The need for randomised treatment studies in neglect research

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Abstract. Purpose: The aim was to review the methodological quality of trials to evaluate rehabilitation for spatial neglect and to determine the overall effectiveness of interventions.

Methods: A systematic literature review and meta-analysis were conducted of trials completed by 2005. Trials identified were independently assessed for methodological quality by two reviewers. Outcomes were analysed as the standardised mean difference and 95\% confidence intervals with random effects models.

Results: 25 trials of neglect rehabilitation were identified, 12 randomised controlled trials and 13 controlled clinical trials. The methodological quality was generally poor with only 4 trials achieving an A rating, i.e. low risk of selection bias. The immediate effect of cognitive rehabilitation on disability was small, 0.26 \([-0.16, 0.67]\) and neither this nor the persisting effect 0.61 \([-0.42, 1.63]\) was statistically significant. The most frequently used standardised neglect test (number of single letters correctly cancelled) favoured the experimental group 0.58 \([0.10, 1.05]\) but was not significant. When cancellation errors were measured there was a small immediate effect favouring the experimental group, of borderline statistical significance, \(-0.65 \([-1.28, -0.01]\) \(p = 0.05\), and a significant persisting effect \(-0.76 \([-1.39, -0.13]\) \(p = 0.02\). Cognitive rehabilitation also significantly improved immediate \((p = 0.01)\) and persisting \((p = 0.02)\) line bisection performance but these findings are based on only four and one study respectively.

Conclusions: The quality of trials identified was poor. Analysis of randomised controlled trials showed some evidence of an effect of intervention on measures of impairment. There was no evidence to support the effects of intervention on measures of disability. Further trials must use methods that reduce bias, have adequate statistical power, and include valid disability outcome measures.

Keywords: Neglect, inattention, meta-analysis, review

1. Introduction

The rehabilitation of spatial neglect is well established and there are examples of effective interventions with individuals\([4,15,19,20]\). However for a treatment to be widely adopted in clinical practice it needs to be shown to generalise from individual cases to the target clinical population. Because no two people are the same and conditions such as neglect are so heterogeneous single case designs, useful for proof of concept, cannot provide the evidence of generalisation that group studies provide. Rehabilitation staff rely on evidence derived from randomised controlled trials (RCT). In an RCT every individual has an equal chance of being allocated to either group, usually but not necessarily a therapy group and a control group. The random allocation process increases the likelihood that the groups
are balanced at baseline. Properly conducted RCTs are the only type of study that can determine whether improvements seen after rehabilitation can be attributed to the rehabilitation rather than to other strong contenders, such as spontaneous recovery or placebo effects. Well conducted RCTs also eliminate the false positive findings that can result from selection bias, causing an imbalance between groups at baseline.

Despite these advantages, there remains a dearth of methodologically sound RCTs of the rehabilitation of spatial neglect. A less robust alternative is to consider controlled clinical trials (CCT) in which two groups receiving different interventions are compared but with no randomisation to groups. In 2002 we published a systematic review of the evidence from RCTs and CCTs [3]. The aim of the present study was to update this review to determine the overall effectiveness of cognitive rehabilitation strategies for neglect.

The methodological quality of the trials determines the conclusions we can draw and the confidence we can have in their findings. There are now published guidelines to enable researchers to design studies in a way which minimises bias and maximises the robustness of the findings [12,16]. The key standards to be achieved relate to randomisation, allocation concealment, ‘blinded’ assessment of outcomes and standardised, reliable, valid measures of outcome. Randomisation should be done using a method that is free from bias and open to verification by an independent observer. While coin tossing is random, it cannot subsequently be verified. The preferred method is a computer generated random allocation sequence held by an independent randomisation centre and a study monitoring body which can check on adherence to the randomisation procedure. Many clinical trials units provide this service, the allocation of patients is not in the control of the researchers who know the patients, and therefore minimises the chance of selection bias. Randomisation should be independent of the people doing recruitment, providing intervention or assessing outcome.

Once patients are allocated to groups, no changes should be made to the allocation. All participants should be followed up, independently of whether they complete the treatment, for an intention to treat analysis [12]. The only exception to follow up should be patients who withdraw consent, but any loss to follow-up should be clear from the study description. A CONSORT diagram [16] is a useful way of summarising these events and is required for publication in several high quality journals. Excluding participants who have further strokes for example renders the trial unrepresentative of clinical practice, as stroke patients will have further strokes. Since adherence to treatment is likely to be a key factor in treatment effectiveness, excluding patients who find treatment unacceptable gives an unrealistic picture of clinical effectiveness. Those dropping out are likely to be a highly selective subgroup i.e. those for whom the treatment is not proving helpful. Untoward chance events are likely to affect participants in both intervention and control groups and therefore if the sample size is adequate such events should be balanced out between the groups.

Outcomes should be assessed by an observer who is unaware of the group allocation of patients. In rehabilitation studies this may be difficult to achieve but guidelines are provided [29]. Most rehabilitation studies can only be conducted single blind, with outcome assessors unaware of the intervention delivered. It is rarely possible to conceal the intervention from the patient or from the person providing the intervention. Outcome measures need to be standardised with established reliability and validity. Developing measures specifically for a study is not considered good practice unless there is no acceptable published measure available and adequate development work has been carried out.

The effectiveness of rehabilitation for spatial neglect is an important issue as many patients have neglect following a stroke. These people tend to progress less well with rehabilitation and it affects long term outcome in independence in activities of daily living and quality of life [15,19,20]. These narrative reviews have summarised the studies on a range of rehabilitation strategies. The strategies can broadly be divided into two major approaches, ‘top down’, in which patients are being trained to compensate for the spatial neglect, and ‘bottom up’ strategies in which the underlying controlling factors responsible for the occurrence of spatial neglect are modified. The ‘top down’ strategies are characterised by scanning training programmes, in which patients were trained to scan visual space to compensate for their failure to attend to one side [10,34]. Scanning training programmes have been shown to reduce impairment [3] but few studies assessed whether treatment effects generalised to daily life. Poor generalisation may be resolved by training patients on daily life tasks [33] but despite the intuitive appeal of targeting real activities, this approach may be limited due to the range of activities requiring training [15]. One major limitation is that it requires patients to be aware of their deficit and to voluntarily maintain orientation of attention to the neglected side.

‘Bottom up’ strategies are characterised by sensory stimulation, to re-map the representation of space.
These have included optokinetic stimulation [22], neck muscle vibration [28] and transcutaneous electrodermal stimulation [27]. Other techniques which involve the manipulation of visual input are eye patching [2], hemi-spatial goggles [38], wearing prisms [26] or prism adaptation training [9,25]. Although patients have benefited on measures of impairment, the effectiveness of the techniques seems to vary [15] and improvement in functional outcomes have not been demonstrated [26]. The advantage of prism adaptation and hemi-spatial goggles is that they are non-invasive, require minimum supervision and do not require the voluntary orientation of attention to the neglected side.

Research has demonstrated that techniques, based on both ‘bottom up’ and ‘top down’ strategies, seem to reduce neglect in treated patients as compared with controls. Effects seem to be small and of short duration. However given that many of the trials contain very small samples it is possible that treatment effects are being missed. A Cochrane review and meta-analysis of trials [3] showed evidence for the effectiveness of treatments on impairment measures. However at that time there were too few studies to determine the effects on functional abilities or for examining long term outcomes. Since then the number of trials has increased. The present review was conducted in conjunction with an update of the Cochrane review. For the latter, which will shortly be published online (www.thecochranelibrary.com) we decided to reduce the risk of selection bias by only including RCTs and excluding the previously included CCTs. For the purposes of the present paper we aimed to examine the effects of intervention on functional outcomes and to assess persisting effects of intervention.

2. Method

We sought all controlled trials in which cognitive rehabilitation was compared to a control treatment for spatial neglect following stroke. Cognitive rehabilitation was broadly defined to include therapy activities designed to directly reduce the level of cognitive deficits or the resulting disability. Drug treatments were not included. Outcomes were classified according to whether they assessed impairment or activity and participation. Standardised measures of impairment included target cancellation, line bisection and figure copying. Outcomes on measures of activity and participation included measures of independence in activities of daily living (Barthel Index, Functional Independence Measure) and questionnaire measures of the effects of neglect on daily life [1,31,39]. The length of follow up to examine persisting effects after the end of the rehabilitation was also considered.

This review was based on the search strategy developed for the Cochrane Stroke Group (www.dcn.ed.ac.uk/csrg). Their specialised trials register was searched by the Review Group Coordinator. In addition, the reviewers searched electronic databases, the National Research Register (July 2005), screened reference lists and used SCISEARCH of the three citation index databases, Science Citation Index (SCI), Social Sciences Citation Index (SSCI) and Arts and Humanities Citation Index (A&HCI) for citation tracking of relevant included studies. The search terms were those of the Cochrane review [3].

Two reviewers independently selected trials using four inclusion criteria (types of trials, participants, interventions and outcome measures) and independently assessed the methodological quality. Differences were resolved by discussion. Study characteristics and outcomes were abstracted. Where these data were not available or unclear from the reports then this was sought and/or confirmed by correspondence with the first author of the publication. Where a crossover design was used [18,28] only data from the first treatment period were considered. Trials in which the same patients were included were only entered once.

All trials identified were reviewed on the extent they met the criteria for high quality research trials [12,16] and classified into categories, listed below, according to the methodological quality. These were based on guidelines for Cochrane reviews [12].

A RCT with concealment of allocation
B/C RCT with unclear (B) or inadequate (C) concealment of allocation

The results from the RCTs were analysed to compare a rehabilitation approach with any other control. Outcomes were treated as continuous and mean and standard deviation data were requested or calculated. Outcomes were analysed as the standardised mean difference and 95% confidence intervals. Random effects models were used.

3. Results

25 trials of neglect rehabilitation were identified, 12 RCTs [5–8,13,23,24,26,27,34,35,38] and 13 CCTs [2,
Table 1
Methodological characteristics of studies identified

<table>
<thead>
<tr>
<th>Trial</th>
<th>Main type of intervention</th>
<th>Rand</th>
<th>Conc</th>
<th>Indep</th>
<th>Outcome Impairment</th>
<th>Outcome Participation</th>
<th>Blind</th>
<th>n</th>
<th>Follow Up</th>
<th>Category</th>
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<tbody>
<tr>
<td>7</td>
<td>Scanning and cueing</td>
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<td>42</td>
<td>X</td>
<td>A</td>
</tr>
<tr>
<td>13</td>
<td>Limb activation/motor cueing</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
<td>50</td>
<td>X</td>
<td>A</td>
</tr>
<tr>
<td>23</td>
<td>Computerised scanning and feedback</td>
<td>√</td>
<td>√</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>30</td>
<td>6 m</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Limb activation</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>36</td>
<td>18–24 m</td>
<td>A</td>
<td></td>
</tr>
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<td>5</td>
<td>Scanning and oral reading</td>
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<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>4</td>
<td>X</td>
<td>B/C</td>
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<td>6</td>
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<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>12</td>
<td>6 w</td>
<td>B/C</td>
<td></td>
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<tr>
<td>8</td>
<td>Feedback of eye movements</td>
<td>√</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>√</td>
<td>18</td>
<td>8 w</td>
<td>B/C</td>
<td></td>
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<tr>
<td>26</td>
<td>Prisms</td>
<td>√</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>√</td>
<td>39</td>
<td>X</td>
<td>B/C</td>
<td></td>
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<td>Scanning with cueing</td>
<td>√</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>√</td>
<td>20</td>
<td>X</td>
<td>B/C</td>
<td></td>
</tr>
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<td>34</td>
<td>Scanning training</td>
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<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>25</td>
<td>X</td>
<td>B/C</td>
<td></td>
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<td>35</td>
<td>Head movement, scanning and feedback</td>
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<td>X</td>
<td>X</td>
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<td>22</td>
<td>2 m</td>
<td>B/C</td>
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<tr>
<td>38</td>
<td>Hemi-blinding goggles</td>
<td>√</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>8</td>
<td>X</td>
<td>B/C</td>
<td></td>
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<tr>
<td>2</td>
<td>Eye patching</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>√</td>
<td>15</td>
<td>3 m</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Scanning</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>√</td>
<td>23</td>
<td>X</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Optokinetic stimulation</td>
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<td>X</td>
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<td>22</td>
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<td>Prism adaptation</td>
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<td>X</td>
<td>√</td>
<td>√</td>
<td>13</td>
<td>5 w</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Perceptual remediation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>77</td>
<td>4 m</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Rod lifting</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>√</td>
<td>14</td>
<td>1 m</td>
<td>E</td>
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</tr>
<tr>
<td>14</td>
<td>Bed orientation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>20</td>
<td>X</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Scanning</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>31</td>
<td>X</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Prisms</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>12</td>
<td>2 h</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>Neck vibration</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>20</td>
<td>2 m</td>
<td>E</td>
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<tr>
<td>30</td>
<td>Video feedback</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>14</td>
<td>3 h</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>Computerised tracking and obstacle course</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>40</td>
<td>X</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>Scanning and spatial assembly</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>√</td>
<td>X</td>
<td>18</td>
<td>1 w</td>
<td>E</td>
<td></td>
</tr>
</tbody>
</table>

Rand – Randomised Con – Concealed allocation Indep- independent person conducting randomisation.
√ reported X not reported/not clear h hours, w weeks, m months.
A RCT with concealment of allocation and ‘blind’ assessment of outcome.
B/C RCT with unclear (B) or inadequate (C) concealment of allocation, and unclear or no ‘blind’ assessment of outcome.
D CCT with ‘blind’ assessment of outcome.
E CCT with unclear or no ‘blind’ assessment of outcome.

9–11,14,17,18,22,25,28,30,33,37]. Two trials included a mixture of randomised and non-randomised patients [28,38]. In one case [38] the authors provided the randomised data so that those cases could be analysed with the other RCTs. Trials are summarised in Table 1.

The method of randomisation was rarely specified in sufficient detail. Of the 12 RCTs, six [7,8,13,23,24,38] described the randomisation process and four [7,13,23,24] achieved adequate allocation concealment (category A). One attempted concealment [8] but this was not considered adequate and seven were judged unclear or inadequate [5,6,26,27,34,35,38]. In the non-randomised trials allocation was by date of admission [11,17,33], alternate [2,22], consecutive batches [25,30], by ward or bed [9,10,14,18], not specified [37] or modified [28]. Few studies adequately described how, or even whether, they had attempted to conceal allocation.

Blinded assessment of outcome was reported in 6 of the 12 RCT’s [7,8,13,24,27,38] and 3 of 13 CCT’s [2,18,22]. The remainder of the trials did not report who conducted the assessments and whether the assessors were blinded or not. Most (21 out of 25) studies measured outcome on impairment measures of neglect, such as cancellation, line bisection and text reading. Several recent studies [5,8,9,11,23,24] used the Behavioural Inattention Test [36], which was analysed either as a total score, as a summary of the behavioural subtests or as individual subtests. Three used questionnaire measures [11,22,28] of the consequences of neglect in daily life. Others (10 out of 25) used generic measures of independence in activities of daily living, such as the Barthel Index [7,13,14,22,27], Frenchay Activities Index [23] and Functional Independence Measure [35].

Outcomes were usually assessed at the end of treatment to determine whether there has been an effect of the intervention but only 5 RCTs and 8 CCTs provided a longer term follow up to determine whether any treatment effects persisted beyond the end of the intervention. Few trials reported losses to follow-up. All category A trials provided this information but for others it was not clear whether no losses to follow-up had occurred or whether researchers excluded those who
failed to complete follow-up. To reduce selection bias outcomes were only analysed for the 306 participants from the 12 RCTs. Six studies reported a measure of disability immediately after the end of rehabilitation on discharge, six with the Barthel Index [7,13,24,26,27] and one with the Functional Independence Measure [25]. One study used the Frenchay Activities Index [23] but the data were not available for this review. Results are shown in Fig. 1.

The overall effect for the six studies (206 participants) measuring immediate effect on disability was small, with a wide confidence interval that included zero 0.26 [−0.16, 0.67] \( p = 0.23 \) and was not statistically significant. Results are shown in Fig. 1. The persistence of effects on disability over time was only assessed in two studies [24,35]. There was no overall evidence for a persisting effect on ADL functioning from these two studies 0.61 [−0.42, 1.63] \( p = 0.24 \).

The number of targets correctly cancelled was measured using four types of targets single letter, double letter, line, and shape. Outcomes for only one of these targets significantly favoured the experimental group: double letter cancellation 1.8 [0.85, 2.76] \( p = 0.0002 \) (one B/C rated study [34]). Four studies with 103 participants used the number of errors cancelling targets [6,23,26,36] and showed a small effect favouring the experimental group, which was of borderline statistical significance, −0.65 [−1.28, −0.01] \( p = 0.05 \). Results are shown in Fig. 2. Only one [23] was A rated. Four studies reporting line bisection performance [26,27,36,38] suggested a favourable outcome for the experimental group −0.84 [−1.36, −0.33] \( p = 0.001 \). However, none of these studies were A rated. Results are shown in Fig. 3. There was no evidence \( (p = 0.35) \) of an overall effect on the three studies using the BIT behavioural subtest summary score [5,8,23]. Therefore, there was evidence that cognitive rehabilitation improved immediate performance on standardised tests of neglect although this varied depending on the test used.

Outcome favoured the experimental group on one of the four cancellation measures and line bisection. There was no evidence in favour of either group on single letter, line or shape cancellation targets or the BIT behavioural subtest score.

Fig. 1. Short-term effects of cognitive rehabilitation on independence in activities of daily living.
N.B. Lincoln and A. Bowen / The need for randomised treatment studies in neglect research

Review: Cognitive rehabilitation for spatial neglect following stroke - 2005 update temp title. (Version 06)
Comparison: 01 Cognitive rehabilitation versus any control: immediate effects
Outcome: 03 Cancellation - numbers of errors

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Experimental</th>
<th>Control</th>
<th>SMD (random) 95% CI</th>
<th>Weight %</th>
<th>SMD (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gottam 1987</td>
<td>6 28.50 (28.20)</td>
<td>6 34.00 (10.80)</td>
<td>18.47 -0.24 [-1.38, 0.90]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robertson 1990</td>
<td>17 43.49 (30.40)</td>
<td>13 45.20 (28.30)</td>
<td>28.66 5.01 [-0.72, 0.73]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rossi 1990</td>
<td>18 2.40 (4.24)</td>
<td>21 9.80 (9.16)</td>
<td>30.20 -0.99 [-1.66, -0.32]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wiart 1997</td>
<td>11 4.00 (4.00)</td>
<td>11 12.00 (7.00)</td>
<td>22.66 -1.35 [-2.29, -0.41]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>52</td>
<td>51</td>
<td>100.00 -0.65 [-1.28, -0.01]</td>
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</tr>
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</table>

Test for heterogeneity: Chi²= 6.78, df = 3 (P = 0.08), I²= 55.7%
Test for overall effect: Z = 2.00 (P = 0.05)

Fig. 2. Short-term effects of cognitive rehabilitation on letter cancellation.

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Experimental</th>
<th>Control</th>
<th>SMD (random) 95% CI</th>
<th>Weight %</th>
<th>SMD (random) 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Rossi 1990</td>
<td>18 0.68 (0.85)</td>
<td>21 2.20 (2.20)</td>
<td>43.48 -0.84 [-1.50, -0.18]</td>
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</tr>
<tr>
<td>Wiart 1997</td>
<td>11 17.00 (14.00)</td>
<td>11 45.00 (25.00)</td>
<td>23.95 -1.33 [-2.27, -0.39]</td>
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<td></td>
</tr>
<tr>
<td>Rusconi 2002</td>
<td>12 4.27 (8.94)</td>
<td>8 17.87 (18.90)</td>
<td>23.48 -0.95 [-1.90, 0.00]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zolot 2002</td>
<td>4 3.75 (3.20)</td>
<td>4 28.30 (22.25)</td>
<td>12.08 0.33 [-1.07, 1.74]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>45</td>
<td>44</td>
<td>100.00 -0.84 [-1.36, -0.33]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi²= 3.76, df = 3 (P = 0.29), I²= 20.1%
Test for overall effect: Z = 3.00 (P = 0.001)

Fig. 3. Short-term effects of cognitive rehabilitation on line bisection.

\[ -1.09 [−2.0, −0.18], p = 0.02 \]. Two studies [8,23] of 31 participants did not find a persisting effect favouring the experimental group on the BIT behavioural subtest summary score \( p = 0.87 \).

4. Discussion

Randomisation to intervention and control groups is essential in research to evaluate the effects of treatment but fewer than half the trials identified used random allocation. Few RCTs specified the methods used for randomisation and few used adequate concealment. In addition, once carried out this was not always adhered to. The principle of randomisation is that it leaves the participants in the groups due to chance to prevent selection bias. Although post-randomisation changes to group membership may balance the groups on variables that can easily be identified (e.g. age, gender), it may introduce selection bias on other variables not measured. Similarly, matching defeats the purpose of randomisation. While groups may be similar on the variables used for matching, there may be selection bias on other characteristic not measured. Once groups are established it is important that a complete follow-up is attempted. The lack of information on attrition is important as an intervention that produces a high level of non-participation will not be generally effective and excluding these people from the analysis leads to a false positive result.

Several CCTs compared patients on different wards or hospitals. The disadvantage is that there may be systematic differences between groups independently of the treatment for neglect being offered, such as differences in admission and discharge policies, staff and in other components of the rehabilitation package. Such performance biases [12] may make evaluation of the intervention for neglect irrelevant. Allocation cannot be concealed when it is determined by ward/hospital admission. Researchers recruiting participants may be influenced if they know that the next patient will be a control or by knowledge of the intervention given to the last person.

Few trials reported blind assessment of outcome. Some attempted to reduce observer bias by including functional outcomes assessed by staff/carers. However
it was unclear whether these were simply independent of the treatment being offered or were unaware of the treatment offered. Expectations are likely to differ if observers know a treatment has been given and this may bias results. It is rarely possible to conceal the intervention from the patient. However greater attempts could be made to deliver a sham or attention placebo intervention. These controls would correct for the novelty effect of new equipment and make others providing routine rehabilitation less aware of the intervention allocation of the participants.

Sample sizes were generally very small. Few studies mentioned conducting a power calculation to determine the sample size needed to detect a clinically significant difference between groups. Given the practical difficulties of conducting trials of rehabilitation for neglect, meta-analysis of several small studies provides an ideal opportunity to examine treatment effects in a larger group of participants. However the trials have to be appropriately designed before such analyses are warranted. Therefore we only included RCTs not CCTs in the updated Cochrane review and meta-analysis. We also conducted separate sensitivity analyses of only the A rated RCTs to examine whether those with B/C ratings inflate the effect size.

Studies generally provided good, detailed and comprehensive descriptions of baseline characteristics of participants. This would enable subgroups to be defined who benefited and who did not benefit from treatment, once the number of trials suitable for inclusion in meta – analysis becomes large enough. Individual patient meta-analysis is increasingly being used to define subgroups on the baseline characteristics and can detect treatment effects when individual studies are small [32].

Meta – analysis also requires that a common outcome is measured although the actual measurement tool used may vary between studies. Many used the Behavioural Inattention Test (BIT) [36] which does provide a common measure of both impairment (conventional tests) and a more ecologically relevant measure (behavioural subtests). Some trials also assessed outcomes on measures of functional abilities, such as the Barthel Index. However, scales developed specifically to assess the functional effects of neglect [1,31,39] may prove to be more sensitive. Since the aim of treatment of neglect is to improve rehabilitation outcomes, future trials must include measures of functional abilities. In the original Cochrane review [3] few trials included assessment of functional outcomes. In the 2005 update the proportion had increased but still only six of the 12 RCTs did so and only two assessed whether it persisted beyond the end of treatment. There needs to be a consensus about the ‘best’ measures and those designing trials need to include these in future in order to facilitate meta-analysis. For clinical purposes it is clearly essential that the benefits outlast the period of intervention, therefore outcomes need to be assessed after the end of treatment. Although this occurred, in some cases the time interval was inadequately short i.e. hours or days.

Overall the results suggest that cognitive rehabilitation shows promise and warrants robust investigation of clinical and cost effectiveness. A range of different rehabilitation interventions exist and although we do not yet have enough evidence to choose between them, we can say that collectively they improve outcome on some measures of impairment and some of these effects persisted after the end of intervention. There was no evidence to support or refute the effect of the interventions on independence in activities of daily living, either at the end of treatment or on follow-up, however this may be because previous studies have been too small and lacked the statistical power to show an impact on gross measures of disability. Improvements in the methodological quality of future trials are required and have been outlined in this paper.

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References


