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Rehabilitation for post-stroke cognitive impairment: an overview of recommendations arising from systematic reviews of current evidence

David C Gillespie[1], Audrey Bowen[2], Charlie S Chung[3], Janet Cockburn[4], Peter Knapp[5] and Alex Pollock[6]

Abstract

Background: Although cognitive impairments are common following stroke, there is considerable uncertainty about the types of interventions that can reduce activity restrictions and improve quality of life. Indeed, a recent project to identify priorities for research into life after stroke determined that the top priority for patients, carers and health professionals was how to improve cognitive impairments.

Objective: To provide an overview of the evidence for the effectiveness of cognitive rehabilitation for patients with stroke and to determine the main gaps in the current evidence base.

Methods: Evidence was synthesised for the six Cochrane reviews relating to rehabilitation for post-stroke cognitive impairment and any subsequently published randomized controlled trials to February 2012.

Results: Data arising from 44 trials involving over 1500 patients was identified. Though there was support for the effectiveness of cognitive rehabilitation for some cognitive impairments, significant gaps were found in the current evidence base. All of the Cochrane reviews identified major limitations within the evidence they identified.

Conclusions: There is currently insufficient research evidence, or evidence of insufficient quality, to support clear recommendations for clinical practice. Recommendations are made as to the research required to strengthen the evidence base, and so facilitate the delivery of effective interventions to individuals with cognitive impairment after stroke.

Keywords

Cognitive impairment, rehabilitation, randomized controlled trial, stroke, systematic review

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[1]Clinical Neuropsychology Service, Western General Hospital, Edinburgh, UK
[2]Stroke Research, University of Manchester, Manchester, UK
[3]Department of Occupational Therapy, NHS Fife, Fife, UK
[4]Retired, UK
[5]Department of Health Sciences, University of York, York, UK
[6]Nursing, Midwifery and Allied Health Professions Research Unit, Glasgow Caledonian University, Glasgow, UK

Corresponding author:
David C Gillespie, Clinical Neuropsychology Service, Department of Clinical Neurosciences (DCN), Western General Hospital, Edinburgh EH4 2XU, UK.
Email: david.gillespie@nhslothian.scot.nhs.uk

Introduction

After stroke most patients experience some disturbance of cognitive functioning,[1,2] and many have enduring difficulties in specific cognitive domains, such as attention and concentration;[3] memory;[4] spatial awareness;[5] perception;[6] praxis;[7] and executive functioning.[8] Although it is possible to have a deficit in one cognitive domain only, usually stroke survivors experience deficits across several domains.[9,10] Cognitive impairment has a significant impact on activities of daily living (ADL)[11] and self-rated quality of life,[12] and it is among the most difficult losses to manage, with high levels of unmet need.[13]

Treatments aim either to restore lost skills or to teach compensatory techniques. However, the evidence base is weak.[14–16] Recently, establishing the best treatment approach for patients with cognitive losses after stroke was identified as a research priority area.[17] In this project: (1) 548 treatment uncertainties were collected; (2) after checking research evidence these were reduced to 226 unique unanswered research questions; (3) 97 people participated in the interim prioritisation process, leading to the identification of 24 shared top priorities; (4) at a final consensus meeting, a representative group of stroke survivors, carers and health professionals decided their research priorities. During the final consensus meeting it was agreed to place the question relating to cognition first in the priority list.[17]

This article should be of interest to clinicians responsible for stroke patients with any cognitive deficit, and will also guide stroke researchers planning future rehabilitation studies for patients with cognitive deficits. The need for such guidance is clear: much previous research has been either small scale or of poor methodological quality, and the same types of methodological limitation have recurred over the years. In order to improve the robustness of cognitive rehabilitation research for stroke, the remaining sections of the current article: (a) outline what is already known about the effectiveness of cognitive rehabilitation treatment approaches from the findings of published systematic review evidence; and (b) make recommendations as to the types of research studies that are required to strengthen the available evidence.

Method

This review is based on Cochrane systematic reviews and randomized controlled trials (RCTs) published since their last search. There are currently Cochrane reviews that synthesise evidence relating to treatments for stroke patients with: (a) attention deficits; (b) memory deficits; (c) spatial neglect; (d) perceptual disorders; (e) motor apraxia; and (f) executive dysfunction. The reviews relating to perceptual disorders and executive dysfunction included studies of mixed aetiology groups (usually stroke and other acquired brain injury), while the other reviews only included studies including participants with stroke. For this synthesis, we removed studies that recruited participants with brain damage other than stroke, unless a subgroup of those with stroke could be identified for which results were reported separately, or 75% or more participants in the sample were individuals with stroke.

As the six Cochrane reviews had different publication dates, if a review had been published more than 12 months previously, more recently published RCTs for that cognitive domain were identified from the results of comprehensive literature searches made available to us by the Clinical Effectiveness and Evaluation Unit of the Royal College of Physicians (RCP) London. These systematic searches (of the computerised databases Medline, AMED, CINAHL, PsycINFO and Embase using keywords for stroke (e.g. cerebrovascular accident) and a full list of terms for the cognitive domains (a) to (f) above) were undertaken for the 2012 edition of the UK *National Clinical Guideline for Stroke*.[16]

We systematically synthesised the characteristics of studies included in the reviews, and summarised the results of meta-analyses, presenting an overview of current knowledge and understanding, and enhancing access to the detailed evidence that is provided within these published reviews. For each review, and supplemented by the additional

RCTs, we explored the recommendations for research considering: (i) evidence relating to the effectiveness of cognitive rehabilitation, and (ii) the key methodological components recommended for future studies in order to address the gaps and uncertainties.

Results

Attention deficits

The review on this topic[18] identified six RCTs,[19–24] which had recruited a total of 223 participants. The RCTs had small sample sizes (range 18–78), with a mean age of under 65 in all but one trial. Inclusion criteria were variable. Treatment duration ranged from 3 to 11 weeks, and was almost all computer-based with the aim of restoring underlying attentional functioning. The control groups in all trials received treatment as usual, with unblinded outcomes on psychometric measures. Few studies assessed functional ability or long-term outcomes (see Table 1, available online).

Meta-analysis found improvement in divided attention immediately following treatment (standard mean difference (SMD) 0.67, 95% confidence interval (CI) 0.35 to 0.98, $p < 0.0001$), but no impact on other attentional domains (e.g. alertness, selective attention, sustained attention; all $p > 0.05$). There was no impact on psychometric test scores in any attentional domain at long-term follow-up (defined as three months post intervention). Nor was there was evidence that interventions for attention deficits improved functional abilities, mood or quality of life either immediately, or late after treatment. No additional literature searches were undertaken because the Cochrane review was recent.

Memory deficits

The Cochrane review[25] identified two trials,[26,27] both of which provided group interventions to a combined total of 18 participants (see Table 1, available online). Treatment was provided over four weeks[26] and 10 weeks,[27] and pragmatic control arms were employed in both investigations. Outcome assessments were unblinded. Although neither study included a functional or quality of life measure, both employed subjective memory questionnaires alongside objective memory test data, and one study reported both short- and longer-term (three months post-treatment) outcomes[27] (see Table 1, available online).

Neither investigation reported improvement on memory tests, or on subjective and objective-rated measures of memory. The RCP searches[16] identified one additional study[28] that found memory improvement on a range of person-centred goals for individuals using an electronic paging reminder system, and replication of this study is required.

Spatial neglect

The review of the rehabilitation of neglect[29] identified 23 trials comprising a total of 628 participants. Sample sizes were mostly small. Twelve were compensatory studies;[30–41] 10 restorative[38,42–50] and two studies combined both approaches[51,52] (see Table 1, available online). Although the interventions were usually well described, and the majority included ADL outcomes, methodological quality of the studies was generally poor. Only six studies[34,39,44,46,49,50] included a follow-up assessment of ADL to determine the long-term impact of intervention, and other meaningful outcomes (e.g. discharge destination, falls, quality of life) were rarely reported.

Meta-analyses demonstrated no *persisting* impact of cognitive rehabilitation on functional disability (SMD 0.31, 95% CI −0.10 to 0.72, $p > 0.05$), standardised neglect assessments (SMD 0.28, 95% CI −0.03 to 0.59, $p > 0.05$) or for immediate effects on ADL (SMD 0.23, 95% CI −0.02 to 0.48, $p > 0.05$). Although treatment resulted in an *immediate* impact on standardised neglect assessments (SMD 0.35, 95% CI 0.09 to 0.62, $p < 0.05$), this was not the case when only studies with the lowest risk of bias were examined (all $p > 0.05$). Also, the impact of intervention when rehabilitation was compared with 'no treatment' vs. 'attention control' was found to be significantly different, suggesting that time spent with a therapist may be the active ingredient rather than therapy content per se. No additional searches were undertaken.

Perceptual disorders

The Cochrane review[53] identified six RCTs[35,54–58] with 338 participants in total. Two studies were excluded from the current article, because >90% of the sample had suffered a traumatic brain injury (TBI),[58] and because separate stroke data were unavailable.[56] This left 275 participants from four trials, on which this evidence is based. Samples ranged from 20–97 participants, and covered a good age range (26–86 years). All studies provided sensory stimulation (e.g. shape recognition tasks), and this was combined with strategy training in one study[54] and functional training in another.[35] Unfortunately, the interventions were described in too little detail to allow replication or implementation into practice. Only one study[54] employed adequate allocation concealment methods, and no study assessed long-term outcome.

No evidence was found for the benefits of treatment on any outcome measure ($p > 0.05$ for perceptual intervention vs. control; and $p > 0.05$ for functional training vs. sensory stimulation). No additional studies were identified in a more recent literature search.[16]

Motor apraxia

The Cochrane review[59] identified three trials incorporating 132 participants.[35,60,61] The trials comprised strategy training;[61] transfer of training;[35] and gesture training[60] (see Table 1, available online). Treatment was delivered over 6 to 19 weeks. Two studies[35,61] measured outcome at the level of function (both with blinded outcome assessment), but none reported on quality of life, patients' or carers' perception of outcome or mood. Only the largest study[61] assessed the persistence of treatment with five month follow-up.

The review found ADL improvement immediately after treatment (mean difference (MD) 1.28, 95% CI 0.19 to 2.38, $p = 0.02$), but not six months post-treatment (MD 0.17, 95% CI −0.41 to 1.75, $p = 0.83$). No additional studies were identified in a more recent literature search.[16]

Executive dysfunction

From the Cochrane review,[62] only five studies provided data on individuals with stroke (211 participants). Four were interventions designed to restore components of executive functioning,[22,63–65] and one trial provided a video feedback compensatory treatment[66] (see Table 1, available online). The overall reporting of methods was poor: only one study reported both allocation concealment and blinding of outcome assessment,[66] and a large number of executive outcomes were used across the studies (e.g. working memory, concept formation, inhibition, mental flexibility). Only two trials measured ADL[63,66] and none considered patient quality of life. No study measured longer-term outcomes.

Meta-analysis found no statistically significant effect of cognitive rehabilitation on primary or secondary outcomes. No additional searches were undertaken because the Cochrane review was recent.

Discussion

Despite research involving over 1500 patients in 44 randomized studies, there is very little strong evidence for the effectiveness of rehabilitation for cognitive deficits found after stroke, and very few direct clinical recommendations can be made. There are, as we will outline, recommendations that can be made for future research.

Current Cochrane review evidence suggests that cognitive rehabilitation for attention deficits, spatial neglect and motor apraxia all improve standardised assessments of impairment immediately following treatment, but that improvements may not persist and (with the possible exception of motor apraxia) do not improve everyday function. There is currently no evidence that memory deficits, perceptual disorders or executive dysfunction respond to the cognitive rehabilitation interventions included in these reviews. Can it, therefore, be concluded that cognitive rehabilitation following stroke is of only limited effectiveness? We do not believe so, because absence of evidence is not the same as evidence of absence. All of the reviews[18,25,29,53,59,62] identified major limitations within the evidence they identified, justifying the decision to place cognitive rehabilitation as the top current research priority.[17] Overall, there is a clear need for methodological improvements in three categories:

(i) sample considerations; (ii) descriptions of interventions; and (iii) measurement of outcome.

As far as sampling is concerned, trials need to recruit larger numbers of participants to ensure sufficient power to detect any impact of treatment. It is important that sample size calculations are carried out for future RCTs, so that studies are adequately powered. There is also a need for research to include samples of stroke survivors that are representative of the population of people with stroke. One important consideration is participant age. To take an example, the Cochrane memory review comprised a study that included only patients aged under 60 years of age[27] and another that recruited from a centre with patients 'who are relatively young' (Doornhein and De Haan, p. 394).[26] The samples in these two studies were in their 40s and 50s, i.e. younger than the typical stroke survivor. An important question is which patients benefit most from cognitive rehabilitation. Do older patients have the same potential for improvement as younger patients? This and related questions can only be answered if researchers recruit stroke samples that are not overly restricted on dimensions of interest, and if appropriate measurements of demographic variables are recorded and reported consistently between trials.

Likewise, more consideration should be given to the therapies that are offered, as well as to their delivery. Treatments should have a clearly stated rationale and should be described in sufficient detail to permit replication. Researchers can consult a recent checklist for the description of rehabilitation interventions to help them do this.[67] Cognitive rehabilitation is a therapy-intensive endeavour, particularly if the time to assess cognitive strengths and weaknesses prior to intervention is taken into account. Most previous studies have involved relatively short periods of therapy. Although the impact of treatment intensity for cognitive rehabilitation after stroke is largely unknown, it has been suggested that much rehabilitation is delivered with inadequate 'dose'.[68] The optimum intervention intensity has yet to be established for post-stroke cognitive impairments and is an important area of future research, particularly for service commissioners. Likewise, little is known about the active ingredients of cognitive rehabilitation. Researchers should consider the use of attention control arms to investigate this issue, so that the direct effect of interventions can be determined, separate from the effects that may result from clinicians showing interest in, and spending time with, patients as suggested by the neglect review.[29]

The fundamental aim of rehabilitation is to improve everyday functioning and yet, many existing studies have been limited to assessing outcome at an impairment level, e.g. on paper-and-pencil tests. We propose that researchers always keep the functional, 'real life' significance of cognitive rehabilitation in mind. It is important to determine the impact of treatment on ADL, mood, quality of life and discharge destination, and also to obtain patient and caregiver views of treatment. The establishment of a core set of outcome measures would be particularly helpful, because this would enable participant data from different studies to be combined using meta-analysis. Also, outcome measurement should not be limited to the short-term (i.e. immediate post-treatment), but should establish whether individuals maintain any improvements over time. Only long-term follow-up can enable both the providers and recipients of cognitive rehabilitation to understand the true costs and benefits of treatment.

As far as trial design is concerned, we believe that future cognitive rehabilitation research should include both explanatory and pragmatic aspects.[69] Most previous research in this area has been explanatory, designed to determine efficacy under optimal conditions; pragmatic trials evaluate the impact of an intervention in routine practice. Both designs are needed to answer the complicated questions posed by rehabilitation research. The former can help us decide if (and how) an intervention works; the latter can reassure us that an intervention is effective in real life settings, an important consideration in resource-limited clinical services. Researchers are encouraged to consult the pragmatic-explanatory continuum indicator summary (PRECIS) tool,[69] and the Medical Research Council (MRC) guidance for complex interventions[70] to help them inform trial design along the pragmatic-explanatory continuum. In doing so,

they might wish to consider the following important issues.

The first is the complex clinical presentations typical of stroke, for cognitive impairments rarely occur in isolation. As an example, stroke survivors with memory impairment[71] and executive dysfunction[72] are at increased risk of depressed mood, which may influence their engagement with rehabilitation, and so negatively impact on outcomes. Future research should aim to study the impact of mood on cognitive rehabilitation outcomes. Of interest to researchers is the finding that improved mood often has a positive impact on cognition.[73,74] Research could compare treatments that aim to improve cognition with those that aim to enhance mood, and determine whether combined cognition-mood interventions might be optimally effective. Combined interventions would be in keeping with comprehensive-holistic rehabilitation programmes as recommended in the recent RCP Stroke Guideline.[16]

A second issue is that of patient preference. Stroke survivors may have significant preferences for treatments,[75] and these preferences are likely to influence engagement. The importance of patient preference in rehabilitation research has been highlighted before;[76] if patients are allocated randomly to treatments that they may not desire, it will be difficult to distinguish between an inherently ineffective treatment and one that failed because it was targeted to patients who were insufficiently motivated to engage with it. These are important concerns because many stroke survivors experience poor awareness of their deficits, and also motivational difficulties.[77] One approach is to conduct a 'patient preference' trial, in which treatment allocation is influenced, at least partly, by what patients would like to receive.

The third issue for researchers to consider is that of cost-effectiveness. This has rarely been reported in trials of cognitive rehabilitation after stroke, but is crucial to health policy and the commissioning of services. The variability in cost data in rehabilitation studies is often much greater than for the clinical outcomes,[78] and so the required sample size is also much greater. Multi-centre recruitment would be one way in which researchers could ensure that their studies had adequate numbers of participants.

Finally, it is notable that this review of published research has been limited to trials of interventions. As well as the complexities and variation of cognitive rehabilitation interventions, factors relating to service delivery also contribute methodological challenges.[79] The current article has not included evaluation of aspects that are crucial to the delivery of care, such as the best tools for screening or diagnosing cognitive impairments, or the required skill mix in rehabilitation teams. These important aspects of care provision should also be the focus of primary and systematic secondary research.

Clinical messages

- There is currently insufficient evidence to make more than a few recommendations concerning cognitive rehabilitation after stroke.
- A review of existing research enables specific recommendations to be made for future research design and execution.

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Conflict of interest

DG, AB, CC, PK and AP are contributing authors of four of the six Cochrane reviews included in the current article, and AP is a member of the Cochrane Stroke Group Editorial Group. AB and PK were members of the Intercollegiate Stroke Working Party (ICSWP) of the Royal College of Physicians London, and together with DG and JC were members of a psychology subgroup that reviewed evidence for the ICSWP.

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