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Relearning Face–Name Associations in Early Alzheimer's Disease

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Preliminary evidence for the effectiveness of cognitive rehabilitation interventions based on errorless learning principles in early-stage Alzheimer's disease (AD) was provided by Clare et al. (1999, 2000, 2001). The present study extends these findings in a controlled trial. Twelve participants meeting criteria for probable AD, with Mini-Mental State Examination scores of 18 or above, were trained in face–name associations using an errorless learning paradigm. Training produced a significant group improvement in recall of trained, but not control, items. Gains were largely maintained 6 months later, in the absence of practice. There were differences in individual response to intervention. Results did not differ according to medication status, and the intervention had no adverse effects on self-reported well-being, but participants who were more aware of their memory difficulties achieved better outcomes.

There is a strong rationale for the development of interventions to assist with memory problems in early-stage Alzheimer's disease (AD). Despite severe episodic memory impairment, some components of memory are relatively preserved (Brandt & Rich, 1995), and a continued capacity for learning means that, given appropriate cognitive support (Bäckman, 1992), memory performance can be facilitated. This effect is evident both in relation to procedural (Zanetti et al., 1997; 2001) and verbal (Camp, Bird, & Cherry, 2000) memory tasks. A recent review of empirically validated treatments for older people (Gatz et al., 1998) classified "memory therapy" as "probably efficacious," indicating that it has some promise and that further research is warranted to extend the evidence base and clarify outstanding questions.

A series of single case evaluations of individually tailored cognitive rehabilitation interventions designed to address everyday memory problems in early-stage AD (Clare, Wilson, Breen, & Hodges, 1999; Clare et al., 2000) produced positive outcomes in five out of six cases, and there was evidence of long-term maintenance of treatment gains (Clare et al., 2001). The improvements could not be attributed to generalized changes in cognitive functioning or behavior. Targets for intervention were chosen by the participants and their partners to maximize clinical relevance. The interventions were based on errorless learning principles (Wilson, Baddeley, Evans, & Shiel, 1994) and involved adaptation of learning methods for which there was prior evidence of potential usefulness (Camp & Stevens, 1990; Hill, Evankovich, Sheikh, & Yesavage, 1987; Thoene & Glisky, 1995; Zanetti, Magni, Binetti, Bianchetti, & Trabucchi, 1994). The results suggested that this approach may be beneficial for a proportion of people with early-stage AD, showed that it can be applied to individually selected and clinically relevant tasks, and countered some of the criticisms that have been leveled at "memory training" (Rabins, 1996; Small et al., 1997) by demonstrating that gains can be maintained for significant periods and by failing to find evidence for any clinically significant negative effect on well-being.

These results were promising, but a number of questions remain unanswered. In considering whether this approach can usefully be applied in clinical practice, it will be necessary to assess what proportion of people with early-stage dementia might benefit, and to establish what factors might help to predict outcome. Therefore, one important next step is to explore the feasibility of applying the techniques in a more standardized way that facilitates comparison between individuals but nevertheless allows some scope for ensuring personal relevance, while also evaluating factors that might help clinicians to determine whether a given individual would be likely to benefit.

The present study represents an initial attempt to evaluate the efficacy of a memory rehabilitation intervention based on errorless learning principles in a standardized, controlled design, and to address the following research questions:

1. To what extent are the positive results achieved in the previously reported single-case series generalizable to a wider group of people with early-stage AD?

2. Is there evidence for long-term maintenance of treatment gains?

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3. Is there evidence for negative effects on the well-being of participants or carers?
4. Do participants receiving acetylcholinesterase-inhibiting medication achieve better learning outcomes than those not receiving medication?
5. Is outcome related to participants' awareness of their memory difficulties?

Method

Participants

Criteria for inclusion in the study were as follows: medical diagnosis of probable AD according to National Institute of Neurological and Communications Disorder and Stroke and Alzheimer's Disease and Related Disorders Association criteria (McKhann et al., 1984), with supporting evidence from neuropsychological tests and scans; minimal or mild AD in keeping with previous studies based on the Addenbrooke's Memory Clinic cohort (Hodges & Patterson, 1995), where minimal corresponds to a Mini-Mental State Examination (MMSE; Folstein, Folstein & McHugh, 1975) score of 24 or above and mild corresponds to a MMSE score of 18–23; impairments predominantly in memory, without widespread general intellectual impairment; absence of major psychiatric disorder; living with a spouse or other relative who was willing to participate; English spoken fluently; and able to give informed consent.

Memory clinic records were reviewed to identify all potentially suitable participants, and new referrals were scrutinized throughout the recruitment period. Referrals were also solicited from local clinical geropsychologists and from the Alzheimer's Society outreach worker. This produced a pool of 18 possible participants of whom 14 agreed to participate; one dropped out and one died, leaving a total of 12 participants who completed all parts of the study.

The participants were nine men and three women aged 57–83 years (mean 71). MMSE scores on entry to the study ranged from 19–29 (mean 23). At 12-month follow-up, MMSE scores ranged from 12–26 (mean 20.9). Half the participants had professional or managerial backgrounds, whereas the remainder had pursued technical, clerical, or caring occupations. Five of the participants were taking either donepezil or rivastigmine, two had discontinued rivastigmine prior to entering the study, and five had never taken acetylcholinesterase-inhibiting medication. One of these began taking donepezil shortly after the one-month follow-up. The carers, all partners, were three men and nine women aged 52–78 years (mean 67.5). Details of participants are summarized in Table 1.

Design

A quasi-experimental pretest posttest design (Cook & Campbell, 1979) was adopted. Participants served as their own controls, receiving training on one set of items and no training on a second matched control set which was presented an equivalent number of times. Level of prior familiarity with the items was established through an initial assessment of visual and verbal recognition memory for the items. All participants performed at ceiling on visual and verbal recognition, indicating that the items represented previously known associations.

This design yielded group data allowing a comparison of performance on free-recall and cued-recall trials at baseline, postintervention, and follow-up assessments for both training and control items. The data could equally be considered as a series of single-case experimental designs involving direct replication. In this regard the design approximated accepted quality standards for empirical validation of treatments using single-case designs, as described by Gatz et al. (1998).

Individual results were reviewed by visual inspection of graphs showing free-recall scores. Analysis of aggregated group data involved comparisons of initial and postintervention free- and cued-recall scores on training and control items, and of initial and postintervention scores on specified questionnaire measures, using repeated measures *t* tests. In addition, postintervention performance on trained items for the currently medicated and never-medicated participants was compared using an independent groups *t* test (Howell, 1997), along with other selected variables.

Pre- and postintervention assessments covered relevant variables, including cognitive functioning, participants' awareness of memory difficulties, participant and carer mood, and carer strain. These allowed for selected within-participant comparisons using repeated measures *t* tests (Howell, 1997) to establish whether there had been any changes on key measures following intervention. Relationship of mean awareness scores and learning outcomes was analyzed using Pearson's product-moment correlation coefficient and controlling for severity of impairment.

Table 1
Participants' Ages, MMSE Scores, Awareness Scores, and Medication Status

Participant	Age (years)	MMSE initial assessment	MARS awareness score[a]	Medication	MMSE 12-month follow-up
George	76	23	27.8	donepezil	21
Heather	65	20	24.8	none	16
Iain	68	27	7.6	donepezil	24
Joel	83	22	11.6	discontinued (rivastigmine)	23
Kathleen	76	26	17.2	none	25
Louis	72	20	24.8	donepezil	23
Martin	77	24	8.8	none	24
Neil	67	29	13.4	none	26
Oliver	65	20	14.8	discontinued (rivastigmine)	19
Paula	57	21	−7.2	rivastigmine	14
Roy	83	19	6.0	none	12
Steve	62	24	24.0	rivastigmine	24

Note. MMSE = Mini-Mental State Examination; MARS = Memory Awareness Rating Scales.
[a] The higher the positive numerical score, the lower the level of awareness. A negative numerical score represents a greater level of awareness. Paula shows the highest level of awareness, followed by Roy, Iain, and Martin. The lowest levels of awareness are shown by George, Heather, Louis, and Steve.

Neuropsychological Assessment

As part of the initial assessment, participants completed a battery of neuropsychological tests assessing general intellectual ability, memory, naming, visuospatial perception, attention, and executive function. The tests used were as follows: (a) National Adult Reading Test (Nelson, 1982; Nelson & Willison, 1991); (b) Raven's Coloured Progressive Matrices (CPM; Raven, Court, & Raven, 1984); (c) Visual Object and Space Perception Battery (Warrington & James, 1991)—Screening, Object Decision, and Position Discrimination subtests; (d) Facial Recognition Test (Benton, Hamsher, Varney, & Spreen, 1983); (e) Graded Naming Test (McKenna & Warrington, 1983; Warrington, 1997); (f) Doors & People Test (Baddeley, Emslie, & Nimmo-Smith, 1994); (g) Digit Span subtest of the Wechsler Adult Intelligence Scale—Revised (Wechsler, 1981); (h) Test of Everyday Attention (TEA; Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994)—Map Search, Elevator Counting and Elevator Counting with Distraction subtests; (i) Dual Performance Task (Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1991); (j) Stroop Test (Trenerry, Crosson, DeBoe, & Leber, 1989); (k) Behavioural Assessment of the Dysexecutive Syndrome (BADS; Wilson, Alderman, Burgess, Emslie, & Evans, 1996)—Key Search and Zoo Map subtests; (l) Hayling and Brixton Tests (Burgess & Shallice, 1997); and (m) verbal fluency (Spreen & Strauss, 1998).

Results of the neuropsychological assessment are summarized in Table 2 (names have been changed to preserve confidentiality). All participants had estimated premorbid intellectual functioning in the average, high average, or superior range. Some were impaired on current global assessment of functioning. As expected, all were impaired on at least one of the memory tests, and some also had impairments on naming and perceptual tasks. Performance on tests of attention, working memory, and executive function was variable, with some showing considerable impairment and others demonstrating preserved functioning.

All participants underwent structural scanning by computerized tomography or magnetic resonance imaging to exclude other possible causes of dementia. All were either normal or showed mild hippocampal atrophy compatible with a diagnosis of AD. Quantitative analyses were not performed.

Standardized Measures

The following standardized measures were used to assess mood, behavior, awareness, and carer strain before and after the intervention:

1. Hospital Anxiety and Depression Scale (HADS; Snaith & Zigmond, 1994). Self-ratings were made by both participants and carers. Separate scores are derived for anxiety and for depression; possible scores range from 0–21 in each case. Cut-points of 8, 11, and 15 indicate mild, moderate, or severe disturbance, respectively.

2. Memory Awareness Rating Scales (MARS; Clare, Wilson, Carter, Roth, & Hodges, in press). Participants and partners completed the Memory Functioning Scale and participants completed the Memory Performance Scale, which is used in conjunction with the Rivermead Behavioural Memory Test (RBMT; Wilson, Cockburn, & Baddeley, 1985). Discrepancy scores were calculated and a mean awareness score was derived for each participant. Higher positive numerical scores on this measure reflect lower levels of awareness. It is possible to achieve negative scores, and these are taken as indicating higher levels of awareness.

3. Behaviour Problems Checklist of the Clifton Assessment Procedures for the Elderly (CAPE; Pattie & Gilleard, 1979). Carers rated participants' behavior and dependency needs using this scale, providing an indication of the severity of dementia from a noncognitive perspective. Possible scores range from 0–36, with higher scores indicating greater severity.

4. Caregiver Strain Index (CSI; Robinson, 1983). Carers rated their subjective experience of strain on this scale. A score of seven or above is viewed as indicative of significant levels of strain.

Materials Used in the Learning Task

For each participant, a set of 12 photographs representing people whom the participant had difficulty in naming was assembled. They were either photographs of people in the participant's social network, photographs of famous people from the Famous Faces Test (Greene & Hodges, 1996), or photographs of currently famous people obtained from newspapers and magazines and digitally manipulated to yield a set of images of uniform size. Pairs of items were matched for gender, nationality, length of name, and other relevant factors (e.g., occupation) as appropriate. Within each pair, one item was selected at random to form part of the training set ($n = 6$) and the remaining item was allocated to the control set ($n = 6$).

Procedures

During initial assessment, 10 baseline free-recall trials were given on the chosen set of faces over three sessions, followed in a subsequent session by one cued recall, one visual recognition, and one verbal recognition trial. When assessing free recall, the participant was shown a photograph and asked for the name of the person depicted. In the cued-recall condition, a photograph was shown with the request "This person's name begins with [initials]; can you tell me the name?" In the visual recognition condition, the task was to select which photograph matched the name from a set of three, including two distractors, one taken from the set of training items, and one taken from the set of control items. Verbal recognition was assessed by asking the participant to select which name matched the photograph from a set of three, again including two distractors, as above.

The intervention was then carried out over six sessions, with one item trained in each session. Order of training was randomly determined. The training method was a replication of that described by Clare et al. (1999). This involved selecting a mnemonic, learning the name using vanishing cues, and rehearsing the name using spaced retrieval (expanding rehearsal), for which a criterion of correct recall after 10 min was established—the predetermined time intervals were 30 s, 1, 2, 5, and 10 min. Should the name not be recalled on a given trial, the procedure was to halve the time interval until correct recall was achieved; in such cases a criterion of a total of eight trials was to be adopted. At the end of each training session, a test trial for the whole set of faces was given. Following each training session, participants were given a copy of the item that had been trained, with the name and mnemonic written on the reverse, and were asked to practice the face–name association during the week. It was suggested that practice be continued until the one-month follow-up trials; after this, practice was discontinued.

Ten postintervention free-recall trials for all trained and untrained faces were given over three sessions. The cued-recall trial was given at the next session. A follow-up assessment of the name-learning task was carried out 1, 3, and 6 months after the end of the postintervention baseline trials. A further follow-up was completed 12 months after the end of the intervention, involving a single visit during which five free-recall trials were followed by one cued-recall trial.

Results

Mean free-recall scores on training and control items for all participants at baseline and postintervention, and at 1-,

Table 2
Results of the Neuropsychological Assessment

Measures (maximum possible score)	George	Heather	Iain	Joel	Kathleen	Louis	Martin	Neil	Oliver	Paula	Roy	Steve
NART errors (50)	6	17	10	3	26	4	6	4	6	8	19	30
NART estimated IQ (M = 100)	123	110	118	127	98	126	123	126	123	121	105	93
CPM raw (36)	33	13	26	29	33	32	27	34	13	16	7	29
Percentile	>95	5–10	75	>95	>95	>95	75–95	>95	5–10	<25	<5	90
GNT raw (30)	21	15	16	3	18	24	22	25	24	20	13	21
Percentile	50–75	10	10–25	<1	25–50	75–90	50–75	90	75–90	50	5	50–75
RBMT profile score (24)	2	5	14	0	5	4	9	5	2	6	2	2
Percentile	<2.5	<2.5	2.5–5	<2.5	<2.5	<2.5	<2.5	<2.5	<2.5	<2.5	<2.5	<2.5
D & P age scaled score (M = 10)	<3	<2	10	<5	<4	<3	<2	10	<3	<1	<4	<1
VOSPB raw scores (20)												
Screening task <15 = <5 percentile	20	20	19	19	20	20	19	19	20	20	10	20
Object Decision <15 = <5 percentile	17	12	19	15	18	18	17	19	17	17	13	19
Position Discrimination <18 = <5 percentile	19	15	20	20	20	19	20	20	20	18	16	20
FR corrected raw (54)[a]	49	43	47	39	51	41	49	46	38	46	41	48
WAIS–R Digit Span												
Digits forward raw score	9	6	5	8	5	7	7	8	4	3	6	6
Digits backward raw score	8	3	4	6	5	4	5	6	3	2	4	5
Age scaled score (M = 10)	19	7	7	16	9	9	14	11	5	3	11	8
Dual Performance dual decrement impaired range > −5.8[b]	−0.76	−1.82	−0.86	−3.31	−0.2	−0.38	0.25	−0.16	0.03	−19.29	−2.16	−1.84
TEA (age scaled score, M = 10)												
Map 1 min age scaled score	7	1	5	5	8	10	6	7	8	<1	2	9
Map 2 min age scaled score	7	<6	7	7	9	9	8	8	7	<4	6	8
EC raw (< 6 = abnormal)	7	5	7	7	7	7	7	7	7	6	—	7
EC with Distraction age scaled score	13	—	6	13	13	13	7	13	—	—	—	—
Stroop Colour Word Score (> 62 = impaired)	91	1	56	—	69	56	66	88	29	—	18	83
Hayling Test profile score (10)	1	6	4	4	4	4	1	5	4	—	1	3
Brixton Test error score	20	44	22	19	33	40	40	23	35	—	50	23
Profile score (10)	5	1	4	5	1	1	1	4	1	—	1	4
BADS profile score												
Key search (4)	4	2	0	1	2	4	2	3	0	3	0	4
Zoo map (4)	3	0	0	1	0	0	1	2	0	—	0	1
Verbal fluency no. correct	61	41	44	26	23	49	54	65	9	14	4	41
Percentile	>90	50	70–80	10–20	10–20	70	80–90	>90	<10	<10	<10	60–70

Note. Cells that contain a dash indicate that the task was either not given or discontinued because the participant found it too difficult. NART = National Adult Reading Test; CPM = Raven's Coloured Progressive Matrices; GNT = Graded Naming Test; RBMT = Rivermead Behavioural Memory Test; D & P = Doors & People; VOSPB = Visual Object and Space Perception Battery; FR = Facial Recognition; WAIS–R = Wechsler Adult Intelligence Scale—Revised; TEA = Test of Everyday Attention; EC = Elevator Counting; BADS = Behavioural Assessment of the Dysexecutive Syndrome.
[a] Score ranges for Facial Recognition are 41–54 = normal; 39–40 = borderline; 37–38 = moderate impairment; and <37 = severe impairment. [b] The dual task decrement is a negative value, with greater negative values representing larger decrements and thus increased difficulty of combining two tasks. It is calculated according to a formula provided by Baddeley et al. (1991). Greene, Hodges, & Baddeley (1995) reported a mean dual-task decrement of −1.4 (D = 2.2) for 30 healthy volunteers with a mean age of 67.9 years. For the present study a cutoff of −5.8 was therefore selected as representing 2 standard deviations below the mean score for the healthy volunteers. Negative values greater than −5.8 were classed as falling into the impaired range.

3-, 6-, and 12-month follow-up, are shown in Figure 1. The marked improvement in performance on trained items from baseline to postintervention phases was statistically significant, $t(11) = -4.408$, $p < .001$, two-tailed. Although practice was discontinued after the 1-month follow-up, gains were largely maintained over the first 6 months of follow-up. A further slight decline observed at 12-month follow-up brought scores on the trained items into line with scores on control items, but performance still remained above baseline levels. For the control items, there was a

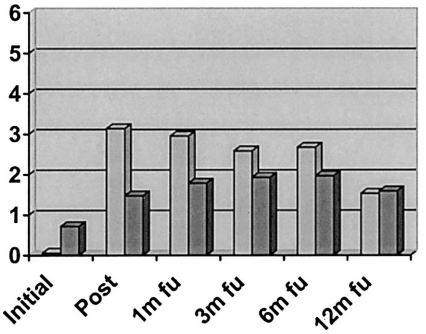


Figure 1. Mean free-recall scores for trained (lighter columns) and untrained (darker columns) items at initial and postintervention (Post) and at 1-, 3-, 6-, and 12-month follow-up (m fu). For initial and postintervention scores of trained items, $p < .001$, and for initial and postintervention scores of untrained items, $p > .05$.

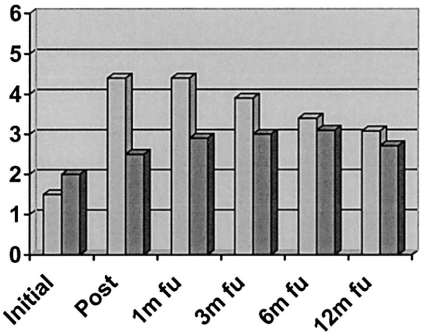


Figure 2. Mean cued-recall scores for trained (lighter columns) and untrained (darker columns) items at initial and postintervention (Post) and 1-, 3-, 6-, and 12-month follow up (m fu). For initial and postintervention scores of trained items, $p < .001$, and for initial and postintervention scores of untrained items, $p > .05$.

slight, nonsignificant improvement in performance between baseline and postintervention assessment, $t(11) = -1.639$, *ns*. The trend to slight improvement on control items continued over the first 6 months of follow-up, after which performance began to decline.

Scores for cued recall of trained and untrained items are shown in Figure 2 (the analysis is based on data from 11 participants, as scores were not available for Roy). Cued recall scores followed a similar pattern to that for free recall, but were slightly higher, indicating that cueing provided a small degree of assistance. There was a significant improvement in cued recall for trained, $t(10) = -4.665$, $p < .001$, two-tailed, but not control items, $t(10) = -1.701$, $p > .05$, two-tailed.

Free-recall scores (maximum six) for each participant on training and control items across all baseline, postintervention and 1-month follow-up trials, and mean free-recall scores achieved on 3-, 6-, and 12-month follow-up trials, are shown in Figure 3. With regard to the trained items, 10 of the participants showed at least some improvement in scores; only 2 participants, Heather and Louis, showed no learning. Seven participants, Iain, Kathleen, Martin, Neil, Paula, Roy, and Steve, showed considerable improvements in performance that were well maintained. Slight improvement, with some maintenance, was shown by George and Joel. Oliver showed a slight improvement in performance at postintervention assessment, but this was not maintained at 1-month follow-up. In summary, just over half of the participants showed clear beneficial effects of the intervention, whereas others showed slight improvement and two showed no learning.

Mean initial and postintervention scores on the HADS, CAPE, and CSI are shown in Table 3. There was very little change in mean score on any measure.

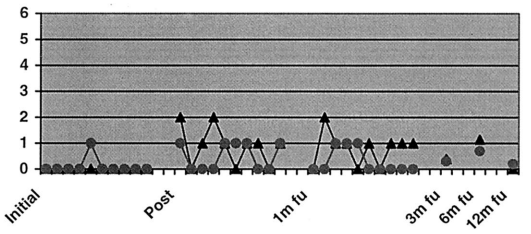
Results for the 5 participants who were taking acetylcholinesterase-inhibiting medication were compared with the results for the 5 participants who had never taken such medication; results for the two groups are summarized in Table 4. Mean free-recall scores at postintervention assessment were almost identical for the currently medicated and never-medicated groups, and there was no statistically significant difference. The two groups did not differ significantly in age, awareness score, initial MMSE score, or current memory ability as indicated by the RBMT Standardized Profile Score, and mean scores on these variables were very similar.

For the whole group of participants, the relationship between learning (postintervention free-recall score) and awareness of memory difficulties (mean MARS discrepancy score) was explored. Mean discrepancy score was inversely correlated with performance on the trained items ($r = -.623$, $p < .05$), showing that a higher level of awareness, as reflected in a low discrepancy score, was related to better learning performance. Mean discrepancy scores showed no relationship with postintervention performance on the untrained control items ($r = .091$, *ns*). Learning outcome was also significantly correlated with MMSE score ($r = .639$, $p < .05$), and there was a significant inverse association between learning outcome and CAPE behavior score ($r = -.668$, $p < .05$), but there was no significant association between learning outcome and age, premorbid IQ, or any other measure.

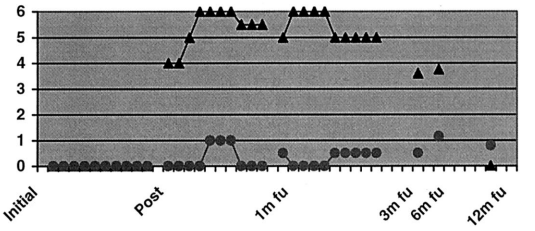
A significant relationship between learning and awareness remained when MMSE score, representing severity of dementia, and CAPE score, representing caregiver's report of behavior, were partialed out ($r = -.764$, $p < .01$). The significant inverse relationship between learning and awareness was maintained in a further analysis controlling for

Figure 3 (opposite). Free-recall scores for individual participants on the trained (triangle) and untrained (circle) items at initial and postintervention (Post) and at 1-, 3-, 6-, and 12-month follow-up (m fu) for the following participants: George, Heather, Iain, Joel, Kathleen (Kath), Louis, Martin, Neil, Oliver, Paula, Roy, and Steve.

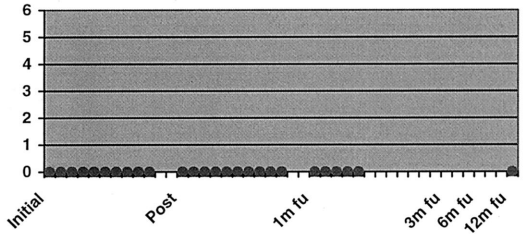
George



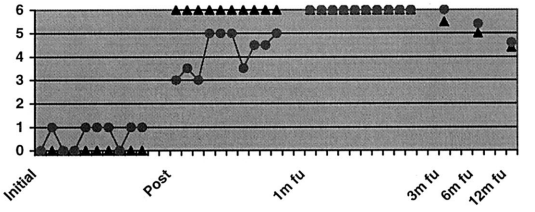
Martin



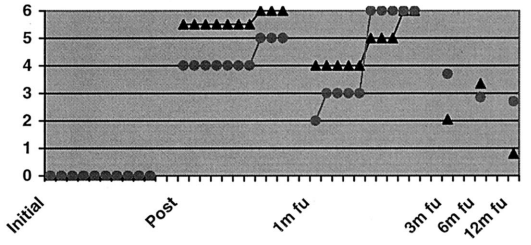
Heather



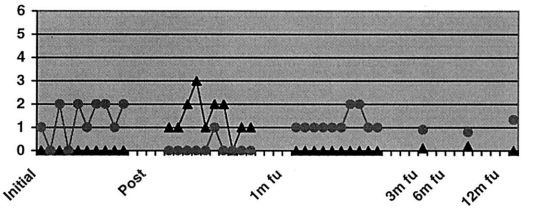
Neil



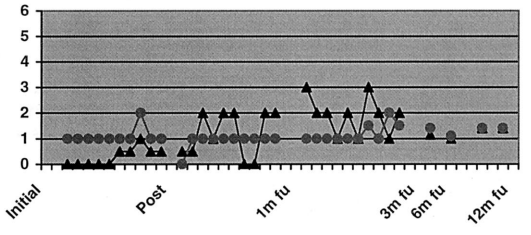
Iain



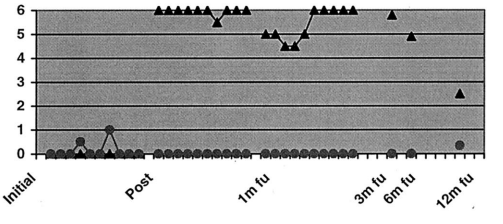
Oliver



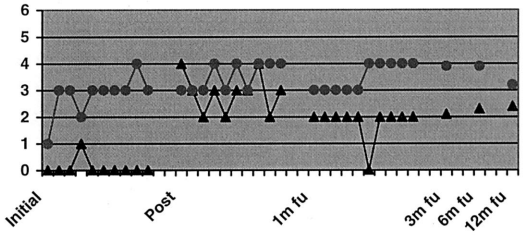
Joel



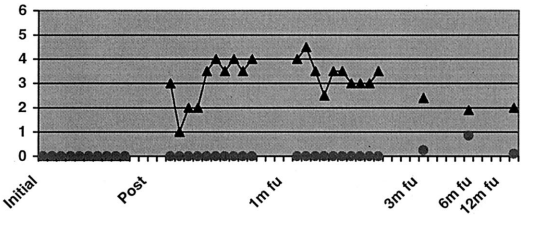
Paula



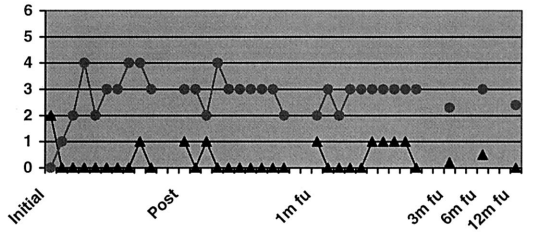
Kath



Roy



Louis



Steve

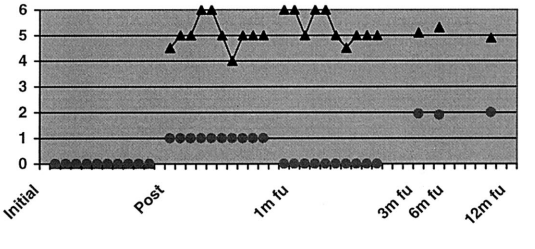


Table 3
Pre- and Postintervention Scores on the Standardized Questionnaire Measures

	HADS anxiety		HADS depression		CAPE behavior scale		CSI		Carer HADS anxiety		Carer HADS depression	
Participant	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
George	4	5	5	2	3	6	0	2	2	1	2	1
Heather	1	1	1	0	13	3	5	5	7	5	9	3
Iain	5	6	3	3	1	0	3	2	5	4	3	2
Joel	7	3	9	3	1	3	0	1	5	7	4	6
Kathleen	9	5	2	1	7	8	5	4	6	3	2	4
Louis	3	1	1	1	9	7	11	11	9	11	8	10
Martin	4	2	1	1	0	0	0	0	8	0	2	0
Neil	9	9	3	3	1	2	0	2	6	7	1	1
Oliver	10	14	5	8	12	12	5	5	3	5	2	3
Paula	0	1	7	3	2	4	3	7	7	7	1	3
Roy	6	4	9	10	1	2	3	0	8	6	0	0
Steve	3	1	1	1	4	7	3	7	11	11	7	7
M	5.1	4.3	3.9	3.0	4.5	5.33	3.2	3.8	6.1	5.6	3.3	3.3
SD	3.2	3.9	3.1	3.2	4.6	4.3	3.2	3.3	2.9	3.4	3.0	3.0

Note. For all scores, $p > .05$. HADS = Hospital Anxiety and Depression Scale; CAPE = Behavior Problems Checklist of the Clifton Assessment Procedures For the Elderly; CSI = Caregiver Strain Index; Pre = preintervention; Post = postintervention.

severity of memory impairment (RBMT standardized profile score) as well as CAPE score and MMSE score ($r = -.75$, $p < .05$).

Discussion

Twelve people with early stage AD participated in a standardized, controlled cognitive rehabilitation intervention involving training in face–name associations based on errorless learning principles. Explicit recall was assessed, and maintenance of gains up to 12 months after the intervention was evaluated. Performance of medicated and never-medicated participants was compared. The relationship between awareness of memory functioning and outcome of the intervention was also explored. Mood, behavior, and carer strain were assessed initially and following intervention.

The intervention produced a statistically significant change in group performance on free recall of trained items and a slight, nonsignificant improvement for control items. Gains were well maintained at 6-month follow-up and scores remained above baseline levels 12 months after the end of the intervention in the absence of further practice. The results provide further support for the efficacy of the errorless learning procedures used in earlier single case studies. These case studies demonstrated that the procedures can be adapted to address individual goals in the real-life context, and thus showed that they have the potential for clinical relevance. Here, the procedures were implemented in a standardized, controlled way to produce a brief, circumscribed intervention that would provide a more stringent test of efficacy. Use of a standard procedure with a fixed number of sessions meant that the learning was not individually paced as in the earlier studies, which may have reduced effectiveness for some participants. Furthermore, it precluded the adaptation of learning strategies to suit individual preferences. Another aspect of the study design that needs to be borne in mind when interpreting the results is that practice was stopped after the 1-month follow-up. Although this provides a useful indication that gains were reasonably well maintained at 6-month follow-up in the absence of practice, clinical interventions need to be designed to support maintenance of gains through continued use of new learning (Bäckman, 1992). Future work will need to return to the real-life setting and continue adapting these procedures, now with demonstrated efficacy, to meet the challenge posed by selecting individual goals, devising appropriate interventions, and conducting these in a therapeutic manner that offers the possibility of more wide-ranging clinical benefits.

It is important to try to understand in what way these cognitive rehabilitation interventions are exerting their beneficial effects. The areas of the brain most affected in the early stages of AD are the medial temporal lobe structures, notably the entorhinal cortex and hippocampus (Braak & Braak, 1991). According to standard views of memory processing, the hippocampal complex plays a critical role in the establishment of new episodic and semantic memories by linking together cortical representations (McClelland, McNaughton, & O'Reilly, 1995; Murre, Graham, & Hodges, 2001). Over time, by rehearsal or reinstatement, connections are established within the cortex which become independent of the hippocampus—so-called long-term consolidation. There is, however, accruing evidence that slower, nonhippocampally dependent processes can support learning of new semantic facts and vocabulary (Kitchener, Hodges, & McCarthy, 1998; Vargha-Khadem et al., 1997). In AD, the earliest pathological changes occur in the medial temporal lobe, notably the entorhinal cortex and hippocampus proper, thus explaining the profound episodic memory deficit found in AD (Hodges, 2000). Because normal hippocampally dependent learning (or relearning) is essentially abolished in AD, one possible hypothesis is that the rehabilitation strategy used here may have operated by slowly reestablishing links between phonological (name) and se-

Table 4
Comparison of Mean Scores and Standard Deviations for Medicated and Never-Medicated Participants

Group	Post-intervention recall score		Awareness score		MMSE score		RBMT standardized profile score		Age (years)	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Medicated ($N = 5$)	3.55	2.8	15.4	14.9	23.0	2.7	5.6	5.0	67	7.6
Never medicated ($N = 5$)	3.46	2.4	14.0	7.4	23.6	4.2	5.2	2.5	73.6	7.5

Note. For all scores $p > .05$. MMSE = Mini-Mental State Examination; RBMT = Rivermead Behavioural Memory Test.

mantic (person-specific) representations in neocortical regions that are less damaged in early AD. If this hypothesis were found to be correct, it is possible that a similar approach would also be effective for learning new semantic information, although clearly the learning or relearning would be expected to occur more reliably where the dementia is less advanced and pathology is confined mainly to the medial temporal areas. However, the results for individual participants in the present study demonstrate that not all benefited equally, and some showed no improvement. Furthermore, although all had significant memory impairments, their neuropsychological profiles differed in other ways. Therefore, different mechanisms might be operating for different individuals. Future studies incorporating neuroimaging data are required to explore further the mechanisms involved in successful relearning.

If it is hypothesized, given the substantial cholinergic inputs to the hippocampus from the basal forebrain cholinergic nuclei via the fornix (Lawrence & Sahakian, 1995), that acetylcholinesterase-inhibiting medication acts to improve hippocampally dependent memory processes via its modulating effect on the medial temporal lobe, the present finding of no difference in learning outcome between the medicated and never-medicated groups can be taken to support the view that relearning was independent of hippocampal function. It should be noted, however, that numbers were small and the reasons for *not* taking medication were varied in this group, including recency of diagnosis or lack of knowledge of diagnosis, unwillingness to accept the diagnosis, or having a preexisting medical condition. Once again, therefore, detailed studies involving larger numbers and incorporating neuroimaging data would be required to explore the mechanisms involved.

Learning outcome in the present study was associated with severity, as assessed by MMSE score and CAPE behavior rating score. The association between learning outcome and severity of dementia is consistent with previous findings indicating that interventions targeting memory functioning are likely to be most beneficial early in the course of dementia, and that as dementia progresses the amount of cognitive support required to facilitate learning or relearning increases (e.g., Bäckman, 1992).

Neither individual differences in terms of age or premorbid ability, nor current score on any neuropsychological measure, appeared predictive of outcome, but learning outcome was significantly associated with awareness of memory difficulties, and this association remained significant when severity of dementia was taken into account. This finding is consistent with previous clinical observations (e.g., Koltai, Welsh-Bohmer, & Schmechel, 2001), but future work could seek to replicate the association in further prospective studies to establish the extent to which the association is robust.

As well as being potentially clinically useful, the association with awareness raises interesting theoretical issues. Neuroanatomical models of unawareness emphasize the role of pathology in right frontal and right parietal areas (Auchus, Goldstein, Green, & Green, 1994; Mangone et al., 1991; Starkstein et al., 1995; Vasterling, Seltzer, Foss, & Vanderbrook, 1995). The participants in the present study did not undergo functional imaging, so it was not possible to explore empirically the relationship between awareness scores and brain pathology. This could be addressed in future studies.

Cognitive neuropsychological models of unawareness emphasize the role of disturbances in executive function (e.g., Schacter, 1989; Stuss, 1991a, 1991b). In the current study, however, there was no clear association between awareness and scores on tests of executive function. Indeed, the participant with the most marked impairment in executive function (Paula) was also the one with the highest rating for awareness. Agnew and Morris (1998) proposed three ways in which unawareness of memory difficulties may arise in dementia: primary anosognosia, resulting from damage to the conscious awareness system; executive anosognosia, resulting from impairment within the executive system; and mnemonic anosognosia, resulting in a failure to update the contents of semantic memory. The ability to update semantic memory may be particularly significant here. The learning task required participants to re-activate previously familiar semantic-phonological associations, whereas the rating of awareness used may have tapped into the extent to which participants' ability to update semantic memory regarding their own situation and functioning was preserved. Future work on awareness in dementia might usefully place more emphasis on the possible role of semantic memory.

The present study aimed to assess the efficacy of the intervention procedures in a brief, standardized, controlled intervention, and was not designed to produce wider clinical benefits. However, because interventions targeting memory functioning in AD have been criticized for negatively affecting well-being, it was important to assess whether any adverse effects were observed. In fact, there was a nonsignificant reduction in patient anxiety and depression scores, and in carer depression scores. The absence of a statistically significant reduction must be considered in the context of the small sample size and the low scores on these measures obtained at initial assessment. The results do not support the view that cognitive rehabilitation is deleterious to well-being, but further work is needed to identify whether this approach can be applied in a way that is beneficial to wider aspects of well-being. This would require a more clinically oriented study targeting individual, personally relevant goals.

The results of the present study must be interpreted in the context of the methodological constraints outlined above. Nevertheless, these findings support the view that a proportion of people with early-stage AD may benefit from cognitive rehabilitation interventions, and suggest that careful assessment of awareness could assist clinicians in determining the suitability of this form of intervention for individual patients.

References

Agnew, S. K., & Morris, R. G. (1998). The heterogeneity of anosognosia for memory impairment in Alzheimer's disease: A review of the literature and a proposed model. *Aging and Mental Health, 2,* 7–19.

Auchus, A. P., Goldstein, F. C., Green, J., & Green, R. C. (1994). Unawareness of cognitive impairments in Alzheimer's disease. *Neuropsychiatry, Neuropsychology and Behavioral Neurology, 7,* 25–29.

Bäckman, L. (1992). Memory training and memory improvement in Alzheimer's disease: Rules and exceptions. *Acta Neurologica Scandinavica, 139*(Suppl.), 84–89.

Baddeley, A. D., Bressi, S., Della Sala, S., Logie, R., & Spinnler, H. (1991). The decline of working memory in Alzheimer's disease. *Brain, 114,* 2521–2542.

Baddeley, A. D., Emslie, H., & Nimmo-Smith, I. (1994). *Doors and people: A test of visual and verbal recall and recognition.* Bury St. Edmunds, England: Thames Valley Test Company.

Benton, A. L., Hamsher, K. d. S., Varney, N. R., & Spreen, O. (1983). *Contributions to neuropsychological assessment.* Oxford, England: Oxford University Press.

Braak, H., & Braak, E. (1991). Neuropathological staging of Alzheimer-related changes. *Acta Neuropathologica, 82,* 239–259.

Brandt, J., & Rich, J. B. (1995). Memory disorders in the dementias. In A. D. Baddeley, B. A. Wilson, & F. N. Watts (Eds.), *Handbook of memory disorders* (pp. 243–270): Chichester, England: Wiley.

Burgess, P. W., & Shallice, T. (1997). *The Hayling and Brixton tests.* Bury St Edmunds, England: Thames Valley Test Company.

Camp, C. J., Bird, M. J., & Cherry, K. E. (2000). Retrieval strategies as a rehabilitation aid for cognitive loss in pathological aging. In R. D. Hill, L. Bäckman, & A. S. Neely (Eds.), *Cognitive rehabilitation in old age* (pp. 224–248). Oxford, England: Oxford University Press.

Camp, C. J., & Stevens, A. B. (1990). Spaced retrieval: A memory intervention for dementia of the Alzheimer's type (DAT). *Clinical Gerontologist, 10,* 58–61.

Clare, L., Wilson, B. A., Breen, K., & Hodges, J. R. (1999). Errorless learning of face–name associations in early Alzheimer's disease. *Neurocase, 5,* 37–46.

Clare, L., Wilson, B. A., Carter, G., Gosses, A., Breen, K., & Hodges, J. R. (2000). Intervening with everyday memory problems in early Alzheimer's disease: An errorless learning approach. *Journal of Clinical and Experimental Neuropsychology, 22,* 132–146.

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,* 477–494.

Clare, L., Wilson, B. A., Carter, G., Roth, I., & Hodges, J. R. (in press). Assessing awareness in early-stage Alzheimer's disease: Development and piloting of the Memory Awareness Rating Scale. *Neuropsychological Rehabilitation.*

Cook, T. D., & Campbell, D. T. (1979). *Quasi-experimentation: Design and analysis issues for field settings.* Boston: Houghton Mifflin.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12,* 189–198.

Gatz, M., Fiske, A., Fox, L., Kaskie, B., Kasl-Godley, J. E., McCallum, T. J., & Wetherell, J. L. (1998). Empirically validated psychological treatments for older adults. *Journal of Mental Health and Aging, 4,* 9–45.

Greene, J. D. W., & Hodges, J. R. (1996). Identification of famous names and famous faces in early Alzheimer's disease: Relationship to anterograde episodic and general semantic memory. *Brain, 119,* 111–128.

Greene, J. D. W., Hodges, J. R., & Baddeley, A. D. (1995). Autobiographical memory and executive function in early dementia of Alzheimer type. *Neuropsychologia, 33,* 1647–1670.

Hill, R. D., Evankovich, K. D., Sheikh, J. I., & Yesavage, J. A. (1987). Imagery mnemonic training in a patient with primary degenerative dementia. *Psychology and Aging, 2,* 204–205.

Hodges, J. R. (2000). Memory in the dementias. In E. Tulving & F. I. M. Craik (Eds), *Oxford Handbook of Memory* (pp. 441–465). Oxford, England: Oxford University Press.

Hodges, J. R., & Patterson, K. (1995). Is semantic memory consistently impaired early in the course of Alzheimer's disease? Neuroanatomical and diagnostic implications. *Neuropsychologia, 33,* 441–459.

Howell, D. C. (1997). *Statistical methods for psychology* (4th ed.). Belmont, CA: Duxbury Press.

Kitchener, E. G., Hodges, J. R., & McCarthy, R. (1998). Acquisition of post-morbid vocabulary and semantic facts in the absence of episodic memory. *Brain, 121,* 1313–1327.

Koltai, D. C., Welsh-Bohmer, K. A., & Schmechel, D. E. (2001). Influence of anosognosia on treatment outcome among dementia patients. *Neuropsychological Rehabilitation, 11,* 455–475.

Lawrence, A. D., & Sahakian, B. J. (1995). Alzheimer's disease, attention and the cholinergic system. *Alzheimer's Disease and Associated Disorders, 9,* 43–49.

Mangone, C. A., Hier, D. B., Gorelick, P. B., Ganellen, R. J., Langenberg, P., Boarman, R., & Dollear, W. C. (1991). Impaired insight in Alzheimer's disease. *Journal of Geriatric Psychiatry and Neurology, 4,* 189–193.

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why are there complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review, 102,* 419–457.

McKenna, P., & Warrington, E. K. (1983). *Graded Naming Test.* Windsor, England: NFER-Nelson.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services task force on Alzheimer's disease. *Neurology, 34,* 939–944.

Murre, J. M. J., Graham, K. S., & Hodges, J. R. (2001). Semantic dementia: Relevance to connectionist models of long-term memory. *Brain, 124,* 647–675.

Nelson, H. E. (1982). *National Adult Reading Test (NART).* Windsor, England: NFER-Nelson.

Nelson, H. E., & Willison, J. R. (1991). *National Adult Reading Test (NART)* (2nd ed.). Windsor, England: NFER-Nelson.

Pattie, A. H., & Gilleard, C. J. (1979). *Clifton Assessment Procedures for the Elderly (CAPE).* Sevenoaks, England: Hodder & Stoughton.

Rabins, P. V. (1996). Developing treatment guidelines for Alzheimer's disease and other dementias. *Journal of Clinical Psychiatry, 57*(Suppl. 14), 37–38.

Raven, J. C., Court, J. H., & Raven, J. (1984). *Manual for Raven's Progressive Matrices and Vocabulary Scales. Section 2: Coloured Progressive Matrices.* London: H K Lewis.

Robertson, I. H., Ward, T., Ridgeway, V., & Nimmo-Smith, I. (1994). *The Test of Everyday Attention.* Bury St Edmunds, England: Thames Valley Test Company.

Robinson, B. C. (1983). Validation of a caregiver strain index. *Journal of Gerontology, 38,* 344–348.

Schacter, D. L. (1989). On the relation between memory and consciousness: Dissociable interactions and conscious experience. In H. L. Roediger III & F. I. M. Craik (Eds.), *Varieties of memory and consciousness: Essays in honour of Endel Tulving.* Hillsdale, NJ: Erlbaum.

Small, G. W., Rabins, P. V., Barry, P. P., Buckholtz, N. S., DeKosky, S. T., Ferris, S. H., Finkel, S. I., Gwyther, L. P., Khachaturian, Z. S., Lebowitz, B. D., McRae, T. D., Morris, J. C., Oakley, F., Schneider, L. S., Streim, J. E., Sunderland, T., Teri, L. A., & Tune, L. E. (1997). Diagnosis and treatment of Alzheimer disease and related disorders: Consensus statement of the American Association for Geriatric Psychiatry, the Alzheimer's Association and the American Geriatric Society. *Journal of the American Medical Association, 278,* 1363–1371.

Snaith, R. P., & Zigmond, A. S. (1994). *The Hospital Anxiety and Depression Scale.* Windsor, England: NFER-Nelson.

Spreen, O., & Strauss, E. (1998). *A compendium of neuropsychological tests: Administration, norms and commentary* (2nd ed.). Oxford, England: Oxford University Press.

Starkstein, S. E., Vazquez, S., Migliorelli, R., Teson, A., Sabe, L., & Leiguarda, R. (1995). A single-photon emission computed tomographic study of anosognosia in Alzheimer's disease. *Archives of Neurology, 52,* 415–420.

Stuss, D. T. (1991a). Disturbance of self-awareness after frontal system damage. In G. P. Prigatano & D. L. Schacter (Eds.), *Awareness of deficit after brain injury: Clinical and theoretical issues* (pp. 63–83). New York: Oxford University Press.

Stuss, D. T. (1991b). Self, awareness and the frontal lobes: A neuropsychological perspective. In J. Strauss & G. R. Goethals (Eds.), *The self: Interdisciplinary approaches* (pp. 255–278). New York: Springer-Verlag

Thoene, A. I. T., & Glisky, E. L. (1995). Learning of face–name associations in memory impaired patients: A comparison of different training procedures. *Journal of the International Neuropsychological Society, 1,* 29–38.

Trenerry, M. R., Crosson, B., DeBoe, J., & Leber, W. R. (1989). *Stroop Neuropsychological Screening Test.* Odessa, FL: Psychological Assessment Resources.

Vargha-Khadem, F., Gadian, D. G., Watkins, K. E., Connelly, A., Van Paesschen, W., & Mishkin, M. (1997, July 18). Differential effects of early hippocampal pathology on episodic and semantic memory. *Science, 277,* 376–380.

Vasterling, J. J., Seltzer, B., Foss, J. W., & Vanderbrook, V. (1995). Unawareness of deficit in Alzheimer's disease: Domain-specific differences and disease correlates. *Neuropsychiatry, Neuropsychology and Behavioral Neurology, 8,* 26–32.

Warrington, E., & James, M. (1991). *Visual Object and Space Perception Battery.* Bury St Edmunds, England: Thames Valley Test Company.

Warrington, E. K. (1997). The Graded Naming Test: A restandardisation. *Neuropsychological Rehabilitation, 7,* 143–146.

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale—Revised (WAIS—R).* San Antonio, TX: The Psychological Corporation.

Wilson, B. A., Alderman, N., Burgess, P. W., Emslie, H., & Evans, J. J. (1996). *Behavioural Assessment of the Dysexecutive Syndrome (BADS).* Bury St Edmunds, England: Thames Valley Test Company.

Wilson, B. A., Baddeley, A., Evans, J. J., & Shiel, A. (1994). Errorless learning in the rehabilitation of memory impaired people. *Neuropsychological Rehabilitation, 4,* 307–326.

Wilson, B. A., Cockburn, J., & Baddeley, A. D. (1985). *The Rivermead Behavioural Memory Test (RBMT).* Bury St Edmunds, England: Thames Valley Test Company.

Zanetti, O., Binetti, G., Magni, E., Rozzini, L., Bianchetti, A., & Trabucchi, M. (1997). Procedural memory stimulation in Alzheimer's disease: Impact of a training programme. *Acta Neurologica Scandinavica, 95,* 152–157.

Zanetti, O., Magni, E., Binetti, G., Bianchetti, A., & Trabucchi, M. (1994). Is procedural memory stimulation effective in Alzheimer's disease? *International Journal of Geriatric Psychiatry, 9,* 1006–1007.

Zanetti, O., Zanieri, G., de Giovanni, G., de Vreese, L. P., Pezzini, A., Metitieri, T., & Trabucchi, M. (2001). Effectiveness of procedural memory stimulation in mild Alzheimer's disease patients: A controlled study. *Neuropsychological Rehabilitation, 11,* 263–272.

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