Acta Psychiatr Scand 2006: 114: 75–90

DOI: 10.1111/j.1600-0447.2006.00789.x

ACTA PSYCHIATRICA
SCANDINAVICA

Review Article

Cognitive training in Alzheimer's disease: a meta-analysis of the literature

Sitzer DI, Twamley EW, Jeste DV. Cognitive training in Alzheimer's disease: a meta-analysis of the literature.

Objective: To systematically review the literature and summarize the effect of cognitive training (CT) for Alzheimer's disease (AD) patients on multiple functional domains.
Method: Effect sizes (Cohen's *d*) were calculated for 17 controlled studies identified through a comprehensive literature review.
Results: An overall effect size of 0.47 was observed for all CT strategies across all measured outcomes. Mean effect sizes were higher for restorative (0.54) than for compensatory (0.36) strategies. Domain-specific effect sizes ranged from 2.16 (verbal and visual learning) to −0.38 (visuospatial functioning). Data are also presented on the relative impact of restorative and compensatory strategies for each domain of functioning.
Conclusion: CT evidenced promise in the treatment of AD, with primarily medium effect sizes for learning, memory, executive functioning, activities of daily living, general cognitive problems, depression, and self-rated general functioning. Restorative strategies demonstrated the greatest overall effect on functioning. Several limitations of the published literature are discussed.

D. I. Sitzer, E. W. Twamley, D. V. Jeste

Department of Psychiatry, University of California, San Diego, CA and VA San Diego Healthcare System, San Diego, CA, USA

Key words: aging; dementia; cognition; memory; rehabilitation; therapy

Elizabeth W. Twamley, Assistant Professor of Psychiatry, University of California, San Diego, Outpatient Psychiatric Services, 140 Arbor Drive, San Diego, CA 92103, USA.
E-mail: etwamley@ucsd.edu

Accepted for publication January 17, 2006

Summations

- Patients with Alzheimer's disease may derive some cognitive and functional benefits from cognitive training.
- Restorative cognitive training strategies demonstrated larger effect sizes than compensatory strategies.
- The largest effect sizes were seen in the domains of learning, memory, executive functioning, activities of daily living, general cognition, depression, and general functioning.

Considerations

- Studies reviewed frequently reported small sample sizes, which we accounted for by weighting the results of each study by sample size.
- Few studies used performance-based measures of daily functioning.
- Most studies combined multiple treatment strategies, making it difficult to evaluate the efficacy of individual strategies.

Introduction

Even in its early stages, the cognitive deficits of Alzheimer's disease (AD) can produce significant functional impairment. Although memory deficits are typically most prominent, impairments in attention, visuospatial functioning, language, reasoning, and executive functioning are common, along with personality changes and behavioral disturbances (for review see 1). Pharmacological strategies for delaying the progression of cognitive deficits and resulting functional impairment have produced mixed results (2–4). Alternative or supplemental treatments to pharmacological interventions include psychosocial treatments targeting cognition, such as cognitive training (CT) for AD patients in the mild to moderate stages of the disease.

For the purposes of our review, CT refers to any non-pharmacologic intervention designed to improve cognitive functioning, regardless of mechanism of action. Typically, CT interventions focus on specific domains of cognitive functioning (such as memory, attention, and problem solving), but more general, cognitively mediated domains of functioning, such as basic and instrumental activities of daily living (ADLs and IADLs, respectively), social skills, and behavioral disturbances can also be targeted. In an effort to be inclusive, given this new area of study, we included all psychosocial interventions that targeted cognition as an outcome variable.

Cognitive training strategies can be divided into two basic categories: compensatory and restorative (5, 6). Compensatory strategies aim to teach new ways of performing cognitive tasks by 'working around' cognitive deficits. Compensatory interventions may use internal strategies such as organizing information by categorizing or visualizing information to be remembered (7), encoding through multiple sensory channels (5), asking questions and paraphrasing during learning (8), and focusing on a single task (8); external strategies such as environmental cues, memory notebooks, and calendars (7, 9); or procedural training to teach complex, higher-order cognitively mediated behaviors such as balancing a checkbook. Restorative strategies attempt to improve functioning in specific domains with the ultimate goal of returning functioning in those domains to premorbid levels. Examples of restorative techniques include spaced retrieval, which requires patients to recall information over longer periods of time; drills, in which patients engage in repeated attention and memory tasks; vanishing cues, in which information is repeatedly presented with diminishing intensity; errorless learning, which involves preventing mistakes during recall trials (7–9); reality orientation therapy, in which orienting information, such as a patient's name, date, time, location, weather, and current events, is continually presented (10); and reminiscence therapy, in which patients discuss remote events in order to place one's life in perspective (11). Although the compensatory/restorative distinction arose in the literature on other clinical populations (such as traumatic brain injury or schizophrenia), these terms seem to apply equally well to AD. For example, let us consider an AD patient's difficulty remembering who is going to visit today. A compensatory approach to this problem might involve writing the visitor's name down in a calendar, whereas a restorative approach might involve repeated cuing and questioning regarding the information to be remembered.

Several reviews have provided detailed descriptions of specific CT strategies that have demonstrated at least minimal impact on the memory and behavior problems of AD (7–9). Although these reviews suggest that CT has some utility in the treatment of AD, the reported effect of these strategies on cognitive and behavioral functioning appears to be small, with the magnitude of effects rarely quantified. Additionally, many of the studies cited in these reviews were case studies or non-controlled studies (12, 13). Other, more methodologically rigorous reviews have led to diverging conclusions. Spector et al. (14) concluded that reality orientation therapy reduced the cognitive and behavioral difficulties associated with dementia. In a similar review of two studies of reminiscence therapy, these authors concluded that there was insufficient evidence to support its use (15). Clare et al. (16) reviewed the literature on the utility of CT for the treatment of memory deficits in AD and vascular dementia. Their strict inclusion criteria resulted in a review of six randomized controlled trials (RCTs) of CT strategies other than reality orientation therapy or reminiscence therapy. The authors concluded that although CT modestly improved some domains of functioning, they were unable to find strong support for the use of CT in the treatment of early-stage AD or vascular dementia. They also noted that their findings should be viewed with caution due to methodological limitations of the studies reviewed.

The current review differs from prior reviews (7–9, 14–16) in that we i) approached the review from a theoretical perspective and classified CT interventions according to their putative mechanism of action (i.e. restorative or compensatory); ii) examined the effects of restorative vs. compensatory approaches across multiple outcomes, allowing for a finer-grained analysis; iii) examined the differential effects of individual and group treatments; iv) examined the differential effects of CT when compared with wait-list control groups and attention-placebo control groups (i.e. those that provided therapeutic contact without CT); and v) evaluated the scientific quality of each study with a formal rating scale and incorporated these ratings into the analyses.

Aims of the study

The objectives of the present review were to: i) systematically review the literature on CT in AD and ii) evaluate the effect of different types of CT techniques on various domains of cognitive and functional abilities. The effects of CT are presented in the form of post-treatment or pretest to post-test difference effect sizes in each individual study and summed across domains of functioning.

Material and methods

Sample of studies

We searched the MEDLINE (years 1953–2004) and PsycINFO (years 1840–2004) databases to identify peer-reviewed reports of controlled trials of CT for AD. The search terms used for this investigation were: 'cognitive rehabilitation,' 'cognitive training,' 'cognitive remediation,' 'memory training,' or 'attention training' and 'Alzheimer's disease.' The MEDLINE search was restricted to English language reports describing clinical trials of human subjects, and returned 77 references. The PsycINFO search was restricted to journal articles and returned 89 references. The studies were then reviewed to determine whether they met the following inclusion criteria: i) a majority of subjects had diagnoses of AD or probable AD, ii) a control condition was present, iii) the experimental condition targeted improvement in at least one domain of cognitive functioning, iv) at least one objective cognitive or functional outcome was measured, v) treatment was provided to patients (as opposed to only caregivers), and vi) enough information was reported to calculate post-test or change score effect sizes. References of included articles and previously published reviews were also examined to identify additional studies not identified by the original MEDLINE and PsycINFO searches. Using these methods, 17 articles were identified for inclusion in this review. Of these 17 reports, one compared a CT protocol with two different control conditions, a wait-list group and an attention-placebo group (17). We used only those effect sizes resulting from the comparison of the CT group with the attention-placebo control group in our analyses, as this was the more rigorous comparison. Two studies compared two different CT interventions to a control group (18, 19). For the purposes of our review, we considered each CT-control comparison a separate study; therefore, our results are based on 19 studies.

All studies provided mean ages of their subjects. Sixteen studies provided information on gender and 10 studies provided information on level of education. The mean sample size for the studies was 16 experimental subjects (range 7–32) and 15 control subjects (range 7–29). The patients were primarily women (62%), with a weighted mean age of 75 years and a weighted mean of 12 years of education.

Evaluation of study methodology

Fourteen of the 19 studies were RCTs. Thirteen studies used wait-list control conditions, whereas six studies used attention-placebo controls. Most interventions used a combination of CT strategies, which were independently categorized by the first two authors as primarily restorative (12 studies) or primarily compensatory (seven studies) based on which type of strategy was predominant in the intervention. There was 100% consensus between the authors. Eight studies employed individual treatment modalities (or an individual dyad including a patient and caregiver), 10 studies used a group format, and one study used a combination of group and individual formats. The length of training sessions ranged from 30 to 90 min. The overall number of training sessions administered varied from five [weekly 1-h sessions for 5 weeks (20)] to 260 [daily 45-min sessions for 1 year (21)].

The methodological rigor of each study was evaluated using a 5-item modified version of the Scale to Assess Scientific Quality of Investigations (SASQI; D.V. Jeste, personal communication). Each study was assigned points for: i) randomization of subjects (3 points), ii) use of a comparison group controlling for non-specific therapeutic factors (i.e. attention-placebo; 3 points), iii) absence of group differences at baseline (2 points), iv) absence of differences between study completers and non-completers (1 point), and v) exclusion of non-AD patients (1 point). Although the SASQI is an objective measure, each of the first two authors individually rated each study. Both authors agreed, with 100% reliability, on the quality of each study. In addition to the SASQI score, 'high quality' studies were defined as those that received the highest scores on each of the first three items.

There was a high degree of variability in tests administered to evaluate the effects of CT on cognitive abilities. In an effort to be inclusive and to analyze the data in a meaningful way, outcome measures were grouped according to the primary domain of functioning evaluated. Although scores on most neuropsychological tests are affected by multiple cognitive abilities, a primary ability is often identifiable for most measures. Domain classification of each measure was based on a consensus of the first two authors using common classification standards (22–25). For some measures (e.g. Alters-Konzentrations Test) the directionality of scoring could not be determined, due to the lack of publicly available (English language) descriptors of the measures; these measures were excluded from the review.

Statistical analysis

Effect sizes were calculated for all post-treatment outcome measures evaluating patients' cognitive abilities and functional behaviors. Effect sizes (Cohen's *d*) were calculated by dividing the difference between the post-treatment CT and control group mean values by the pooled standard deviation (26) for each neuropsychological test. When available, pretreatment to post-treatment change scores and standard deviations were used in place of post-treatment scores (e.g. 27, 28; where pretreatment mean values were different between groups). For measures on which low scores indicate better performance, formulas were adjusted so that a positive effect size always represented improved performance. We then weighted each effect size by multiplying by the study sample size. After effect size weighting, measures were grouped by primary cognitive domain evaluated by the measure. Mean weighted effect sizes were calculated for each cognitive domain, and converted back to Cohen's *d* by dividing by the total number of observations within each domain. Differences between studies comparing CT to wait-list vs. attention-placebo controls, restorative vs. compensatory CT strategies, and individual vs. group formats, were evaluated using *t*-tests (29).

Results

Sample size, patients' age, gender, education, type of CT, type of control condition, duration and modality of training, outcome measures, effect sizes, SASQI scores, identification as a 'high quality' study, and study follow-up information were evaluated and are presented in Table 1. SASQI scores for each study ranged from 3 to 10 (maximum), with a mean score of 6.07 (SD = 2.50). Five studies were identified as 'high quality' studies (17, 20, 30–32). Most studies were not classified as high quality because they did not control for non-specific therapeutic factors (18–19, 21, 27–28, 33–35, 37–39). One study that provided an adequate control condition (30) did not randomize subjects to treatment or control conditions. Fourteen studies randomized subjects to treatment and control groups (17–20, 23, 24, 30–35); six reports controlled for non-specific therapeutic factors (17, 20, 30–32, 36); 17 investigations had comparable scores between treatment and control groups on baseline variables (17–21, 30–39); four studies reported no differences on baseline measures between completers and non-completers (18, 30, 36); and nine studies used samples homogeneous for AD (17, 20, 21, 30–32, 37–39).

The weighted mean effect size for all CT strategies across all outcome domains was 0.47 (SD = 0.45). Studies comparing CT to a wait-list control group demonstrated nonsignificantly greater effect sizes than did those comparing CT to attention-control placebo groups ($d = 0.53$, SD = 0.47 vs. $d = 0.36$, SD = 0.58, respectively; $t(17) = 0.67$, $P = 0.511$). Reports on restorative strategies yielded nonsignificantly greater mean effect sizes than did those on compensatory approaches ($d = 0.54$, SD = 0.59 vs. $d = 0.36$, SD = 0.27, respectively; $t(16.5) = 0.92$, $P = 0.370$). Studies providing individual treatment evidenced nonsignificantly greater mean effect sizes than did those providing group treatment ($d = 0.69$, SD = 0.54 vs. $d = 0.33$, SD = 0.43, respectively; $t(16) = 1.60$, $P = 0.129$).

The analyses described above were repeated for the five high quality studies. The overall weighted effect size for all high quality CT reports was 0.16 (SD = 0.18). For these high quality studies, there were no statistically significant differences between restorative and compensatory strategies ($d = 0.12$, SD = 0.27 vs. $d = 0.15$, SD = 0.09, respectively; $t(3) = 0.14$, $P = 0.897$) or between individual treatment and group treatment ($d = 0.20$, SD = 0.24 vs. $d = 0.04$, SD = 0.07, respectively; $t(3) = 0.90$, $P = 0.434$).

The mean weighted effect sizes for each domain of functioning are presented in Table 2. The greatest overall effect was seen for performance-based measures of ADLs ($d = 0.69$, SD = 0.16). The mean weighted effect size on measures of cognitive functioning was 0.50 (SD = 0.54). Mean weighted effect sizes on informant- and self-ratings were 0.56 (SD = 0.41) and 0.26 (SD = 0.43), respectively. Weighted effect sizes for measures that focused primarily on learning (acquisition of novel information) were higher than those that focused primarily on memory (delayed recall of previously learned information; e.g. verbal learning $d = 0.50$, verbal memory $d = 0.03$).

The highest weighted effect sizes for compensatory strategies were in the domains of performance-based ADLs ($d = 0.69$, SD = 0.16), informant-rated cognitive problems ($d = 0.68$, SD = 0.00), and verbal and visual learning and memory ($d = 0.65$, SD = 0.00). The highest

Table 1a. Randomized Controlled Trials of Cognitive Training for Individuals with Alzheimer's Disease

Study Study Sample SASQI Score *High quality study.	n, Age (A = mean years) Gender (G = % male) Education (E = mean years)	Experimental Condition (EC) Compensatory (C) vs. Restorative (R)	Control Condition (CC)	Duration and modality of training	Outcome measure/s	Effect size/s (immediate)	Follow-up duration and effect size/s
Loewenstein et al. (2004) (32) Mildly impaired AD patients taking cholinesterase inhibitors SASQI = 9*	EC n = 25 CC n = 19 EC, CC A = 78, 74 G = 60, 58% E = 13, 14 MMSE = 23.4, 24.5	i) Face-name associations through spaced-retrieval technique and cognitive support (R) ii) Memory notebook w/calendar (C) iii) Activation of procedural and motor memory through manipulation of objects (C) iv) Computerized attentional training (R) v) Training to make change from $20 (C) vi) Balancing a checkbook by hand, using a calculator, bill paying (C) Overall = Compensatory	Mental Stimulation Training: Commercially available computer games (matching tasks); playing games like Hangman; word searches; asked to recall events from within the past few days	24 to 45-min sessions twice per week, for 12–16 weeks 24 total sessions Individual			3 month follow-up
					Face-Name		
					Learning	0.65	0.43
					Delayed recall	0.46	0.46
					Orientation	0.59	0.66
					Continuous Performance Test		
					Omissions	0.02	−0.13
					Commissions	−1.73	−1.17
					Reaction Time	1.32	0.38
					Object Memory		
					Learning	−0.14	0.08
					Delayed recall	−0.24	−0.09
					Modified Making Change Task (DAFS)	0.50	0.22
					Balance Checkbook (DAFS)		
					Hand	0.46	0.30
					Calculator	0.72	0.49
					Informant Questionnaire Cognitive Decline in the Elderly		
					Patient	−0.02	0.37
					Informant	0.68	0.09
					Center for Epidemiologic Studies Depression Scale		
					Patient	−0.01	0.39
					Informant	0.32	0.04
					Bayer Activities of Daily Living Scale	0.26	0.05
					Revised Memory and Behavior Problems Checklist		
					Number of problem behaviors	0.04	−0.08
					Frequency of problem behaviors	0.19	−0.27
Cahn-Weiner et al. (2003) (30) Mildly impaired AD patients taking cholinesterase inhibitors SASQI = 10*	EC n = 17 CC n = 17 EC, CC A = 78, 76 G = 52, 29 % MMSE = 24.3, 25.1	Memory Training: Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE): mnemonic strategies with exercise and practice (C) and practice tests (word lists). (ACTIVE training was shortened from 10 to 6 weeks due to higher functioning patients; 2 modules were presented: categorization and visualization) Overall = Compensatory	Education and support group	1 session per week for 6 weeks 6 total sessions Group			8 week follow-up
					Hopkins Verbal Learning Test		
					Total Learning	0.41	0.03
					Delayed Recall	−0.39	−0.34
					Recognition	−0.04	0.15
					Brief Visual-Spatial Memory Test-Revised		
					Total Learning	−0.09	−0.06
					Delayed Recall	0.12	0.13
					Recognition	0.11	0.46
					Boston Naming Test	−0.06	−0.15
					Controlled Oral Word Association Test	0.28	0.14
					Judgment of Line Orientation	−0.38	−0.47

Table 1a. (Continued)

Study Study Sample SASQI Score *High quality study.	n, Age (A = mean years) Gender (G = % male) Education (E = mean years)	Experimental Condition (EC) Compensatory (C) vs. Restorative (R)	Control Condition (CC)	Duration and modality of training	Outcome measure/s	Effect size/s (immediate)	Follow-up duration and effect size/s
					Trail Making Test		
					A	0.53	0.60
					B	0	−0.02
					Activities of Daily Living Questionnaire	−0.42	−0.15
					Everyday Memory Questionnaire	0.80	0.34
Davis et al. (2001) (20) Probable AD SASQI = 9*	EC n = 19 CC n = 18 EC, CC A = 69, 73 G = 53, 33% E = 15, 13 MMSE = 21.8, 22.8	Spaced retrieval (R) Peg task (C) Face-name training with pegs (C) Attention Process Training (APT) at home (R) Overall = Restorative Participants advanced to the next type of training if there was time after completing the previous level of training to criterion	Clinic visits consisting of unstructured conversations, recitation of overlearned material (alphabet), video tapes	5 1-h weekly sessions 5 total sessions Individual	MMSE	−0.25	No follow-up data
					WMS-R Logical Memory		
					Immediate Memory	−0.15	
					Delayed Memory	−0.28	
					WMS-R Visual Reproduction	0	
					Immediate Memory	0.18	
					Delayed Memory		
					WAIS-R Digit Span		
					Forward	−0.34	
					Backward	0.21	
					Quality of Life-Patient	−0.44	
					Verbal Series Attention Test		
					Seconds	−0.02	
					Errors	−0.23	
					Controlled Oral Word Association Test		
					Letters (CFL)	−0.20	
					Animals	−0.05	
					Supermarket	−0.11	
					Tapping Test		
					Dominant	0.50	
					Nondominant	0.38	
					Geriatric Depression Scale	0.28	
Koltai et al. (2001) (27) Mild–moderate dementia SASQI = 3	EC n = 14 CC n = 8 EC, CC A = 73, 74 G = 47% E = 15, 15 MMSE = 22.9, 26.6	Memory Coping Program (MCP): Spaced retrieval (R) Face-name associations (R) Verbal elaboration (C) Concentration strategies (self talk) (C) External aids (C) Coping strategies (C) Overall = Compensatory	Wait list	Group: 1-h weekly sessions for 5 weeks Individual: 1-h weekly sessions, with caregivers included in last 15-min for 6 weeks 11 total sessions Group and Individual	MMSE	−0.36	No follow-up data
					CERAD		
					Word List Memory - Total	−0.43	
					Word List Memory - Recall	0.57	
					Everyday Memory Questionnaire		
					Self	0.38	
					Informant	0.73	
					Geriatric Depression Scale		
					Self	0.49	
					Informant	0.06	

Table 1a. (Continued)

Quayhagen et al. (2000) (34) Mild-moderate dementia, mostly AD SASQI = 5	EC n = 21 CC n = 15 A = 75 G = 63% E = 15 DRS Total > 100	Cognitive Stimulation: Caregiver cognitively stimulates patient through memory provoking (R), problem-solving (R), and conversational fluency activities (R) Overall = Restorative	Wait list	1 h per day, 5 days per week for 8 weeks 40 total sessions Individual (couple)	Immediate Memory Composite WMS Logical Memory I WMS Visual Reproduction I Dementia Rating Scale - Memory Delayed Memory Composite WMS Logical Memory II WMS Visual Reproduction II Verbal Fluency Composite Controlled Oral Word Association (Letters and Animals) Dementia Rating Scale - Initiation Problem Solving Composite Geriatric Coping Schedule Dementia Rating Scale–Conceptualization Memory and Behavior Problems Checklist – Part A – Behavior Functioning	1.08 1.31 1.45 1.41 0.77	No follow-up data
Bach et al. (1995) (33) Mild-moderate dementia patients recently admitted to a long-term geriatric residential care facility SASQI = 5	EC n = 22 CC n = 22 EC, CC A = 83, 83 G = 11% No measure of general mental status	Reactivating Occupational Therapy and Functional Rehabilitation: Memory drills (R) Manual/creative activities (R) Self–management (shopping list, plan leisure activities) (C) Overall = Restorative	Functional Rehabilitation: functional occupational therapy, physical therapy, speech therapy	1-h sessions, twice per week for 24 weeks 48 total sessions Group	Benton Test Grunberger Verbal Memory Test Nuremberg Aged Persons Inventory Number Symbol Test Latent Learning Hamilton Depression Scale Depression Status Inventory Scale of Well-being	1.09 2.05 1.03 2.11 1.06 1.23 1.13	No follow-up data
Quayhagen et al. (1995) (30) Possible or probable AD with mild-moderate decline SASQI = 9*	EC n = 25 CC1 n = 28 CC2 n = 25 A = 74 G = 65% E = 13 DRS Total ≥ 90	Cognitive Stimulation (R): Drills lead by caregiver focusing on the domains of memory, problem-solving, and social interaction Overall = Restorative	CC1: placebo: passive cognitive stimulation (observation of activities without enforced participation) CC2: Wait list	1-h sessions, 6 days per week for 12 weeks 72 total sessions Individual	 Dementia Rating Scale - Total General Memory Composite Dementia Rating Scale - Memory WMS Logical Memory I WMS Figural Memory WMS Visual Reproduction I Nonverbal Memory Verbal Memory	 CC1 CC2 0.36 0.65 0.43 0.54 0.46 0.92 0.34 0.07	6 month follow-up CC1 CC2 0.22 0.62 0.25 0.50 0.23 0.71 0.20 0.16

Table 1a. (Continued)

Study Study Sample SASQI Score *High quality study.	n, Age (A = mean years) Gender (G = % male) Education (E = mean years)	Experimental Condition (EC) Compensatory (C) vs. Restorative (R)	Control Condition (CC)	Duration and modality of training	Outcome measure/s	Effect size/s (immediate)	Follow-up duration and effect size/s
					Fluency Total Dementia Rating Scale – Initiation Controlled Oral Word Association Test Problem Solving Total Dementia Rating Scale– Conceptualization Geriatric Coping Schedule	0.55 0.80 0.44 0.69	0.17 0.46 0.24 0.33
Heiss et al. (1994) (31) Memory clinic outpatients with AD SASQI = 9*	EC n = 18 CC n = 17 EC, CC A = 66, 67 G = 59, 56% MMSE = 20.6, 21.6	Computer-based cognitive training (R) for memory, perceptual, motor tasks Overall = Restorative	Social support: weekly, 1-h meetings to talk about personal problems and management of daily life	EC: 2 1-h sessions per week for 6 months CC: 1 h session per week for 6 months EC: 48 total sessions CC: 24 total sessions Group	MMSE Verbal Selective Reminding Recognition Hits False positive Corsi's Block span Reaction Time Fragmented Picture Test (difference) 1st Presentation 2nd Presentation Controlled Oral Word Association Test Supermarket Orientation	0.01 −0.23 0.17 0.15 −0.31 0.14 0.01 0.09 0.03 0.47 −0.13	No follow-up data
Breuil et al. (1994) (35) Dementia outpatients SASQI = 5	EC n = 32 CC n = 29 EC, CC A = 76, 78 G = 31, 48% MMSE > 9	Elaboration (C) Overall = Compensatory	Wait list	2 1-h sessions per week for 5 weeks 10 total sessions Group	CERAD Mini Mental State Word List Global Score (CERAD + ADL measure) CERAD Verbal Fluency	 0.72 0.37 0.64 0.03	No follow-up data

Table 1a. (Continued)

Beck et al. (1988) (28) Residents of a VA geriatric unit or community nursing home with moderate cognitive impairment SASQI = 3	EC n = 10 CC n = 10 EC, CC A = 74, 76 G = 50, 30% MMSE = 24.3, 25.1	Training exercises (R) for attention and reading, concentration on detail, and remembering Overall = Restorative	Wait list	30 to 40-minute sessions, 3 times per week for 6 weeks 18 total sessions Individual	Attention and Reading (Cancellation task) Remembering Digits Verbal Concentration Identical match Different Spatial Orientation	0.63 0.78 0.09 −0.33 −0.25	No follow-up data
Baines et al. (1987) (18) Moderately to severely cognitively impaired residents of an authority home for the elderly SASQI = 6	EC n = 5 CC n = 5 EC, CC A = 81, 80 G = 7% CAPE Information/ Orientation = 5.4, 5.9 Mental Ability = 6.8, 7.4	Reality Orientation Therapy (R) Overall = Restorative	Wait list	30 min per day, 5 days per week for 4 weeks 20 total sessions Group	CAPE Information/Orientation Mental Ability Behavior Life Satisfaction Indices Holden 5-point Communication Scale Problem Behavior Rating Scale	 0.20 −0.15 1.47 0.05 −1.36 0.82	4 week follow-up 0.46 0 1.64 0.28 −1.03 1.03
Baines et al. (1987) (18) Moderately to severely cognitively impaired residents of an authority home for the elderly SASQI = 6	EC n = 5 CC n = 5 EC, CC A = 83, 80 G = 7% CAPE Information/ Orientation = 5.8, 5.9 Mental Ability = 8.2, 7.4	Reminiscence Therapy (R): audio/slide program of pictures of scenes from personal photographs, books, magazines, newspapers, domestic articles Overall = Restorative	Wait list	30 min per day, 5 days per week for 4 weeks 20 total sessions Group	CAPE Information/Orientation Mental Ability Behavior Life Satisfaction Indices Holden 5-point Communication Scale Problem Behavior Rating Scale	 −0.05 0.36 0.38 0.11 −1.40 0.69	4 week follow-up 0.67 0.26 0.85 0.48 −0.61 0.96
Zarit et al. (1982) (19) Probable mild–moderate dementia SASQI = 6	EC n = 14 CC n = 10 EC, CC A = 75, 75 E = 11, 11 MSQ ≥ 2 errors	Imagery (C) Overall = Compensatory	Wait list	1.5-h sessions (with caregivers), twice per week for 3.5 weeks 7 total sessions Group	Recall Trials Daily Tasks Unrelated Word List Unfamiliar Word Pairs Familiar Word Pairs Recognition Trials Daily Tasks Unrelated Word List Unfamiliar Word Pairs	 0.23 0.71 1.08 0.55 −0.11 −0.32 0.40	No follow-up data

Table 1a. (Continued)

Study Study Sample SASQI Score *High quality study.	n, Age (A = mean years) Gender (G = % male) Education (E = mean years)	Experimental Condition (EC) Compensatory (C) vs. Restorative (R)	Control Condition (CC)	Duration and modality of training	Outcome measure/s	Effect size/s (immediate)	Follow-up duration and effect size/s
					Familiar Word Pairs	0.45	
					Caregiver Reports		
					Memory Problems	0.45	
					Behavior Problems	0.21	
Zarit et al. (1982) (19) Probable mild to moderate dementia SASQI = 6	EC n = 11 CC n = 10 EC, CC A = 70, 75 E = 16, 11 MSQ ≥ 2 errors	Problem-solving: group leaders made suggestions for how to cope with specific memory problems (C) Overall = Compensatory	Wait list	1.5-h sessions (with caregivers), twice per seek for 3.5 weeks 7 total sessions Group	Recall Trials		No follow-up data
					Daily Tasks	0.10	
					Unrelated Word List	0.88	
					Unfamiliar Word Pairs	0.86	
					Familiar word pairs	0.54	
					Recognition trials		
					Daily Tasks	−0.11	
					Unrelated Word List	−0.62	
					Unfamiliar Word Pairs	0.55	
					Familiar Word Pairs	0.61	
					Caregiver Reports		
					Memory Problems	0.26	
					Behavior Problems	0.45	

ADL = Activities of Daily Living; CAPE = Clifton Assessment Procedures for the Elderly; CERAD = Consortium to Establish a Registry for Alzheimer's Disease; DAFS = Direct Assessment of Functioning Scale; DRS = Dementia Rating Scale; IADL = Instrumental Activities of Daily Living; MMSE = Mini-Mental State Examination; MSQ = Mental Status Questionnaire; SASQI = Scale to Assess Scientific Quality of Investigations; WAIS = Wechsler Adult Intelligence Scale; WMS = Wechsler Memory Scale.

Table 1b. Non-Randomized Controlled Trials of Cognitive Training for Individuals with Alzheimer's Disease

Study Study Sample SASQI Score * High quality study	n, Age (A = mean years) Gender (G = % male) Education (E = mean years)	Experimental Condition (EC) Compensatory (C) vs. Restorative (R)	Control Condition (CC)	Duration and modality of training	Outcome measure/s	Effect size/s (immediate)	Follow-up duration and effect size/s
Requena et al. (2004) (21) Elderly day-care attendees with AD SASQI = 6	EC n = 18 CC n = 18 EC, CC A = 77, 71 G = 28, 17% MMSE = 19.4, 19.4	Cognitive stimulation (R); Stimulation in: orientation, bodily awareness, family and society, self-care, reminiscing, household activities, animals, people and things. Used visual stimuli under computer control Overall = Restorative	Wait list	Daily 45-minute sessions for 1 year 260 total sessions Group	MMSE Alzheimer's Disease Assessment Scale (cognitive) Clinical Developmental Stage of Dementia (FAST) Geriatric Depression Scale	1.26 0.40 0.95 0.04	No follow-up data
Zanetti et al. (2001) (37) Probable AD patients with mild – moderate cognitive impairment in day hospital treatment SASQI = 3	EC n = 11 CC n = 7 EC, CC A = 78, 74 G = 1, 14% E = 6, 5 MMSE = 20, 19	Procedural memory training, with prompts and modeling for ADLs and IADLs (C) Overall = Compensatory	Wait list	Daily 1-h sessions, 5 days per week for 3 weeks 15 total sessions Individual	Time to complete (Independent) Activities of Daily Living	0.93	No follow-up data
Schreiber et al. (1999) (36) Mild moderately impaired AD or vascular dementia SASQI = 9*	EC n = 7 CC n = 7 EC, CC A = 81, 79 G = 29, 17% MMSE = 21	Computer based training: finding objects in a 3-D virtual apartment, with increasing degrees of difficulty (increasing number of objects to find) with aid of instructor when needed (R) Overall = Restorative	Nondirected conversation with therapist	5 to 30-minute sessions per week for 2 weeks 10 total sessions Individual	Nuremberg Aging Inventory Figure Picture Rivermead Behavioral Memory Test Picture Route Immediate Route Delayed	 0.30 1.67 0.45 2.16 2.35	No follow-up data
Zanetti et al. (1995) (38) Mild to moderate AD in day hospital patients SASQI = 3	EC n = 16 CC n = 12 EC, CC A = 73, 68 E = 5, 7 MMSE = 18.4, 20.0	Reality Orientation Therapy (R) Overall = Restorative	Wait list	45-minute sessions, 5-days per week for 4-weeks 20 total sessions Group Some patients completed multiple cycles (1–4 cycles)	MMSE Activities of Daily Living measure Independent Activities of Daily Living measure Geriatric Depression Scale	0.75 –.31 –.04 0.14	No follow-up data
Quayhagen et al. (1989) (39) AD patients SASQI = 5	EC n = 10 CC n = 6 EC, CC A = 68, 67 G = 40, 17% E = 13, 14 Mental status errors = 5.1, 4.3	In-home training focusing on conversation skills, memory-provoking exercises, and problem-solving techniques (R) Overall = Restorative	Wait list	1-h per day, 6 days per week for 16 weeks 96 total sessions Individual	 Total Cognitive Functioning Attention Initiation Conceptualization Calculation Logical Memory Problem Solving Frequency of Memory and Behavior Problems Frequency of Memory Problems Frequency of Behavior Problems	 1.27 2.22 0.68 0.95 1.01 0.98 1.48 0.57 0.15 0.84	4 month follow-up 1.99 2.72 1.40 1.80 1.16 1.50 1.68 0.85 0.52 1.32

ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; MMSE = Mini-Mental State Examination; SASQI = Scale to Assess Scientific Quality of Investigations.

Table 2. Mean weighted effect sizes, standard deviations, and number of subjects for each domain of functioning

Domain of functioning	Overall ES (SD) (*n*)	Restorative ES (SD) (*n*)	Compensatory ES (SD) (*n*)
Overall cognitive	0.50 (0.54) (545)	0.67 (0.62) (339)	0.22 (0.16) (206)
General cognitive functioning	0.38 (0.46) (308)	0.37 (0.45) (225)	0.40 (0.46) (83)
Attention and processing speed	0.37 (0.70) (230)	0.48 (0.78) (152)	0.16 (0.33) (78)
Verbal learning	0.50 (0.68) (316)	0.68 (0.89) (154)	0.34 (0.32) (162)
Verbal memory	0.03 (0.27) (173)	−0.07 (0.22) (72)	0.10 (0.29) (101)
Visual learning	0.30 (0.46) (261)	0.48 (0.44) (183)	−0.12 (0.02) (78)
Visual memory	0.00 (0.19) (115)	0.18 (0.00) (37)	−0.08 (0.18) (78)
Verbal and visual learning	2.16 (0.00) (14)	2.16 (0.00) (14)	–
Verbal and visual memory	0.67 (0.76) (149)	0.73 (0.90) (105)	0.53 (0.00) (44)
Verbal learning and memory	−0.23 (0.00) (35)	−0.23 (0.00) (35)	–
Visual learning and memory	0.73 (0.27) (30)	0.73 (0.27) (30)	–
Verbal and visual learning and memory	1.03 (0.66) (177)	1.16 (0.72) (133)	0.65 (0.00) (44)
Working memory	0.17 (0.52) (108)	0.17 (0.52) (108)	–
Language	0.08 (0.51) (240)	0.09 (0.65) (145)	0.06 (0.04) (95)
Motor speed	0.44 (0.00) (37)	0.44 (0.00) (37)	–
Executive functioning	0.66 (0.55) (139)	0.87 (0.46) (105)	0.00 (0.00) (34)
Visuospatial functioning	−0.38 (0.00) (34)	–	−0.38 (0.00) (34)
Performance-based activities of daily living	0.69 (0.16) (62)	–	0.69 (0.16) (62)
Overall informant ratings	0.56 (0.41) (325)	0.75 (0.47) (180)	0.32 (0.07) (145)
Informant-rated activities of daily living	−0.07 (0.30) (106)	−0.18 (0.00) (28)	−0.04 (0.34) (78)
Informant-rated memory problems	0.53 (0.25) (117)	0.15 (0.00) (16)	0.59 (0.22) (101)
Informant-rated cognitive problems	0.80 (0.14) (80)	0.95 (0.00) (36)	0.68 (0.00) (44)
Informant-rated behavior problems	0.48 (0.33) (161)	0.81 (0.17) (72)	0.22 (0.13) (89)
Informant-rated depression	0.63 (0.50) (110)	1.23 (0.00) (44)	0.23 (0.12) (66)
Overall self-ratings	0.26 (0.43) (231)	0.32 (0.48) (165)	0.14 (0.21) (66)
Self-rated memory problems	0.38 (0.00) (22)	–	0.38 (0.00) (22)
Self-rated cognitive problems	−0.02 (0.00) (44)	–	−0.02 (0.00) (44)
Self-rated depression	0.34 (0.40) (211)	0.43 (0.43) (145)	0.16 (0.24) (66)
Self-rated quality of life	−0.26 (0.25) (57)	−0.26 (0.25) (57)	–
Self-rated general functioning	1.13 (0.00) (44)	1.13 (0.00) (44)	–

ES, effect size; SD, standard deviation; *n*, number of subjects.

weighted mean effect sizes for restorative strategies were in the domains of verbal and visual learning ($d = 2.16$, SD = 0.00), informant-rated depression ($d = 1.23$, SD = 0.00), verbal and visual learning and memory ($d = 1.16$, SD = 0.72), and self-rated general functioning ($d = 1.13$, SD = 0.00).

Six reports provided follow-up data, with a mean length of follow-up of 4.5 months. The overall mean weighted effect size for CT at follow-up was .30 (SD = 0.41), with nonsignificantly greater effect sizes in wait-list control studies ($d = 0.70$, SD = 0.74) than in attention-placebo control studies ($d =$ 0.14, SD = 0.09; $t(2.1) = 1.31$, $P = 0.318$). Follow-up effect sizes for restorative strategies ($d = 0.58$, SD = 0.65) were nonsignificantly greater than were those for compensatory strategies ($d = 0.10$, SD = 0.07; $t(4) = 0.98$, $P = 0.381$), and individual treatment evidenced nonsignificantly greater effect sizes than did group treatment at follow-up ($d = 0.64$, SD = 0.79 vs. $d = 0.20$, SD = 0.15, respectively; $t(2.1) = 0.95$, $P = 0.436$).

Discussion

The results from the 19 controlled trials of CT reviewed suggest that, in general, CT can improve the cognitive and functional abilities of AD patients. The range of effect sizes, however, was large. Using Cohen's (26) description of effect size magnitude (0.2 = small, 0.5 = medium, 0.8 = large), small effects were observed in some domains (e.g. visual learning and motor speed), whereas larger effects were observed in other domains (e.g. executive functioning, verbal and visual learning, and ADLs). These findings are consistent with several other reviews (7–9) suggesting that there is some benefit to using CT for AD patients, and paint a somewhat more optimistic picture than do the Clare et al. (16) and Spector et al. (14, 15) reviews. The discrepant conclusions drawn from our review and the Clare et al. (16) review may have resulted from our less strict inclusion criteria, leading to a broader range of interventions reviewed.

Although a small effect size was observed for CT in general, examining subgroups of studies presents a somewhat different perspective. As might be expected, differential effects of CT are observed when compared with different control groups. Stronger effects were observed for investigations comparing CT to wait-list controls rather than to attention-placebo controls. This may suggest that much of the benefit derived from CT may result from the consistent focused attention received by participants and general cognitive stimulation provided through scheduled interpersonal interactions. Prior research has demonstrated that maintaining higher levels of mental activity can have a protective effect and delay the onset of noticeable cognitive decline (40).

A differential impact on cognition and functional ability was observed for different types of CT. The most efficacious CT interventions were those that used restorative strategies, such as general cognitive stimulation (e.g. prompting recall of remote memories, practicing conversation skills, problem-solving, reading, and engaging in creative activities), computerized visuospatial drills, and memory drills emphasizing repetition. Four of the five reports with the most beneficial results employed general stimulation techniques. This further supports the notion that simply maintaining higher levels of mental activity may have a beneficial effect on cognitive functioning, and underscores the potential role that family members might play in providing general cognitive stimulation.

Compensatory techniques (e.g. visualization, procedural memory training, and external devices) appeared to be less effective than restorative strategies at improving cognitive and functional abilities. Although compensatory strategies have been demonstrated to improve functioning in other populations with cognitive and functional impairments (41, 42), and a small effect size was observed in the current review, the difficulties experienced by AD patients may present a unique challenge to teaching compensatory strategies. Although AD patients may be able to learn some of these techniques, they may forget to use them. Utilizing the AD patients' relatively preserved implicit and procedural memory systems (9) to make these strategies habitual may improve outcomes. With a mean duration of treatment of 5.7 weeks in the studies reviewed, it is unlikely that the techniques taught became habits.

Greater effect sizes were observed for studies using individual treatment modalities over group modalities. It is unclear whether these individual modalities were better tailored to the specific needs of each individual, or if the benefit over group modalities was due to more individualized attention. Regardless of the answer, this finding provides further evidence for the potential impact of individualized attention from family members on the cognitive and functional abilities of AD patients.

There was a high level of variability in the effects of CT on different domains of functioning. The greatest overall effect was observed on measures of performance-based ADLs. This effect was based on two reports (32, 37) that used compensatory procedural memory strategies to train patients in the performance of specific ADLs. Performance on trained activities was evaluated, whereas performance of untrained ADLs was not measured; therefore, we are unable to determine if any generalization of skills occurred. Even if training on specific tasks does not generalize to other daily activities, patients' autonomy and sense of self-reliance may be improved through their ability to better perform trained tasks. No studies providing CT targeting only cognition reported results of performance-based measures of ADLs, again limiting conclusions regarding generalizability of effects.

Medium overall effects were observed for informant ratings of cognition and behavior, but smaller effects were observed on self-rating measures, probably due to AD patients' lack of awareness of their deficits. A medium overall effect was found for cognitive performance. Within the domain of cognitive functioning, however, there were negative or minimal effects (e.g. on visuospatial functioning and language), small effects (e.g. on motor speed and visual learning), medium effects (e.g. on executive functioning), and large effects (e.g. on verbal and visual learning). CT appeared to have an immediate effect on combined measures of verbal and visual learning and memory; however, due to the lack of effects on more pure measures of verbal memory ($d = 0.03$) and visual memory ($d = 0.00$), we suspect that CT may show promise for improving learning, but not memory.

Studies identified as high quality painted a less optimistic picture of the efficacy of CT for AD. These studies demonstrated lower overall effect sizes, and no differences between restorative and compensatory strategies were observed. The difference between the high quality studies and the remaining studies is probably due to methodological differences between the studies. The high quality studies used attention-placebo control groups whereas most other studies used wait-list controls. If AD patients do benefit from general cognitive stimulation, this may explain the smaller effect sizes for studies using attention-placebo control groups.

The few studies that provided follow-up data suggest that gains acquired during treatment may be maintained an average of 4.5 months after discontinuing the treatment. Similar to immediate treatment effects, maintenance of treatment gains was better in studies that compared CT with a wait-list control group, used an individual treatment modality, and for restorative CT strategies. In progressive diseases such as AD, it may not be possible to maintain gains in cognitive or functional abilities, but the follow-up findings in the literature suggest that the rate of decline may be slower in patients receiving CT.

Limitations

The relatively small number of published well-controlled studies of the efficacy of CT in AD patients limited the number and types of analyses we performed. Additionally, the sample sizes of the studies reviewed here are relatively small (mean = 36, range 10–61). Thus, the studies' effect sizes were weighted by sample size. We also identified several problems related to the outcome measures employed in the reports reviewed here, including variability in outcome measures between studies, making cross-study comparisons difficult. Additionally, there were relatively few performance-based measures of functional abilities, which should be included along with cognitive measures to assess change in daily functioning abilities. Functional outcomes are probably best measured with performance-based tests, rather than informant reports, which have multiple inherent biases and limitations. Only two studies in the current review used performance-based measures of daily functioning (32, 37) and no studies used measures of real-world functioning.

Multiple CT techniques were often used in combination to create CT protocols for each study, making it difficult to evaluate the efficacy of a single strategy. By categorizing the studies as primarily compensatory or restorative, we evaluated the effect of each category of techniques rather than each individual strategy. Further complicating this process were the incomplete descriptions of CT regimens provided in several studies. It may be helpful in future research to evaluate a single CT strategy at a time and present a detailed description of the training provided. The identification of individually effective strategies would aid in the development of more effective combinations of strategies.

Concern over the maintenance of treatment gains is warranted, given the degenerative nature of AD. The current review provides some evidence that treatment gains may be maintained over a period of a few months. However, these results are based on only six reports that provided follow-up data.

Restorative and compensatory CT strategies were reviewed in this paper; however, we did not review environmental manipulations, which are commonly included in the treatment of AD (43), due to a lack of controlled studies in this area. Such manipulations include the use of bright lights in the early evening in order to reduce the effects of sundowning, name-tags to help reduce memory demands, and clear labels around the living quarters. Although the effect of environmental manipulation on inappropriate behavior in AD has been studied (see 44 for review), these studies are primarily uncontrolled and do not target specific cognitive impairments.

The results of this meta-analysis may be positively skewed because of publication bias. We relied on published reports for our data and it is not possible to know how many unpublished studies of CT demonstrated no effect on cognition or cognitively mediated behavior.

It should also be noted that several domain scores, including the very large effect size for verbal and visual learning, represent results of a single study and are not aggregate scores. These scores are less robust than scores reflecting multiple studies and may have resulted from extraneous, study-specific factors.

Future directions

Several suggestions for future research are implied by the findings of this review. It appears that CT may improve the cognitive and functional abilities of AD patients, or at least slow the rate of decline. These effects seem to be largest in the domains of learning, informant-rated cognitive problems, self-rated general functioning, and performance-based measures of functional abilities. Training patients in the performance of IADLs could increase the length of time they are able to remain independent and decrease burden on caregivers. Effectiveness studies using larger samples in various settings (e.g. retirement communities, family members' homes, nursing facilities) will aid with dissemination. The generalizability of treatment effects to everyday behaviors will also be an important outcome. Performance-based measures of IADLs may be used to evaluate the effects of treatment on daily functioning. The economic impact of providing CT for AD patients will also be of interest, as will its effects on relatives and caregivers. Ultimately, the most effective treatments will probably involve a combination of pharmacotherapy, CT, and caregiver involvement.

Acknowledgements

This work was supported, in part, by the National Institute of Mental Health grants P30MH066248-03 and T32MH019934-11 and by the Department of Veterans Affairs.

References

1. Rosenstein LD. Differential diagnosis of the major progressive dementias and depression in middle and late adulthood: a summary of the literature of the early 1990s. Neuropsychol Rev 1998;**8**:109–167.
2. Cummings JL. Use of cholinesterase inhibitors in clinical practice: evidence-based recommendations. Am J Geriatr Psychiatry 2003;**11**:131–145.
3. Lanctot KL, Herrmann N, Yau KK et al. Efficacy and safety of cholinesterase inhibitors in Alzheimer's disease: a meta-analysis. CMAJ, 2003;**169**:557–564.
4. Rockwood K. Size of the treatment effect on cognition of cholinesterase inhibition in Alzheimer's disease. J Neurol Neurosurg Psychiatry 2004;**75**:677–685.
5. Bellack AS, Gold JM, Buchanan RW. Cognitive rehabilitation for schizophrenia: problems, prospects, and strategies. Schizophr Bull 1999;**25**:257–274.
6. Spaulding WD, Fleming SK, Reed D, Sullivan M, Storzbach D, Lam M. Cognitive functioning in schizophrenia: implications for psychiatric rehabilitation. Schizophr Bull 1999;**25**:275–289.
7. Backman L. Utilizing compensatory task conditions for episodic memory in Alzheimer's disease. Acta Neurol Scand 1996;**165**(suppl.):109–113.
8. Mahendra N. Direct interventions for improving the performance of individuals with Alzheimer's disease. Semin Speech Lang 2001;**22**:291–304.
9. De Vreese LP, Neri M, Fioravanti M, Belloi L, Zanetti O. Memory rehabilitation in Alzheimer's disease: a review of progress. Int J Geriatr Psychiatry 2001;**16**:794–809.
10. Taulbee LR, Folsom JC. Reality orientation for geriatric patients. Hosp Community Psychiatry 1966;**17**:133–135.
11. Woods RT, Portnoy S, Head D, Jones GMM. Reminiscence and life review with persons with dementia: which way forward? In: Jones GMM, Meisen BML, eds. Care giving in dementia: research and applications. pp 137–161. New York: Tavistock/Routledge, 1992.
12. Brush JA, CAMP CJ. Spaced retrieval during dysphagia therapy: a case study. Clin Gerontol 1989;**19**:96–99.
13. Clare L, Wilson BA, Carter G, Breen K, Gosses A, Hodges JR. Intervening with everyday memory problems in dementia of the Alzheimer type: an errorless learning approach. J Clin Exp Neuropsychol 2000;**22**:132–146.
14. Spector A, Orrell M, Davies S, Woods B. Reality orientation for dementia. Cochrane Database Syst Rev 2000;Issue 3:Art. No.: CD001119. DOI: 10.1002/14651858. CD001119. This version first published online: 24 July 2000 in Issue 3, 2000.
15. Spector A, Orrell M, Davies S, Woods RT. Reminiscence therapy for dementia. Cochrane Database Syst Rev 2000;Issue 3:Art. No.: CD001120. DOI: 10.1002/14651858.CD001120. This version first published online: 24 July 2000 in Issue 3, 2000.
16. Clare L, Woods RT, Moniz Cook ED, Orrell M, Spector A. Cognitive rehabilitation and cognitive training for early-stage Alzheimer's disease and vascular dementia. Cochrane Database Syst Rev 2003;Issue 4:Art. No.: CD003260. DOI:10.1002/14651858.CD003260. This version first published online: 20 October 2003 in Issue 4, 2003.
17. Quayhagen MP, Quayhagen M, Corbeil RR, Roth PA, Rodgers JA. A dyadic remediation program for care recipients with dementia. Nurs Res 1995;**44**:153–159.
18. Baines S, Saxby P, Ehlert K. Reality orientation and reminiscence therapy: a controlled cross-over study of elderly confused people. Br J Psychiatry 1987;**151**:222–231.
19. Zarit SH, Zarit JM, Reever KE. Memory training for severe memory loss: effects on senile dementia patients and their families. Gerontologist 1982;**22**:373–377.
20. Davis RN, Massman PJ, Dood RS. Cognitive intervention in Alzheimer's disease: a randomized placebo-controlled study. Alzheimer Dis Assoc Disord 2001;**15**:1–9.
21. Requena C, Ibor MI, Maestu F, Campo P, Ibor JJ, Ortiz T. Effects of cholinergic drugs and cognitive training on dementia. Dement Geriatr Cogn Disord 2004;**18**:50–54.
22. Twamley EW, Bondi MW. The differential diagnosis of dementia. In: Ricker JH, ed. Differential diagnosis in adult neuropsychological assessment. New York: Springer Publishing Company, Inc., 2004:276–326.
23. Knopman D, Selnes O. Neuropsychology of dementia. In: Heilman KM, Valenstein E, eds. Clinical neuropsychology, 4th edn. New York: Oxford University Press, 2003:574–616.
24. Fields RB. The dementias. In: Snider PJ, Nussbaum PD, eds. Clinical neuropsychology. Washington, DC: American Psychological Association, 1998:211–239.
25. Lezak MD. Neuropsychological assessment. New York: Oxford University Press, 1995.
26. Cohen J. A power primer. Psychol Bull 1992;**112**:155–159.
27. Koltai DC, Welsh-bohmer KA, Schmechel DE. Influence of anosognosia on treatment outcome among dementia patients. Neuropsychol Rehabil 2001;**11**:455–475.
28. Beck C, Heacock P, Mercer S, Thatcher R, Sparkman C. The impact of cognitive skills remediation training on persons with Alzheimer's disease or mixed dementia. J Geriatr Psychiatry 1988;**21**:73–88.
29. Petiti DM. Meta analysis, decision analysis and cost effectiveness analysis. Oxford: Oxford University Press, 1994.
30. Cahn-weiner DA, Malloy PF, Rebok GW, OTT BR. Results of a randomized placebo-controlled study of memory training for mildly impaired Alzheimer's disease patients. Appl Neuropsychol 2003;**10**:215–223.
31. Heiss WD, Kessler J, Mielke R, Szelies B, Herholz K. Long-term effects of phosphatidylserine, pyritinol, and cognitive training in Alzheimer's disease. A neuropsychological, EEG, and PET investigation. Dementia 1994;**5**:88–98.
32. Loewenstein DA, Acevedo A, Czaja SJ, Duara R. Cognitive rehabilitation of mildly impaired Alzheimer's disease patients on cholinesterase inhibitors. Am J Geriatr Psychiatry 2004;**12**:395–402.
33. Bach D, Bach M, Bohmer F, Fruhwald T, Grilc B. Reactivating occupational therapy: a method to improve cognitive performance in geriatric patients. Age Ageing 1995;**24**:222–226.
34. Quayhagen MP, Quayhagen M, Corbeil RR et al. Coping with dementia evaluation of four nonpharmacologic interventions. Int Psychogeriatr 2000;**12**:249–265.
35. Breuil V, De Rotrou J, Forette F et al. Cognitive stimulation of patients with dementia: preliminary results. Int J Geriatr Psychiatry 1994;**9**:211–217.
36. Schreiber M, Schweizer A, Lutz K, Kalveram KT, Jancke L. Potential of an interactive computer-based training in the rehabilitation of demetia: an initial study. Neuropsychol Rehabil 1999;**9**:155–167.
37. Zanetti O, Zanieri G, Di Giovanni G et al. Effectiveness of procedural memory stimulation in mild Alzheimer's disease patients: a controlled study. Neuropsychol Rehabil 2001;**11**:263–272.
38. Zanetti O, Frisoni GB, De Leo D, Dello Buono M, Bianchetti A, Trabucchi M. Reality orientation therapy in Alzheimer's disease: useful or not? A controlled study. Alzheimer Dis Assoc Disord 1995;**9**:132–138.

39. Quayhagen MP, Quayhagen M. Differential effects of family-based strategies on Alzheimer's disease. Gerontologist 1989;**29**:150–155.
40. Fratiglioni L, Paillard-Borg S, Winblad B. An active and socially integrated lifestyle in late life might protect against dementia. Lancet Neurol 2004;**3**:343–353.
41. Twamley EW, Jeste DV, Bellack AS. A review of cognitive training in schizophrenia. Schizophr Bull 2003;**29**:359–382.
42. Cicerone KD, DahlberG C, Kalmar K et al. Evidence-based cognitive rehabilitation: recommendations for clinical practice. Arch Phys Med Rehabil 2000;**81**:1596–1615.
43. Raskind MA. Psychopharmacology of noncognitive abnormal behaviors in Alzheimer's disease. J Clin Psychiatry 1999;**60**:45–49.
44. Cohen-Mansfield J. Nonpharmacologic interventions for inappropriate behaviors in dementia: a review and critique. Am J Geriatr Psychiatry 2001;**9**:361–381.