, S. L., Farlow, M. R., Doody, R. S., Mohs, R., Friedhoff, L. T., & Group, T. D. S. (1998). A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease. *Neurology*, *50*, 136–145.

Rosen, W. G., Mohs, R. C., & Davis, K. L. (1984). A new rating scale for Alzheimer's disease. *American Journal of Psychiatry*, *141*, 1356–1364.

Salmon, D. P., Thal, L. J., Butters, N., & Heindel, W. C. (1990). Longitudinal evaluation of dementia of the Alzheimer type: A comparison of three standardized mental status examinations. *Neurology*, *40*, 1225–1230.

Tariot, P. N., Solomon, P. R., Morris, J. C., Kershaw, P., Lilienfeld, S., & Ding, C. (2000). A 5-month, randomized, placebo-controlled trial of galantamine in AD. *Neurology*, *54*, 2269– 2276.

Wechsler, D. (1955). *Wechsler Adult Intelligence Scale Manual*. New York, NY: Psychological Corporation.

Winblad, B., Engedeal, K., Soininen, H., Verhey, F., Waldemar, G., Wimo, A., Wetterholm, A. L., Zhang, R., Haglund, A., & Subbiah, P. (2001). A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD. *Neurology*, *57*, 489–495.

Manuscript received July 2003
Revised manuscript received March 2004