

Systematic Review of Neuropsychological Outcomes in Dementia from Cognition-Based Psychological Interventions

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Key Words

Cognition · Dementia · Neuropsychology · Cognitive training · Cognitive stimulation

Abstract

Background/Aims: Although there is increasing evidence for the effectiveness of cognition-based psychological interventions in dementia, little is known about which neuropsychological domains are more amenable to change. **Method:** A systematic search identified randomised controlled trials grouped according to intervention type (cognitive training/cognitive stimulation). Methodological quality was evaluated. **Results:** Of the 129 studies identified, 18 met the inclusion criteria; 11 were 'Cognitive Training' and 7 'Cognitive Stimulation'. For Cognitive Training, it was not possible to conclude which (if any) domains are most amenable to change. For Cognitive Stimulation, there was good evidence for general cognitive enhancement, more specifically in language and memory. **Conclusions:** Further in-depth trials are needed to determine neuropsychological processes more clearly.

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Introduction

In recent years, psychosocial interventions for dementia have become widely used and evaluated [1]. The development of psychological cognitive interventions for de-

mentia was originally stimulated by evidence from the neuroscience literature. This suggested that the adult brain retains significant neuronal plasticity and therefore has the capacity for regeneration and compensation [2–5]. 'Dementia' encompasses a variety of disorders involving impaired cognition including memory, language, praxis, visuospatial and perceptual function and executive functions such as planning, organising and sequencing. Three main categories of cognition-focused psychological interventions have been described [6]: (1) cognitive training involves guided practice on a set of standard tasks designed to promote particular cognitive functions such as memory, attention or executive function, with the assumption that regular practice may improve or maintain functioning in that domain, (2) cognitive rehabilitation describes interventions that aim to build on preserved areas of cognition by developing strategies or using external aids to compensate for functional difficulties and (3) cognitive stimulation employs a range of activities and discussions aimed at the general enhancement of cognitive functioning, where tasks are more general, emphasise implicit as opposed to explicit learning and usually depend on the integration of various cognitive functions (e.g. memory, attention, language and problem-solving). Cognitive training and cognitive rehabilitation tend to be individualised approaches that are guided by needs, for example, it may be important for an individual to be able to dress themselves or learn the names of friends at a day centre. In contrast, cognitive stimulation usually

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1420–8008/12/0344–0244\$38.00/0

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runs in a group format, often following a programme known as ‘CST’ [cognitive stimulation therapy, see [40)].

Existing systematic reviews evaluating the efficacy of psychological cognitive interventions in dementia have generally only looked at change on the most widely used, generic measures of cognition, i.e. the Mini Mental State Examination (MMSE) and the cognitive subscale of the Alzheimer’s Disease Assessment Scale (ADAS-Cog) [7–9]. One review looked at change on more specific measures of cognitive function [7], but unfortunately grouped cognitive training and cognitive stimulation with other psychological interventions, labelling them all as ‘restorative strategies’ and not exploring differential effects on cognition. Our review aims to identify which neuropsychological domains show improvements or maintenance of function in people with mild to moderate dementia in relation to participation in cognition-focused psychological interventions.

Methods

Inclusion Criteria

Only randomised controlled trials (RCTs) published in English in peer-reviewed journals were considered for inclusion. Additional criteria relating to study participants, interventions and outcome measures were used to select studies which met the quality criteria and were relevant to the aim.

Type of Participants

- Diagnosed with dementia using validated, systematic diagnostic criteria such as DSM-IV-TR [10] or ICD-10 [11].
- Mild to moderate dementia as estimated by a standardised measure such as the MMSE [12] or Clinical Dementia Rating (CDR) [13].

Types of Interventions

- Aimed primarily at improving or maintaining cognitive function: techniques, therapy, groups, training, strategies or stimulation that directly and explicitly target cognitive functioning.
- Acceptable control conditions including ‘no treatment’, ‘treatment as usual’, another active treatment or placebo.

Types of Outcome Measures

- Evaluated in terms of change from baseline on at least one standardised measure of cognitive function.

Search Methods for Identification of Studies

Studies were identified by searching ALOIS (www.medicine.ox.ac.uk/alois), the specialized register of the Cochrane Dementia and Cognitive Improvement Group including records from a range of sources i.e. Medline, Embase, PsycINFO and Cinahl. No start date was used for the search in order to include as many studies as possible. The search was limited to RCTs. Search terms were ‘dementia’ or ‘Alzheimer disease’ and at least one of the following:

‘cognitive’, ‘memory’, ‘reality’, ‘orientation’, ‘stimulation’, ‘rehabilitation’, ‘training’, ‘remediation’ and ‘retraining’. Additionally, the terms were entered into PsycINFO. Abstracts were read to determine whether each study met inclusion criteria.

Categorisation of Studies

The above definitions of ‘Cognitive Stimulation’ and ‘Cognitive Training’ were used [6]. None of the studies eligible for inclusion involved ‘Cognitive Rehabilitation’, hence it was excluded. Scores on most neuropsychological tests can be affected by multiple cognitive abilities; however, a primary ability is usually identifiable. Measures were grouped by the primary domain of cognition evaluated. Measures for which the primary domain could not be identified due to lack of information (e.g. Syndrom Kurztest) were excluded. The methodological quality of each study was objectively rated using the Jadad scale for evaluating RCTs [14], which gives studies up to 5 points according to randomisation, blinding, whether dropouts are described, method of randomisation and method of double-blinding. A study was designated ‘high quality’ if it scored 3–5, ‘medium quality’ if it scored 2 and ‘low quality’ if it scored 0 or 1.

Results

Searches identified 129 potential studies, 18 of which met the inclusion criteria, 11 being cognitive training and 7 being cognitive stimulation. A heterogeneous range of measures was used to evaluate cognitive change. The two most frequently used measures were the MMSE [12] and the ADAS-Cog [15]. Both are used as measures of global cognitive ability. The MMSE is a brief measure used clinically to screen for cognitive impairment. It contains items that assess orientation to time and place, attention and calculation, language and immediate and delayed recall. The ADAS-Cog is frequently used as a primary efficacy measure in clinical trials of medication for Alzheimer’s disease [16]. It consists of three subscales: memory, praxis and language; however, only the overall score out of 70 tends to be reported.

Cognitive Training Interventions

Full details of the 11 cognitive training interventions can be found in tables 1 and 2. Four were rated as high-quality, 3 as medium-quality and 4 as low-quality. Studies varied somewhat in content, both for the treatment and comparison groups. In terms of comparison groups, 2 studies used a waiting-list control, 2 used a treatment-as-usual control group and 1 used two comparison groups: medication only and placebo medication. The remaining 6 studies all used a placebo comparison group in order to control for general effects of therapist attention and/or social interaction. Five studies evaluated cognitive train-

Table 1. Cognitive training studies: key characteristics and findings

First author	Quality rating (score/5) studies	Num-ber of participants	Diagnosis of participants	Antidementia medication use	Standardised objective cognitive outcome measures ¹	Assessment intervals	Statistically significant findings and trends
Beck [27]	low (1)	20	AD or mixed dementia	Not reported	Cognitive Skills Battery [59] involving letter cancellation, digit span, story recall and object matching	At baseline and post-intervention	Trend towards improvement in CT group on Digit Span compared to control group ($p < 0.10$). Both CT and control groups declined significantly on the object-matching tasks ($p < 0.01$ and $p < 0.05$, respectively).
Bottino [19]	medium (2)	13	Probable AD based on ICD-10 and NINCDS-ADRD criteria	All taking ChEI for 2 months	MMSE, ADAS-Cog, WAIS-R Vocabulary, WAIS-R Block Design, WMS-R Digit Span, TMT, Semantic Fluency (animals), BNT and FOME	At baseline and post-intervention	Improved performance on MMSE ($p = 0047$) and Backward Digit Span ($p = 0018$) at post-intervention in CT group compared to control group. Trend towards improvement in CT group on ADAS-Cog ($p = 0092$).
Cahn-Weiner [22]	high (5)	34	Probable AD based on NINCDS-ADRD criteria	All taking ChEI throughout intervention	HVLT-R, BYMT-R, BNT, COWA, JOLO, TMT and MMSE	At baseline, post-intervention and 8-week follow-up.	None.
Davis [20]	high (3)	37	Probable AD based on NINCDS-ADRD criteria	Intervention group $n = 5$ placebo group $n = 4$	MMSE, WMS-R LM, WMS-R VR, WAIS-R Digit Span, VSAT, COWA, Category Fluency and Finger-Tapping Test	At baseline and post-intervention.	Trend towards improvement in CT group on VSAT seconds ($p < 0.10$).
De Vreese [17]	low (1)	18	AD based on NINCDS-ADRD or DSM-IV criteria	All taking ChEI for 3 months	MMSE and ADAS-Cog	At baseline, post-intervention and 26 weeks.	At 26 weeks both combined and ChEI only groups improved on the ADAS-Cog compared to a decline in the placebo group. The combined group demonstrated a significant improvement on the MMSE compared to the ChEI only ($p = 0019$) and placebo groups.
Galante [18]	low (1)	11	AD based on NINCDS-ADRD criteria	All taking ChEI for at least 3 months before inclusion.	MMSE, MODA, Bisyllabic Word Repetition Test, Prose memory, Corsi's blocks, Digit cancellation, Raven's Coloured Progressive Matrices, semantic and phonemic verbal fluency, "denomination", constructional apraxia and ideomotor apraxia for superior limbs	At baseline, post-intervention and 3-month and 9-month follow-up.	Mean MMSE score in CT group remained stable over time. Decline in control group on MMSE at 9 months compared to both baseline ($p = 004$) and at 3-month follow-up ($p = 0008$).
Heiss [23]	medium (2)	80	Probable AD based on NINCDS-ADRD	Not reported	MMSE, verbal selective reminding task, orientation, praxis, fragmented pictures test, reaction time, block span test and "supermarket" task	At baseline and post-intervention.	CT plus phosphatidylserine group showed a non-significant trend for improvement in the MMSE, block span and orientation measures. The other groups showed no improvement, and on some measures a slight trend towards cognitive decline.
Koltai [21]	medium (2)	22	Dementia	Not reported	CERAD test battery (MMSE, a list-learning and memory task, abbreviated BNT, category fluency, Rosen figures of constructional praxis) and EMQ (self- and relative-rated)	At baseline and post-intervention.	None.
Loewenstein [26]	high (3)	44	Possible or probable AD based on NINCDS-ADRD	All on stable dose of ChEI for at least 8 weeks before inclusion	List-Learning Task from the CERAD test battery, WMS-III LM, WAIS-III Digit Span, TMT, Category Fluency Test, MMSE orientation items and CPT	At baseline, post-intervention and 3-month follow-up.	Improvement in CT group on MMSE orientation items and CPT reaction time relative to baseline, at post-intervention and at 3-month follow-up. Control group had fewer commission errors on the CPT at post-intervention.

Table 1. (continued)

First author	Quality rating (score/5)	Number of studies	Diagnosis of participants	Antidementia medication use	Standardised objective cognitive outcome measures ¹	Assessment intervals	Statistically significant findings and trends
Quayhagen 1995 [24]	high (3)	78	Possible or probable AD	Not reported	DRS, Memory Composite Score (memory factor from DRS plus WMS-R LM I, Figural Recall and VRI), Fluency Composite Score (COWA, initiation factor from DRS, category fluency), WMS-R Visual Memory Span and Digit Span	At baseline, post-intervention and 6-month follow-up.	Improvement in CT group on DRS (p = 0004), non-verbal memory (p = 0006) and fluency (p = 0005) at post-intervention. Waiting-list group declined at post-intervention and 6-month follow-up across all measures. Placebo group declined on some items and maintained baseline on others.
Quayhagen 2000 [31]	low (1)	103	Possible or probable AD, vascular or Parkinson's dementia	Not reported	Immediate-Memory Composite (memory factor from DRS plus WMS-R LM I and VR I), Delayed-Memory Composite (WMS-R LM II and VR II), Verbal-Fluency Composite (COWA, animal fluency and initiation factor from DRS), and Problem-Solving Composite (GCS and DRS conceptualisation factor)	At baseline and 4 weeks after intervention.	Improvement in CT group on delayed memory (p = 0029), problem solving (p = 0009) and verbal fluency (p = 0018).

¹ Please refer to table 3 for full titles of all measures.

ing in combination with acetylcholinesterase inhibitors (ChEIs). Studies also varied significantly in terms of length of intervention (range 4–24 weeks, $M = 10.5$, $SD = 6.6$), number of sessions delivered (range 5–72, $M = 25.3$, $SD = 20.9$) and mode of delivery. Some interventions were delivered by a clinician or member of the research team, some by computer and some using a combination of professional and family-caregiver facilitation. Three studies looked at group interventions, whereas the remaining studies looked at individual interventions.

General Cognitive Function. Eight of the 11 studies used a measure of general cognitive function as an outcome measure, with 7 using the MMSE and 2 using the ADAS-Cog. Three studies provided some evidence for enhancement of general cognitive function, but 2 of these were rated as being of low methodological quality [17, 18] and 1 as being of medium quality [19]; these 3 were also the smallest out of all of the studies and 2 of them failed to control for general effects such as therapist attention and social interaction [17, 19]. There were no significant differences in the remaining 4 studies that employed the MMSE [20–23], 2 high-quality and 2 medium-quality studies. A ‘high quality’ study [24] used the Dementia Rating Scale [25] to measure general cognitive ability, finding statistically significant improvements after intervention relative to both waiting-list and placebo-control groups. However, baseline data for each of the groups were not reported and so the findings could also be due to group differences in baseline scores.

Learning and Memory. All but 1 [17] of the 11 studies of cognitive training interventions used at least one test of learning and memory as an outcome measure. The aforementioned high-quality study [24] found significant improvements in non-verbal and delayed memory. One study [20] found that both intervention and control groups (consisting of unstructured conversation, questioning and reciting overlearned material) improved significantly on verbal and non-verbal memory. They suggested that these findings may be due to small practice effects. In the remaining studies, no significant changes in measures of learning and memory were found; although 2 of these were rated as being of high quality [22, 26], they all had relatively small sample sizes and may therefore have lacked power to detect an effect.

Orientation. Only 2 studies measured orientation. One [26] trained participants on the orientation items from the MMSE and used the same items as an outcome measure, finding significantly higher scores at both the post-intervention and 3-month follow-ups. Another [23] did not find any statistically significant improvements in

Table 2. Cognitive training studies: contents and format of interventions and control conditions

First author	Contents of cognitive training intervention	Format of intervention	Control group(s)
Beck 1988 [27]	Training in the areas of attention, reading, concentration on detail and remembering (n = 10).	6 weeks, 18 sessions, 30–40 min, 3 sessions per week, individual. Setting: geriatric unit of a Veterans Administration hospital and 4 community nursing homes Delivered by: research assistants	Treatment-as-usual (n = 10).
Bottino 2005 [19]	Orientation, reminiscence, training in use of external memory aids using errorless learning, discussion of interesting topics, face-name association plus activities-of-daily-living training, external social activities and support group for caregivers (n = 6).	20 weeks, 20 sessions, 90 min, 1 session per week, in groups. Setting: not reported Delivered by: not reported	Routine treatment (ChEI only) (n = 7).
Cahn-Weiner 2003 [22]	Memory training programme involving visualisation and categorisation techniques (n = 17).	6 weeks, 6 sessions, 1 session per week, in groups. Setting: clinic Delivered by: clinical neuropsychologist	Placebo. Didactic educational presentations but no memory training. Equivalent format and duration (n = 17).
Davis 2001 [20]	Face-name association and spaced retrieval plus participation in home “attention exercises” directed by caregivers (n = 19).	5 weeks, 5 sessions, 1 h, 1 session per week of individual sessions plus home attention exercises 30 min per session, 6 sessions per week. Setting: clinic and home Delivered by: ‘Examiner’ and caregiver	Placebo. Unstructured conversation, questioning, reciting overlearned material and watching videotapes about general health issues. Equivalent format and duration to individual sessions (n = 18).
De Vreese 1999	Cognitive training aimed at (re)training memory (in particular autobiographical and implicit), language and executive abilities associated with Reality Orientation Therapy, to be repeated at home by the carer (n = 9).	12 weeks, 24 sessions, 45 min, 2 sessions per week, individual sessions with caregiver present. Setting: not reported Delivered by: not reported	ChEI only (n = 9). Placebo medication (n = 9).
Galante 2007 [18]	Computerised exercises targeting memory, attention, language, non-verbal intelligence, visual perception and spatial cognition (n = 7).	4 weeks, 12 sessions, 1 h, 3 sessions per week, individual. Setting: not reported Delivered by: computer	Semi-structured interviews on current affairs and autobiographical history. Equivalent format and duration (n = 4).
Heiss 1993 [23]	Computerised training covering memory, perceptual and motor tasks selected according to level of impairment (n = 18).	24 weeks, 48 sessions, 1 h, 2 sessions per week, individual. Setting: not reported Delivered by: computer	Placebo. Social support (n = 17). Additional intervention groups: cognitive training plus pyritinolol (a vitamin B ₆ analogue, 2×600 mg/day) (n = 17) cognitive training plus phosphatidylserine (a phospholipid, 2×200 mg/day) (n = 18).
Koltai 2001 [21]	Spaced retrieval, face-name association, verbal elaboration, concentration/over repetition, use of external memory aids and ways of coping. Carers joined the last 10–15 min of each session when available (n = 14).	5 weeks, 5 sessions, 1 h, 1 session per week, individual or small groups of 4 (results pooled). Setting: not reported Delivered by: first author	Waiting-list control (n = 8).
Loewenstein 2004 [26]	Face-name association, object recall, functional tasks, orientation to time and place, visuo-motor speed of processing and use of a memory notebook (n = 25).	12–16 weeks, 24 sessions, 45 min, 2 sessions per week, individual. Setting: not reported Delivered by: not reported	Mental Stimulation condition: interactive computer games involving memory, concentration, and problem-solving skills. Equivalent format and duration (n = 19).

Table 2. (continued)

First author	Contents of cognitive training intervention	Format of intervention	Control group(s)
Quayhagen 1995 [24]	Memory, problem-solving and conversation activities (n = 25).	12 weeks, 72 sessions, 1 h, 6 sessions per week, individual. Setting: home Delivered by: caregiver plus weekly sessions with member of research team.	Placebo. Similar activities offered for the same amount of time but designed to encourage passive observation rather than active participation (n = 28). Waiting-list control (n = 25).
Quayhagen 2000 [31]	Memory-provoking, problem-solving and conversational-fluency activities (n = 21).	8 weeks, 40 sessions, 1 h, 5 sessions per week, individual. Setting: participant's home Delivered by: caregiver, plus modelling of the intervention by member of the research team	Waiting-list control (n = 15) Additional intervention groups: dyadic counselling (n = 29) early-stage day care consisting of structured activities including discussions, physical exercise and outings (n = 16) dual supportive seminar (n = 22)

orientation following their cognitive training intervention.

Attention/Working Memory. Seven studies used a digit span test and/or a spatial span test as a measure of attention/working memory. Two [19, 27] found a significant improvement on a digit span task; however, one [27] was rated as low-quality and there were statistically significant differences in baseline characteristics between groups despite randomisation. In the remaining studies, no significant differences were found. One study [20] used the Verbal Series Attention Test [28] as an additional measure of attention/working memory, finding insignificant but positive trends. Another [26] used the Continuous Performance Test (CPT) [29] as a further measure of attention/working memory, with mixed results. Participants in the intervention group showed significant improvements in the time score of the CPT at both the post-intervention and 3-month follow-up. However, the number of commission errors appeared to increase significantly whereas the placebo group achieved a significantly lower number of commission errors at the post-intervention follow-up. It is important to note that they [26] used the CPT as one of the training tasks in their cognitive intervention.

Language. Only 4 studies investigated the impact of cognitive training on language. Three [19, 21, 22] found no significant differences between intervention and control groups on the Boston Naming Test [30]. One [18] did not find any significant changes on a word repetition task. Of note, these were all relatively small studies that may have lacked power to detect an effect.

Executive Function. Verbal fluency tasks were used as outcomes in 8 studies. Only 2 [24, 31] found a significant improvement in verbal fluency relative to the control group. Two [26, 19] used the Trail-Making Test [32], a measure of response inhibition and set-shifting, finding no significant differences. One [29] found a significant change over time on a problem-solving composite score for participants in their cognitive intervention group.

Praxis and Motor Function. Only 3 studies measured praxis as an outcome. One of the highest-quality studies [20] did not find any statistically significant group differences on the finger-tapping test which measures self-directed manual motor speed [33]. One study [21] did not report the outcomes on a measure of constructional praxis which they used as part of the CERAD (Consortium to Establish a Registry for Alzheimer's Disease test battery) [34], suggesting that results were not significant. Another [18] did not find any significant differences on measures of constructional and ideomotor apraxia; however, with

a sample size of just 11, it is hard to draw conclusions from this study.

Visual Perception. A range of tests of visual perception were employed including Benton, Hannay and Varney's [35] Judgement of Line Orientation [22], a cancellation task [18], a fragmented-pictures test [23] and an object-matching task [27]. None of these studies reported any significant findings for tests of visual perception.

Cognitive Stimulation Interventions

Full details of the 7 cognitive stimulation studies can be found in table 3. Studies varied somewhat in terms of the comparison group(s) used, with 1 using 'psychosocial support', 5 using 'treatment-as-usual' or 'no treatment' and 1 using basic stimulation and ChEI medication. Four studies evaluated cognitive stimulation in combination with a stable dose of ChEI [36–39]. Studies varied in terms of length of intervention (range 5–52 weeks; $M = 19.9$, $SD = 16.2$) and number of sessions delivered (range 10–103; $M = 51.7$, $SD = 33.9$). There was some heterogeneity in the mode of delivery, with 4 studies evaluating groups and 3 evaluating individual interventions. Most interventions were delivered by a clinician or member of the research team, but in 1 study the intervention was delivered by computer and in another by family caregivers.

General Cognitive Function. All 7 studies used at least one measure of general cognitive function as an outcome measure and all used the MMSE. Five of these found significant results in the intervention group compared to the controls. The ADAS-Cog was employed as an additional outcome measure in 4 studies, all finding significant improvements [36, 37, 39, 40]. One study [41] measured general cognitive function using the Kingston Dementia Rating Scale [42] and found that both their cognitive-stimulation ('enhanced reality orientation') and 'social interaction' groups showed significant improvements 1 week after intervention, returning to baseline levels at 10 weeks. The treatment-as-usual control group's scores did not change over time. Six out of the 7 studies, including the highest-quality, most methodologically rigorous studies [36, 37, 40] found positive effects on at least one measure of general cognitive functioning.

Learning and Memory. One study [3] found a non-significant trend towards improvement on both a word-list memory task and an 'association' test in their cognitive stimulation group. Another [43] analysed the memory subscale of the ADAS-Cog but found no statistically significant effects. This subscale is, however, based solely on a word-list learning and recall item which may lack ecological validity. The remaining studies of cognitive stim-

ulation interventions did not use detailed measures of learning and memory.

Language. One trial [3] did not analyse the results of the naming section of the CERAD test battery [33] due to a high proportion of ceiling effects. For another trial [39], a subsequent analysis of the significant ADAS-Cog changes [43] showed that, of the three subscales, 'language' was the only one to show significant changes. Within this subscale, 'spoken language' and 'commands' changed significantly.

Executive Function. Only 1 trial was evaluated for this [3]; verbal fluency was measured and no significant group differences were reported.

Praxis. Only 1 trial [3] used a specific measure of praxis. The results could not be analysed due to a ceiling effect. Another study [40] found no significant effects on the praxis subscale of the ADAS-Cog.

Discussion

It is not possible to state with any certainty which cognitive domains show improvements or maintenance of function in people with dementia participating in cognition-focused psychological interventions. In cognitive training research, more attempts have been made to examine changes in objective cognitive measures, rather than solely relying on measures of general cognitive function. Learning and memory, attention/working memory and the initiation aspect of executive function are the most evaluated areas, yet results are inconclusive in all three areas. In terms of other dementia-relevant cognitive domains (praxis, orientation, visual perception, language and other aspects of executive function) more work is needed to determine whether improvement or maintenance of function is feasible. The studies to date have been significantly limited by small sample sizes, with reduced statistical power. It is difficult to ascertain whether the content of the intervention was linked to outcome, as there are so many confounding factors such as mode of delivery, length of intervention and study quality. There were only 2 high-quality studies with significant results [26, 24]; the former described their activities in detail (e.g. face-name association, object recall, functional tasks and orientation) and the latter more broadly (memory, problem-solving and conversation), yet it may be that there was some overlap between these two interventions.

Two large, methodologically rigorous RCTs of cognitive stimulation have been conducted [37, 40], both find-

Table 3. Cognitive stimulation studies: key characteristics and findings

First author	Quality rating: score/5	Number of studies	Diagnosis of Participants	Anti-dementia medication use	Contents of cognitive stimulation	Duration and format of intervention	Control group	Standardised objective cognitive outcome measures ¹	Assessment intervals	Statistically significant findings and trends
Breuil 1994 [3]	2	56	Dementia based on DSM-III criteria	None	Activities such as categorisation and association (n = 29)	5 weeks, 10 sessions, 1 h, 2 sessions per week, groups of 10. Setting: not reported. Delivered by: a doctor and a psychologist	Not described (n = 27)	CERAD test battery ² , picture pair associate test, immediate associate memory and verbal fluency	At baseline, 1 week and 7 weeks.	Significant improvement in MMSE scores (p < 0.01) and non-significant improvement in word-list memory (p = 0.09) and 'association test' (p < 0.10) scores in intervention group relative to control group.
Gerber 1991 [41]	2	24	Probable AD based on DSM-III criteria	Not reported	Enhanced reality orientation including exercises, self-care, food preparation and orientation (n = 8)	10 weeks, 40 sessions, 1 h, 4 sessions per week, in groups. Setting: inpatient Psychiatric Hospital. Delivered by: not reported	Regular hospital care which did not include group activities (n = 8). Social interaction during recreational activities (n = 8)	KDRS	At baseline, 1 week post-intervention and 10 weeks post-intervention	Improvement in intervention and social interaction groups at 1 week post-intervention on the orientation (p < 0.05) and language (p < 0.01) subscales, but returned to baseline levels at 10 weeks. No change in control group.
Olazaran 2004 [36]	3	84	MCI (n = 12), mild AD (n = 48) and moderate AD (n = 24) based on NINCDS-ADRDA criteria	All ChEI treated for at least 1 month before inclusion	Reality orientation, cognitive exercises, social and psychomotor activities plus psychosocial support (n = 44)	1 year, 103 sessions, 3.5 h, 2 sessions per week, groups of 7–10. Setting: non-medical outpatient unit. Delivered by: not reported	Psychosocial support only (n = 40)	ADAS-Cog and MMSE	At baseline, 1, 3, 6 and 12 months	Significant improvement in ADAS-Cog in intervention group at 1 month (p = 0.05). Intervention group maintained MMSE and ADAS-Cog scores at 6 months compared to significant deterioration in control group (p = 0.03 and p = 0.01, respectively).
Onder 2005 [37]	3	156	Probable AD based on NINCDS-ADRDA criteria	All treated with ChEI for at least 3 months before inclusion	Orientation, discussion of topics of general interest, attention, memory and visuospatial exercises (n = 79)	25 weeks, 30 min, 3 sessions per week, individual, informal stimulation throughout the day also encouraged. Setting: participant's Home. Delivered by: caregiver	No treatment (n = 77)	MMSE and ADAS-Cog	At baseline and 25 weeks.	Significant improvement in MMSE and ADAS-Cog scores in intervention group compared to a decline in the control group (p = 0.02 and p = 0.01, respectively).

Table 3. (continued)

First author	Quality rating: score/5	Number of studies	Diagnosis of Participants	Anti-dementia medication use	Contents of cognitive stimulation intervention	Duration and format of intervention	Control group	Standardised objective cognitive outcome measures ¹	Assessment intervals	Statistically significant findings and trends
Onor 2007 [38] Italy	2	16	AD based on DSM-IV criteria	All ChEI treated for at least 6 months before inclusion	Reality orientation, occupational therapy and reminiscence therapy plus psychoeducation for caregivers (n = 8)	4 months, 60 min, 3 sessions per week. Setting: not reported. Delivered by: psychologist	No treatment (n = 8)	MMSE and MODA	At baseline, 2 and 4 months (MMSE). At baseline and, 4 months (MODA)	None.
Spector 2003 [40] 2010 [43] UK	3	201	Dementia based on DSM-IV criteria	None	Themed sessions incorporating orientation, reminiscence, multisensory stimulation and information processing (n = 115)	7 weeks, 14 sessions, 45 min, 2 sessions per week, groups of 5-8. Setting: day centres and residential homes. Delivered by: researcher	Usual activities (n = 86)	MMSE and ADAS-Cog	At baseline and post-intervention	Significant improvement in MMSE (p = 0.044) and ADAS-Cog (p = 0.014) scores in intervention group compared to control group. Significant improvement on language subscale of ADAS-Cog (p = 0.01)
Tarraga 2006 [39] Spain	1	46	Probable AD	All ChEI treated for at least 12 months before inclusion	IMIS of cognitive stimulation in addition to an IPP (n = 15)	24 weeks, 20 min of IMIS, 3 sessions per week plus 8 h of daily IPP. Setting: day centre. Delivered by: computer	IPP only (n = 16). ChEI only (n = 12)	ADAS-Cog, MMSE, SKT, (BNT, verbal fluency and RBMT story recall subtest - not administered to ChEI group due to 'manager' limitations)	At baseline, 12 and 24 weeks	At 12 weeks, intervention group and IPP group superior to ChEI group on ADAS-Cog (p < 0.05). At 24 weeks intervention group superior to ChEI group on ADAS-Cog (p < 0.05) and intervention and IPP groups superior to ChEI group on MMSE (p < 0.05). No change in SKT across 3 groups. Other measures not analysed.

AD = Alzheimer's disease; BNT = Boston Naming Test [30]; BVM-T-R = Brief Visual Spatial Memory test - revised [46]; MCI = mild cognitive impairment; CERAD = Consortium to Establish a Registry for Alzheimer's Disease [33]; COWA = Controlled Oral Word Association [47]; CT = cognitive training; DRS = The Mattis Dementia Rating Scale [25]; EMQ = Everyday Memory Questionnaire [48]; FOME = Full Object Memory Evaluation [49]; GCS = Geriatric Coping Schedule [50]; HVL-T-R = Hopkins Verbal Learning test - revised [51]; IMIS = interactive multimedia internet-based system; IPP = integrated psychostimulation program; JOLO = Judgement of Line Orientation [35]; KDRS = Kingston Dementia Rating Scale [41]; MODA = Milan Overall Dementia Assessment [52]; RMBT = Rivermead Behavioural Memory test [53]; SKT = Syndrom Kurztest [54]; TMT = Trail-Making test [32]; VSAT = Verbal Series Attention Test [28]; WAIS-R/WAIS-III = Wechsler Adult Intelligence Scale - revised/3rd edition [55, 56]; WMS-R/WMS-III = Wechsler Memory Scale - revised/3rd edition [57, 58].

ing significant improvements in general cognitive function. This finding has been supported by the smaller studies. There is robust evidence for improved cognitive functioning for people with dementia using cognitive stimulation, confirmed by the recent Cochrane review [9]. Only 1 study provided results for more detailed neuropsychological outcome measures [3] and another attempted to examine the subscales of the ADAS-Cog [43]. Results suggest that language and possibly memory may be the cognitive domains most amenable to change following cognitive stimulation.

Limitations

Neuropsychological tests are not necessarily indicative of the effects that these interventions may have on cognitive performance in everyday life, and the ecological validity of neuropsychological tests is typically moderate [44]. Moreover, it is not always evident how a change in a measure will translate practically for an individual. In addition, assumptions about the quality of the studies were based solely on the information provided and methodological details were often omitted from the report.

Further Research

Larger scale, trials of quality are needed to further investigate the neuropsychological outcomes of cognitive training and cognitive stimulation, in order to increase the understanding of which aspects of cognition are more amenable to change. It has been suggested [7] that the aim

of cognitive rehabilitation is to improve function and/or wellbeing, rather than to improve performance on cognitive tests per se. This may imply that functional outcomes reflecting individualised rehabilitation goals may be more suitable than further neuropsychological investigations. Future trials should use more sensitive neuropsychological tests. Participation in stimulating activities may lead to enhanced activation of neurons in the brain. Therefore, improved performance in cognitive function could reflect enhanced functioning of the existing neuronal networks typically used to perform these tasks or enhanced recruitment of alternative neuronal networks [5]. Functional brain imaging studies are required to further explore these hypotheses. Another recommended area for future research is the development of a more suitable and comprehensive neuropsychological test battery for people with mild to moderate dementia. There are weaknesses in existing batteries; the CERAD [34], for example, may be prone to floor and ceiling effects [3].

Conclusion

This review does not specifically indicate which aspects of cognitive performance are most likely to improve following cognitive stimulation or cognitive training. Nonetheless, there is strong evidence to support the widespread clinical use of cognitive stimulation, and this is advocated in UK government guidelines [45]. Research investigating the optimum implementation of cognitive stimulation would be beneficial, as the content, frequency, duration, format, delivery mode and number of sessions of the interventions in this review varied considerably. It would be helpful to know which strategies and activities are the most important, in order to implement these in clinical practice.

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