Cognitive rehabilitation for people with early-stage Alzheimer’s disease: preliminary results from a randomised controlled trial of an individual, goal-oriented approach

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Cognition as a focus of intervention in early-stage Alzheimer’s

• Cognitive abilities are a crucial component of human functioning in everyday life, affecting a vast range of activities and interactions as well as the nature of subjective experience itself.

• Cognitive change is a central, defining feature of Alzheimer’s (AD).

• There is evidence for cognitive plasticity, demonstrated through retained abilities, new learning, and behaviour change in people with early-stage AD (Fernandez-Ballesteros et al., 2003; Clare, 2007).

• Changes in patterns of brain activation in response to memory tasks may reflect compensatory recruitment of additional neural resources in AD (Sperling et al, 2003; Grady et al, 2003; Pariente et al, 2005).

• This suggests cognition-focused intervention should be beneficial. However, cognitive training involving structured practice in cognitive tasks shows few direct benefits for people with AD and is unlikely to produce improvements in everyday functioning.
An innovative approach to intervention: cognitive rehabilitation

• Cognitive rehabilitation (CR) interventions aim to tackle directly those difficulties considered most relevant by the person with dementia and his or her family members or supporters. Goals for rehabilitation are selected collaboratively, and interventions designed to tackle these goals are devised and implemented by the therapist in the person’s everyday setting (Clare, 2007). CR is not exclusively ‘cognitive’ – an alternative term is ‘rehabilitation of individuals with cognitive impairments’ (Sohlberg & Mateer, 2001).

• A Cochrane systematic review found no RCTs of CR, but promising evidence from single case experimental designs and small group studies suggested that significant improvements in targeted areas could be achieved for some participants (Clare et al 2003/2007). The need for RCTs was noted.

• Trial design and outcome evaluation in rehabilitation presents challenges because goals are typically highly individualised, and therefore innovative approaches to measurement are needed.
The focus of cognitive rehabilitation in early-stage dementia

Onset/progression of dementia

‘Impairment’
Cognitive & related changes

‘Disability’
Limitations on engaging in activity

‘Handicap’
Restrictions on social participation

Personal and social context

WHO 1980, 1998

‘Impairment’
‘Disability’
‘Handicap’
Applying cognitive rehabilitation in early-stage AD

- selecting personal rehabilitation goals – relevant to daily life – and devising interventions to help in achieving these, drawing on evidence-based rehabilitation methods, with the aim of improving performance and enhancing self-efficacy and coping.

- developing interventions to address goals that adopt compensatory and/or restorative approaches – e.g. introducing or developing the use of memory aids and strategies, maintaining or relearning practical skills, and making the most of remaining memory ability.

- cognitive difficulties may be addressed through identifying effective methods of taking in and recalling important information, and finding ways of improving attention and concentration.

- supporting emotional well-being, for example through managing mood and dealing with anxiety.

- involving a family member or other supporter where available.

Clare, 2007
RCT of cognitive rehabilitation: Hypotheses

Cognitive rehabilitation will improve performance and satisfaction with performance for selected goals, compared to conditions that do not directly address individual goals.

These improvements will be reflected in changes in brain activation in participants receiving cognitive rehabilitation, which are not seen in participants in other conditions.

Based on available evidence, improvements on neuropsychological tests are not anticipated.
RCT of cognitive rehabilitation: trial protocol

Recruitment: Memory Clinic attenders, diagnosis of AD, MMSE 18 or above, stabilised on AChEI medication

Randomisation

Baseline assessment

8 weeks: Medication only (NT)

8 weeks: Relaxation therapy + medication (RT)

8 weeks: Cog rehab + medication (CR)

Post-intervention assessment

Follow up: 6 months later

Oct 2005 – March 2009
Funded by Alzheimer’s Society, UK
Outcome measures for participants with dementia

1. Primary outcome
   Goal performance and satisfaction – Canadian Occupational Performance Measure (COPM)*

2. Secondary outcomes
   Quality of life
   Mood
   Memory
   Memory self-appraisal
   Verbal fluency
   Attention
   Quality of Life in AD (QoL-AD)
   Hospital Anxiety and Depression Scale (HADS)
   Rivermead Behavioural Memory Test (RBMT-II)
   Memory Awareness Rating Scale (MARS)**
   Controlled Oral Word Association
   Test of Everyday Attention, Map Search and Elevator Counting with Distraction sub-tests

3. Neuroimaging
   Brain activation while performing an associative encoding and recognition task during fMRI scanning*

* Initial and post-intervention only; ** initial and six month follow-up only
Outcome measures for carers

Post-intervention and six month follow-up

Quality of life: WHOQoL-BREF

Mood: General Health Questionnaire (GHQ-12)
Hospital Anxiety and Depression Scale (HADS)

Strain: Relatives’ Stress Scale
The cognitive rehabilitation intervention

8-session structured programme combining work on individual goals with supporting components

Central feature
• Intervention to address an individual therapy goal taken from COPM initial assessment
• Some participants also worked on a second goal identified during the sessions

Supporting elements
• Review of practical strategies and intervention to improve on these
• Strategies for learning and retaining information
• Practice with maintaining attention and concentration
• Strategies for managing anxiety and stress

Caregiver was involved where available and willing
Practice was undertaken in between sessions
RCT of cognitive rehabilitation: final status

Approached n= 202
Expressed interest and appeared potentially eligible n= 84
Decided not to participate n = 8

Initial assessment n=76
Ineligible n = 5, discontinued n= 2

Randomised n=69

CR
Allocated n=23
Completed n=21
Discontinued n=2
Post-intervention assessment n=21

RT
Allocated n=24
Completed n=23
Discontinued n=1
Post-intervention assessment n=23

NT
Allocated n=22
Completed n=21
Discontinued n=1
Post-intervention assessment n=21
## Sample characteristics

<table>
<thead>
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<th>CR n=23</th>
<th>RT n=24</th>
<th>NT n=22</th>
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<tr>
<td>Female</td>
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<td>13</td>
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<tr>
<td>Male</td>
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<td><strong>Diagnosis</strong></td>
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<tr>
<td>AD</td>
<td>17</td>
<td>21</td>
<td>18</td>
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<tr>
<td>Mixed AD and vascular</td>
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<td>3</td>
<td>4</td>
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<tr>
<td><strong>Medication</strong></td>
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<tr>
<td>Donepezil</td>
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<td>16</td>
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<td>Rivastigmine</td>
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<td>3</td>
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<tr>
<td>Galantamine</td>
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### Participant characteristics

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<th>RT</th>
<th>NT</th>
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<tbody>
<tr>
<td>n</td>
<td>Mean (sd), range</td>
<td>Mean (sd), range</td>
<td>Mean (sd), range</td>
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<tr>
<td><strong>Age</strong></td>
<td>23</td>
<td>76.35 (6.24) 64-89</td>
<td>24</td>
</tr>
<tr>
<td><strong>Years of education</strong></td>
<td>23</td>
<td>10.83 (1.92) 9-17</td>
<td>24</td>
</tr>
<tr>
<td><strong>MMSE score/30</strong></td>
<td>23</td>
<td>23.3 (3.15) 18-27</td>
<td>24</td>
</tr>
<tr>
<td><strong>IADL self-rating</strong></td>
<td>21</td>
<td>15.86 (6.17) 8-28</td>
<td>24</td>
</tr>
<tr>
<td><strong>PSMS self-rating</strong></td>
<td>21</td>
<td>7.1 (1.76) 6-11</td>
<td>23</td>
</tr>
<tr>
<td><strong>Mths current medication</strong></td>
<td>23</td>
<td>17.57 (15.5) 1-60</td>
<td>23</td>
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</table>
What goals did participants identify?

Sixty-six participants identified a total of 213 goals (an average of 3.15 each, range 1 - 5) in the following domains:

• Memory (102) e.g.  
  remembering where they had put things  
  remembering things they have been told  
  reducing repetitive questioning

• Performing practical skills and activities (42) e.g.  
  resuming or increasing activities  
  learning a new skill

• Concentration (21)
• Naming and word finding (21)
• Organisation (11)
• Social interaction (6)
• Visual recognition (4)
• Orientation (4)
• General well-being (2)

*CR participants worked on one or two goals during the intervention.*
Primary outcome: goal performance and satisfaction

COPM performance: Significant effect of intervention F(2,60) 8.147 p.001 CR>RT=NT
Effect sizes CR vs. RT 1.175 (0.526-1.823); CR vs. NT 0.908 (0.248-1.568)

COPM satisfaction: Significant effect of intervention F(2,60) 7.88 p.001 CR>RT=NT
Effect sizes CR vs. RT 1.222 (0.569-1.874); CR vs. NT 0.865 (0.208-1.521)
Secondary outcomes: summary of significant differences

Participants with dementia

Post-intervention:
Anxiety. Significant decrease in anxiety (HADS)  :  $F_{2,60} = 4.07, \ p<.05$;
NT showed more reduction in anxiety than RT ($1.246 \pm 1.122$)

Six-month follow up:
Memory self-assessment. Memory Performance Scale:  $F_{2,47}=4.6, \ p<.05$
CR rated their memory performance better than NT ($6.228 \pm 5.174$)

Carers

Post intervention:
Quality of Life. WHOQoL-BREF social relationships:  $F_{2,21}=10.76, \ p<.01$
CR and RT carers rated their QoL in this area better than NT carers
(CR > NT $1.048 \pm 1.195$; RT > NT $2.2 \pm 1.269$)
fMRI results

In total 19 participants were scanned. They scored significantly higher on MMSE than the non-scanned participants (24.79 vs. 22.22, $t_{66} = 3.402$, $p < .05$)

The scanned participants were 7 from CR and 12 from the other two conditions forming a combined Control group. The CR group had significantly higher COPM performance and satisfaction scores post-intervention.

Significant between-group differences were observed post-intervention, although the two groups did not differ significantly in task performance, with the CR group showing greater activation in all cases:
- Right fusiform face area – CR > Control, during encoding and retrieval
- Right temporo-parietal junction – CR > Control, during encoding and retrieval
- Right medial prefrontal cortex – CR > Control, during encoding and retrieval
- Right parahippocampal area – CR > Control, during retrieval
Neural activations in right fusiform face area (FFA) during encoding and retrieval

Bar charts in upper and lower left panels show the percentage signal change in FFA for the CR and Control groups during pretest and posttest.

Right panels show the event-related average waveforms of BOLD signals during encoding and retrieval. Participants in the CR group showed an increase in BOLD waveform after intervention during both encoding and retrieval. Significant Group (CR vs. Control) x Time (Pretest vs. Posttest) interaction effects were observed for both encoding and retrieval, \( F(1, 16)=21.34, p<0.001; F(1, 16)=11.60, p<0.005 \), respectively.
### Summary of therapy goals addressed in the CR group (n= 21)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory (9)</td>
<td>Remember what happened yesterday</td>
</tr>
<tr>
<td></td>
<td>Reduce repetitive questioning</td>
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<tr>
<td>Skills and activities (6)</td>
<td>Crochet a bolero following a written pattern</td>
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<td></td>
<td>Handling money – pay with correct amount in coins</td>
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<tr>
<td>Concentration (4)</td>
<td>Remember what was doing after being distracted</td>
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<tr>
<td>Learning a new skill (2)</td>
<td>Learn to use a mobile phone</td>
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<tr>
<td></td>
<td>Learn to use the computer to email a friend</td>
</tr>
<tr>
<td>Organisation (2)</td>
<td>Improve use of calendar to remember non-routine events</td>
</tr>
<tr>
<td>Naming (2)</td>
<td>Remember names of people at keep fit class</td>
</tr>
<tr>
<td>Memory/organisation/naming (1)</td>
<td>Know who will be visiting – remember name and link with calendar entry</td>
</tr>
<tr>
<td>Well-being (1)</td>
<td>Manage day-time sleepiness</td>
</tr>
</tbody>
</table>
Goal achievement ratings:
12 goals (46%) fully achieved
13 goals (50%) partially achieved
1 goal (4%) not achieved

CR: within-group improvements in ratings for the specific goals addressed in therapy (n=21)
Future developments: issues to consider

Brief intervention:
- Limited number of goals could be addressed
- Limited time to show improvement on some of the specific goals

Maintenance of gains:
- Need to identify how to assess longer term maintenance
- Are the goal performance and satisfaction measures valid over a longer follow-up period?

What other measures may be appropriate:
- Mood and QoL were not sensitive to change in the participants
- What else might we realistically expect to be targeting?

Additional questions still to be addressed:
- What factors predict whether someone will benefit?
- How can this approach best assist caregivers?
- Can neuroimaging data help us to target rehabilitation efforts more effectively?
Conclusions

• Cognitive rehabilitation appears to offer some benefits for people with early-stage AD and represents one possible treatment option.

• Collaborative intervention addressing individually-relevant goals can enhance aspects of everyday functioning and satisfaction with performance.

• Assessing goal performance and satisfaction provides a sensitive and specific measure of change.

• It appears that improvements in performance may be mirrored in alterations in brain activation, although these findings are exploratory.

• The findings offer valuable information about ways of improving support for people with early-stage AD, which will be followed up in future research.
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Thank you for your attention!

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