Introduction

Unilateral spatial neglect is a disorder that has, for many years, intrigued and frustrated researchers and clinicians working in the area of stroke rehabilitation. A vast literature exists on the subject of neglect, much of it published by neuropsychologists and neurologists. Many of these papers aim to identify the underlying causal mechanisms, in terms of the neuroanatomical structures and cognitive processes involved. More recently, research has focused on evaluation of rehabilitation strategies to reduce the disabling effects of neglect. Various research designs have been used to examine whether a particular approach is effective or not. These range from single-case experimental designs (where the individual acts as their own control) through to randomized controlled trials (RCTs). In the latter, comparisons are made between (typically) two groups, one randomly assigned to receive the therapy approach under investigation and the other assigned to the control treatment.

The present review paper aims to discuss the evidence for the effectiveness of neglect rehabilitation based on single cases and RCTs. A comparison will be made of the types of evidence that each design can produce, in terms of the sorts of clinical questions they can best answer. A definition of neglect will be provided, the epidemiology of neglect presented and the adverse effects on the individual with stroke described. The review will also summarize the balance of evidence from single case designs, RCTs and finally the findings from a recent Cochrane meta-analysis. The overall aim of the present paper is to make recommendations for clinicians working with people with neglect following a stroke, and to highlight future research directions.

Research designs

Before discussing the existing evidence for the therapy of neglect, it is worth contrasting the principles behind the two very different experimental methods frequently used in rehabilitation research in this area. Single-case experimental designs and RCTs answer very different research questions. Single-case designs are typically useful for testing whether the therapy ‘could’ work, i.e. proof of concept. For example, we can test whether an intensive, resource-heavy therapy regime, provided by a specialist research therapist, for a highly motivated individual with little or no comorbidity appears to be effective for that individual. However, a positive finding from one individual cannot be generalized to a clinical population. Nor can we conclude that a possible therapeutic effect observed following an idealistic therapy regime would be replicable in a non-research setting, i.e. if provided in a limited dose, to a heterogeneous population, by the usual clinical staff, in the usual clinical setting. Whilst RCTs can also be used to investigate proof of concept, their key advantage over single-case designs is in producing unbiased generalizable data. In reality, RCTs are required to determine whether the therapy ‘does’ work rather than whether it ‘could’ work, i.e. whether there is, on average, evidence of effectiveness over and above any spontaneous recovery or placebo effects. The key question for a health care provider is most often not can it work in principle but would it work for my patients, if delivered within the constraints of my existing resources.

Of course, the RCT or single-case design is simply a framework around which a research project is structured. The choice of framework is necessary but not sufficient to ensure the quality and utility of the resulting evidence. Other methodological choices, such as the validity of the primary outcome measure, are crucial. A highly statistically significant effect from an RCT is not
a guarantee of a clinically significant effect if the outcome measure chosen was of dubious clinical significance to service users, providers or purchasers. This point should be considered when reviewing existing effectiveness data.

UK and international evidence-based initiatives
By way of setting a context for this review, it is also worth highlighting UK and international initiatives to develop stroke services on the basis of robust research-based evidence of effectiveness. In the UK, a Royal College of Physicians (RCP) Intercollegiate Working Party published evidence-based Clinical Guidelines for the management of stroke.1 The first edition included a section on rehabilitation but did not specifically address neglect in detail. The RCP guidelines are currently being expanded and the second edition will include a section on the management of neglect.

Internationally, the Cochrane collaboration aims to promote evidence-based practice. This is achieved through the publication of systematic reviews and meta-analyses of RCTs, which are published in the Cochrane library. There are forty-nine topic ‘review groups’ including one specifically dedicated to stroke. As their mission statement states, the Cochrane Collaboration ‘is an international organization that aims to help people make well-informed decisions about healthcare by preparing, maintaining, and promoting the accessibility of systematic reviews of the effects of healthcare interventions’.2 In the 1990s, Professor Nadina Lincoln from the University of Nottingham initiated a Cochrane review of neglect. This has recently been published in full3 and in summary4 format.

What is neglect?
Neglect can impair a person’s ability to see, hear or move in a certain part of their environment. Neglect is often referred to as unilateral or hemispatial, as it disproportionately affects one side more than the other (but see below). The most widely quoted definition of neglect is a description of the resulting behavioural disabilities: ‘fails to report, respond, or orient to novel or meaningful stimuli presented to the side opposite a brain lesion.’5 This definition does not describe the causal mechanism of neglect, but does make the important point that it is not due to sensory or motor impairments. However, many individuals with neglect will also have a hemiplegia or hemianopia. It is important that co-existing impairments must be taken into account in planning a therapeutic approach for neglect.

Neglect can affect a person’s ability to carry out many everyday tasks such as eating, reading and getting dressed.6 These disabilities are likely to be due to impairment of attentional direction to the space around us. Stroke may differentially affect our ability to direct our attention in the visual, auditory or tactile modalities. Stroke survivors may also make very few movements with their affected limb, even if it has adequate power and strength (motor neglect). They may also have difficulties in making movements towards and exploring the contralesional space with the ipsilesional (unaffected) limb. Since different types of neglect can occur, several different terms are used in clinical practice, e.g. visual neglect, motor neglect, hemi-neglect, inattention.7

Neglect can also affect different areas of space. These have been divided into three main categories: personal space, peripersonal space, and extrapersonal space. Personal space refers to the area of the individual’s body. Neglect of this area of space may manifest in some of the most striking clinical features of neglect such as not shaving one side of the face or brushing hair on only one side of the head. Peripersonal space refers to the space around the body which is within reaching distance.8 Neglect in peripersonal space may manifest clinically in symptoms such as not eating food on one side of the plate, or being unable to find objects in one side of space. Extrapersonal space concerns the area which is beyond reaching distance.9 Neglect in this area of space may be less evident from everyday observation unless stroke survivors are mobile. It may manifest as bumping into objects or doorways in navigation. Peripersonal and extrapersonal areas have previously9,10 both been referred to as extrapersonal space, sometimes subdivided into ‘near’ and ‘far’. Neglect may occur in one or all of these areas of space. For example an individual may have neglect in personal but not peripersonal space or vice versa.10

The different aspects of neglect often co-occur, and so neglect is commonly regarded as a syndrome. However, there is some evidence that different aspects of neglect may manifest independently. It is reasonable to assume that dif-
different disorders require type-specific rehabilitation approaches. A therapy for neglect of near space will not necessarily be effective for neglect of far space. Although people do sometimes neglect their ipsilesional side, most researchers and clinicians focus on the far more common neglect of contralesional space. This paper will focus on contralesional neglect.

Before proceeding, it is worth clarifying two important issues. Although terms such as unilateral and hemispatial often preface the term neglect, these are perhaps misleading. A left hemianopia (or a left hemiplegia) typically affects the area or functioning to the left of the body’s midline. However, a left-neglect does not have a neat midline split. Neglect appears to exist along a gradient. Some left-neglect patients may be perfectly able to move and look across their midline into part of their left hemispace. However, their spatial awareness will decrease the further left they go. Others may have such a severe neglect that they appear completely pulled towards their right side and are unable (automatically) to move or look at things even to the near right of their midline.

The second issue to clarify is the intriguing finding that patients may be able to attend voluntarily to things they cannot attend to automatically. Someone who is unaware of a fork placed on the left side of their dinner plate may suddenly ‘see’ it if the clinician draws their attention away from the right, e.g. by the clinician tapping the table on the left and asking the patient to concentrate on where the sound is coming from. Hence many of the rehabilitation strategies (described later) work on providing a cue (visual, auditory or tactile) to prompt the person to voluntarily attend to the neglected area. A very frustrating aspect arises from the fact that the apparently miraculous treatment effect of eliciting voluntary or effortful action is short-lived. A few minutes later, the patient returns to dependence on their impaired automatic attentional system and ‘loses’ yet another piece of cutlery.

Measuring neglect

Therapists often identify neglect using their clinical judgement, based on subjective observation of individual performance on everyday tasks. This identification of neglect means therapists are aware of the real-life manifestations of neglect in an individual, and can therefore target rehabilita-

tion. However, formal assessment of neglect remains important to quantify neglect, assess which types of neglect are present, and monitor change.8

The World Health Organization disease classification system11 has recently been updated to a ‘components of health’ classification.12 This framework for describing the health situation of a person comprises three main levels. Impairment – describes problems with body structure or function (including the mind); activity (previously disability) – describes performing tasks or actions; participation (previously handicap) – describes individual experience and involvement in everyday life-situations.

Measurement can occur at any of these levels. In neglect, some of the traditional paper and pencil assessments would be classified as being at the level of impairment. Other more functional measures are at the level of activity.

There are several widely used traditional impairment level measures of neglect. Cancellation tasks require individuals to search a visual array for target items, and to put a line through all target items. These arrays may consist of targets only, or of targets and distractors. Typically, people with left-sided neglect cancel targets on the right of the array only. People with neglect tend to start tasks on the right, rather than the left as healthy people do.13 Line bisection is another commonly used paper and pencil assessment. It requires individuals to put a mark in the centre of a line presented to them. Such traditional assessments of neglect are usually restricted to the peripersonal domain, and so they are insensitive to personal and extrapersonal neglect.

Measures of neglect at the level of activity have also been developed. For example,14 there are scales for therapists to rate patients’ neglect behaviour. More objective standardized assessments of neglect that are functionally relevant are also available. The behavioural inattention test (BIT) is a battery which includes traditional measures of neglect, and ‘behavioural’ measures.15 The impact of neglect on real life means that both activity and impairment level measures are important in diagnosis and therapy planning.

Diagnosis of neglect should not be made using a single assessment. As discussed above, neglect may manifest in many ways, and different assessments may be sensitive to different aspects of neglect. Usually more than one test is
administered. Test batteries for neglect\textsuperscript{15,16} have been developed, which are favoured for several reasons. Firstly, the differing sensitivities of neglect tests mean that use of a single test may only identify a subset of patients actually affected.\textsuperscript{17,18} Furthermore, batteries can include assessments of several different aspects of the neglect syndrome.

**Epidemiology**

The reported rate of occurrence of neglect following stroke has varied from as high as 90\%\textsuperscript{19} to as low as 8\%.\textsuperscript{20} The variability in the figures is due to methodological differences between studies, such as the operational definition of neglect, selection criteria for patients and method of assessment employed.\textsuperscript{7,21,22} Although an accurate estimate of the rate of occurrence is not presently available, a previous review found that, in sixteen of the seventeen studies making the comparison, contralesional neglect occurs more often after right than left hemisphere stroke.\textsuperscript{21}

For many people, the initial highly visible signs of neglect disappear within one month of stroke.\textsuperscript{22} The period of most rapid spontaneous recovery is the first ten days\textsuperscript{23} up to the first month.\textsuperscript{24} Neglect continues to improve beyond this although at a slower rate and may be barely perceptible after three months.\textsuperscript{21,23,24} For example, an initial frequency of 41\% dropped to 9\% after three months in the absence of any neglect-specific rehabilitation.\textsuperscript{24}

In a previous review of one of the present authors, four of the seventeen studies (comparing right- and left-hemisphere stroke groups) provided longitudinal data with which to determine whether recovery is more common for either group.\textsuperscript{21} A reduction in the frequency of neglect appeared more likely following left-hemisphere stroke.\textsuperscript{21}

Although neglect may resolve spontaneously, it can also be an enduring and disabling condition.\textsuperscript{23,24} Neglect is associated with poor performance on activities of daily living,\textsuperscript{22,24–26} and suboptimal response to therapy.\textsuperscript{27} The quality of the evidence for the rehabilitation of neglect will be considered in those individuals with a persisting disability. However, it should be remembered that reliable epidemiological data are essential to ensure that RCTs of therapy have adequate statistical power. The necessary data includes the proportion of patients likely to experience neglect following stroke and the extent of natural recovery over time. Unfortunately, as described above, the current epidemiological data are less than adequate.

**Evidence for specific therapy approaches**

In this section, different types of therapy used in neglect rehabilitation will be outlined. The rationale for the therapy is first explained, followed by the evidence from single-case designs and then from RCTs (if available). This section will be followed by a description of the Cochrane review and meta-analysis. This paper excludes other group studies, e.g. before and after trials. Our justification is that the results of such studies are misleading, as they do not account for temporal changes, e.g. spontaneous recovery.

**Scanning training**

Scanning training aims to compensate for difficulties attending to the left by encouraging full scanning of the environment. Scanning training has been investigated whilst the participant is static and mobile in a wheelchair.\textsuperscript{28,29} Early studies used a machine to train scanning behaviour.\textsuperscript{30,31} This machine facilitated: (1) tracking a target around the edge of the board by looking and pointing at it; (2) reporting which of two rows of lights on the board were lit. The programme also included reading training and cancellation tasks using perceptual anchors and cues (see below). Pizzamiglio and colleagues developed a series of tasks using sequential scanning, including a computer-based task, reading and copying tasks, figure description and copying a drawing on to a dot matrix.\textsuperscript{32,33} Robertson et al. tried to automate the scanning training process.\textsuperscript{34} To start with, scanning tasks were computerized, but a therapist implemented the self-instructional training.\textsuperscript{34} Self-instructional training is a behavioural technique that trains individuals to use their own verbal instruction to guide behaviour. The aim was that ultimately both components of the therapy would be automated.\textsuperscript{34} Edmans and Lincoln found little benefit of either scanning or perceptual training on impairment level measures in four single cases.\textsuperscript{35} Investigation of five single cases, using multiple baseline by subject designs, found positive effects on a measure similar to the training task, but this did
not generalize to other impairment or activity level measures. Studies incorporating a mobile element, in addition to static training, have succeeded in achieving improvements on impairment and activity level measures. However, further single cases with static and mobile scanning training showed improvements only on the trained tasks, without generalization to other neglect measures. Mobile training requires high levels of physical ability (being able to stand and rotate the trunk). This may restrict its applicability to a small number of people.

Several small RCTs have been conducted on scanning training. Although slightly higher numbers of participants were recruited, outcome data are only available on twenty-two to thirty participants. These were typically described as severely impaired and were one to five months poststroke. The group assigned to active therapy received from sixteen to twenty hours. One study delivered computerized scanning therapy. The method of randomization was unclear and possibly flawed in all but one study. There were differences between the two groups on certain baseline assessments, with the experimental group scoring better than the control group on some measures which were then used to determine outcome. In one study the groups differed in dose as well as type of therapy. The experimental group received five hours per week whilst the control group only received three hours. Only two studies compared outcome at the activity level. However, there were baseline differences between the groups on the activity level measure in one study and the other was not adequately randomized.

Overall, single-case designs and RCTs evaluating scanning training have had mixed results. Several of the approaches were not limited to scanning training and included other elements (described below), for example reading training, visual cues, and perceptual anchors. It may be that these additional elements can account for the varying outcomes across studies. Further, adequately sized and appropriately designed RCTs are required before the approach could be said to have an evidence base.

**Visual cueing approaches**

Participants with neglect are able to respond to cues, and the use of cues during a task temporarily reduces right-sided bias. Most of the scanning training programmes discussed above incorporated cues. Visual cues include the use of coloured strips or numbers down the left side of the page or screen which participants are verbally directed to process. These cues are gradually reduced or faded as training progresses. Other research has used the left arm as a perceptual anchor. Here, the left arm is positioned to the far left of the activity and participants are encouraged to look across to it.

Two single cases showed improvement on impairment and activity level measures of neglect with use of the left arm as a perceptual anchor, both after treatment and at follow-up. A single case of neglect dyslexia also showed improvement on reading tasks using this sort of self-generated cue.

Despite its wide use in conjunction with other rehabilitation strategies, and its well-established temporary benefits in theoretical studies, the effects of visual cueing alone on functional ability have not been adequately evaluated in single case designs or RCTs (see above on RCTs of scanning).

**Alteration of visual input**

It is suggested that altering visual input can influence symmetry of brain activation levels, and central mechanisms involved in spatial representation. Prism goggles have aimed to shift the visual field to the right in neglect participants during mental imagery tasks, daily activities, and while performing a pointing task. Also, covering the right eye with a patch, or blocking the right side of each lens of a pair of glasses aimed to alter visual input.

Several single-case designs have been conducted into prisms and eye-patching. Wearing prism goggles during mental imagery tasks ameliorated the effects of neglect in two single cases. A recent case report urges caution in the use of eye patches after observing that patching the right eye in a case with neglect worsened performance on a line-bisection task. A case study of adapted glasses, which blocked out the right side of each lens, observed that use of these glasses coincided with a reduction in the number of collisions in an individual with chronic neglect. However, they did not result in consistent improvements in performance of tests of neglect.

There is some promising evidence from RCTs, although the studies have been small and possibly
underpowered to demonstrate statistically significant differences between groups. Wearing prism goggles during everyday activity over a one-month period led to improved performance on impairment, but not activity level measures in the experimental group (n=18) compared to a slightly larger control group. Although the method of group allocation was unclear, there were no measured differences at baseline. In another RCT, brief exposure to prism goggles during pointing activity improved performance. Again this was only on impairment level neglect measures. An RCT of eye-patching has also been reported.

However, although group allocation was concealed from the outcome assessors, it was not truly random. Participants wore patches on the right eye or the right half of each eye or not at all for three months. The authors concluded that the half-eye patch group improved more on the functional independence measure (FIM) than controls, while the whole-eye patch group did not differ significantly from controls. However, this conclusion should be considered with some caution. The groups were very small (seven to eight people), and again were not equivalent at baseline on the activity level outcome measure.

As yet, there is no evidence from single-case designs or RCTs to support the implementation of visual field blocking or prism goggles in routine practice. Despite their potential, prisms have not demonstrated effects on activity level measures in a long-term rehabilitation approach. However, further research is warranted.

Visual imagery

Visual imagery techniques are beginning to be used in neglect rehabilitation. Their rationale is that, in neglect, the mental representation of space is impaired. Intensive imagery rehabilitation (40 sessions, each lasting for 50 minutes) has used various techniques including room imagery and path description. An alternative visual imagery technique, aimed to teach participants to think of their head and eyes like a lighthouse. The strategy was to imagine they were a lighthouse, to scan fully left and right, using eye and head turning. Paper-and-pencil and computer task were used to practise the strategy, and errors were pointed out. Participants walked with the therapist and tried to locate items with and without cues (e.g. shoulder tapping). Cues were faded out with improvements. Posters of a lighthouse were given to the patient, family and other staff. Other therapists were instructed to encourage the strategy in other goal-related therapy sessions.

Two single cases were reported as improving significantly on impairment and activity-level neglect measures, using room imagery and path description. These effects were maintained until six months post-intervention. Although the observed improvements were large, one cannot causally attribute this to the intervention, since an AB single-case design was used with only one pre-test, and one post-test. Essentially, this is simply a before and after design and cannot distinguish between therapy effects and temporal changes (e.g. spontaneous changes over time). The chi-squared test used was not an appropriate statistic for this experimental design, because it is designed for nominal rather than interval data.

Thirty-one participants took part in a trial described as an RCT two months after stroke onset. The amount of therapy provided to the experimental group was brief: an initial session followed by three half-hour sessions. This controlled trial used consecutive admissions rather than randomization to allocate to groups. It was unclear whether or not outcome assessors were blinded to group allocation. The primary outcome measure was a non-standard tool developed by the researcher. Some improvements were reported, although they were only observed on tasks similar to those used during training. The research design was inadequate to evaluate the effectiveness of this therapy approach. In conclusion, visual imagery is a newly emerging approach, which at present has no adequate evidence base.

Limb activation

There has been considerable research into limb activation, although this is largely theoretical rather than aimed at evaluating rehabilitation. Using the left hand to respond resulted in reduced contralesional neglect on target location and line-bisection tasks, in comparison to using the right hand. The mechanism of this improvement has been debated. Halligan and Marshall concluded that since movement of the right hand in left space also ameliorated neglect, the effects observed with use of different responding hands were a result of external perceptual cueing rather than contralateral limb activation itself. However,
participant performance on a cancellation task was improved by movement of the affected (left) limb out of sight of the participant, suggesting that the beneficial effects were due to the limb activation itself and could be observed independently of perceptual cueing. Further, intentional movement of the affected (left) limb resulted in better performance on a neglect task than when the movement was passively produced by the experimenter. This suggests that active involvement was necessary in order to benefit from this approach. Robertson and North explain the mechanism of limb activation, using the premotor theory of attention. Within this framework, the action and perception systems are very closely linked. Activating the action system (i.e. by moving the affected limb) can cause increased activation of perceptual and attentional systems resulting in reduced neglect behaviour.

Experimental work with limb activation has been applied as a rehabilitation tool after brain injury. Limb activation was elicited by experimenter instruction, or prompting by a buzzer device (the neglect alert device) during therapy sessions, and routine activities of daily living. Other research has used the limb activation technique in a quite different way. One study used five minutes of hand tapping prior to completion of a self care programme. Another study gave an instruction to try to move the left arm, and to look at it while trying to make a movement. This was applied during conventional therapy sessions and with different sorts of activities (including language, motor, and ADLs). Self-instructional training (described above) was used to encourage spontaneous and regular use of the left arm in this study.

Single-case designs have shown beneficial effects of limb activation at both the level of impairment and activity, although not all cases completed both types of measure. These positive effects have lasted up to six weeks. The relatively short maintenance is due to the short follow-up period used, and so it is not known if effects could last longer.

An RCT of limb activation compared to traditional therapy found that limb activation resulted in improvement on impairment but not activity level measures. The authors described the rationale for the approach as follows: movements of the affected limb in the deficit hemispace led to a summation of activation of the affected receptive fields of two distinct but linked spatial systems for personal and extrapersonal space, resulting in improvements in attentional skills and appreciation of spatial relationships on the affected side. In essence, they proposed a system of spatio-motor cueing. The study group consisted of forty-seven subjects two to fourteen days post stroke-onset (a further three subjects died before outcome was assessed). Allocation to groups was done in blocks using computer-generated random numbers, and people blinded to group allocation conducted assessments. There were no baseline differences between groups. A small but positive effect of therapy on the Barthel Index (BI) was found. At outcome assessment, the experimental group had a better average BI (14.2) than the control group average. The standardized mean difference (0.62) had a 95% confidence interval of 0.04 to 1.21 (see Figure 3). There was no effect on destination of discharge, i.e. the experimental group was no more likely than the controls to be discharged to their own home.

In summary, limb activation techniques have shown beneficial effects in single-case designs and one RCT. The technique has been administered for varying durations, from four hours to just five minutes per day, and has been applied in different ways. There is no clear recommendation as to how the technique is best used, for how long, or the extent to which benefits are maintained. Most studies have used limb activation that is encouraged or directed by a therapist. One limitation is the necessity for participants to voluntarily move their contralesional limbs. Stroke survivors are often unable to move their affected limbs because of hemiplegia, or if they can, it may require great effort, thus limiting the number of people with whom this technique could be used. However, the technique shows promise and further RCTs to examine longer-term effects on activity level measures are required.

Awareness training

Neglect is associated with anosognosia and people with neglect are largely unaware of their difficulties. It is argued that if individuals are to use compensatory strategies, they must be aware of their own difficulties. Awareness of specific aspects of neglect-related behaviour has been explored. It was assumed that the proprioceptive and visual feedback provided from attempting to
pick up a horizontal rod from its centrepoint would enable the person to realize their errors in misjudging the centre of the rod. In fact, this led to significant short-term (twenty minute) improvement on impairment neglect measures. Although a theoretical investigation into the effects of feedback, it suggests that this is an area that holds potential for rehabilitation strategies. Video feedback has been used to increase awareness of difficulties in neglect. This allows the neglected (left) side of space to be projected to the attended (right) side of the screen for viewing. Video feedback has also been used in conjunction with compensatory strategies.

Two studies have used single-case methodology to investigate visual feedback. In the study of Soderbck et al., four single cases received video feedback which led to improvement on the trained task without generalization. Tham et al. evaluated the provision of daily sessions, over a four week period, of an awareness-training programme. They included video feedback, participant therapist discussion, therapeutic narratives, and strategy generation. Different activities and environments were used during the sessions. They identified clinically significant changes in ADLs, awareness, and impairment and activity level neglect measures, although maintenance of these benefits was not clear.

Two RCTs have evaluated visual feedback. Feedback of eye movements was investigated in an RCT of seventeen people who were on average one month poststroke. Participants wore glasses, which tracked their eye movements. A buzzer sounded when they had not looked to the left for fifteen seconds. In order to stop the buzzer they had to move their eyes to the left. Participants receiving this intervention did not improve more on impairment or activity level neglect measures than controls. Another RCT evaluated a single training session including immediate video feedback for fourteen people within two weeks poststroke. There was no effect on either impairment measure (see line bisection data in Figure 1). However, this was a small trial and may well have been statistically underpowered.

The evidence to date from small RCTs contradicts that from single-case designs. At present there is no justification for implementing visual feedback into routine practice unless as part of a trial.

Sustained attention training

Neglect is strongly associated with impairments of the ability to sustain attention, therefore, improvements in sustained attention might lead to improvements in neglect. A study with eight single cases with left-sided neglect used self-instructional training to improve sustained attention. This technique trained individuals to use verbalization to control their sustained attention system. This was practised during a number of vigilance tasks for five hours in total. Improvements on measures of neglect (impairment and activity level) and sustained attention were observed. Effects were maintained for up to two weeks. A further single case improved significantly on a non-standardized activity level measure at the end of a ten-day intervention period with a much shorter duration of daily training.

There are no RCTs of this approach. However, the theoretical link between sustained attention and neglect, coupled with the promising findings from single-case designs suggests this approach may be worth further investigation.

Tactile stimulation

Vibration of the muscles of the left side of the neck has been used as a rehabilitation approach for neglect. The rationale is that muscle vibration leads to the interpretation that the muscles have been lengthened, thus altering the person’s internal co-ordinate framework. Electrical stimulation of the skin on the left side of the neck (which does not result in muscle activation) and on the left hand has also been used. The possible effect of skin stimulation is one of cueing, i.e. the person is cued to attend to the site of the stimulation. These studies predict a differential effect for stimulating muscles versus skin.

Several single-case designs have been carried out, often with more than ten cases. Vibration of the muscles of the left side of the neck during task performance induced changes in target detection and body-centre judgements in participants with neglect. In another study, electrical stimulation of the left side of the neck did not affect performance on target detection tasks. Fifteen minutes of electrical stimulation applied to the left side of the neck or the left hand led to improved performance on impairment-level tasks immediately after stimulation. Similar improvements
Comparison: 01 Cognitive rehabilitation versus control treatment of spatial neglect: immediate effects
Outcome: 04 Line bisection

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Test for heterogeneity chi-square=5.70 df=4 p=0.22
Test for overall effect z=2.62 p=0.009

were also identified on mental imagery neglect tasks after electrical stimulation of the left side of the neck.74

There are no RCTs of tactile stimulation of the neck or hand. The evidence to date from single-case designs is growing but is not convincing. Where there is a possible effect in an individual, it tends not to persist after the stimulation ends.

Evidence from the Cochrane systematic review

As described above, many techniques for rehabilitating neglect have been investigated, some of them within RCTs. Most of the existing RCTs are described under the section dealing with that particular therapy approach. In 2002, a Cochrane systematic review and meta-analysis of randomized and controlled trials was published.3 This combined all the therapy approaches to examine the overall evidence for therapy for neglect following stroke. The study had several objectives: to investigate effectiveness at the level of impairment, activity (disability) and destination on discharge from hospital, and to determine whether any effects persisted beyond the end of therapy. This latter question is required to justify a recommendation to change routine clinical practice. The key aim of any therapy is to promote independence.

The full details of the methods and results of this meta-analysis are available in the published review.3 In brief, studies from 1966 to 2000 were considered for inclusion. Fifteen were included, although not every study provided data with which to answer all of the research questions. For example, only six studies included an activity-level outcome measure and only four investigated persisting effects beyond the end of therapy. The studies were small (see Table 1) with the largest study providing outcome data on 63 participants.

The Cochrane Collaboration recommends a system for judging the quality of the design and conduct of trials. As shown in Table 1, only three were classified as Category A (adequate) for randomization and allocation concealment. Much of the information required for quality assessment was unclear or unavailable, and so six studies were classified as B (unclear). The remaining six were classified as inadequate (C). This method of quality rating allows for a review of the combined studies (all 15) and potentially of only the A-rated studies. The evidence from A-rated studies is clearly of greater reliability and more importance, as these are less likely to contain bias.

From the fifteen studies, there was evidence that rehabilitation resulted in significant and persisting improvements on some impairment level assessments. (As they are fully available elsewhere,3 only

Table 1. A summary of the 15 studies included in the Cochrane review of neglect

<table>
<thead>
<tr>
<th>Main therapy approach</th>
<th>Number of data sets collected</th>
<th>Cochrane quality rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye patching53</td>
<td>15</td>
<td>C</td>
</tr>
<tr>
<td>Visual scanning and self-prompting79</td>
<td>12</td>
<td>B</td>
</tr>
<tr>
<td>Auditory feedback of eye movements from adapted glasses70</td>
<td>17</td>
<td>A</td>
</tr>
<tr>
<td>Perceptual remediation80</td>
<td>63</td>
<td>C</td>
</tr>
<tr>
<td>Limb activation/motor cueing25</td>
<td>47</td>
<td>A</td>
</tr>
<tr>
<td>Bed orientation81</td>
<td>20</td>
<td>C</td>
</tr>
<tr>
<td>Visual scanning55</td>
<td>31</td>
<td>C</td>
</tr>
<tr>
<td>Visual scanning, reading and copying35</td>
<td>23</td>
<td>C</td>
</tr>
<tr>
<td>Computerized scanning and feedback28</td>
<td>30</td>
<td>A</td>
</tr>
<tr>
<td>Prisms50</td>
<td>39</td>
<td>B</td>
</tr>
<tr>
<td>Video feedback66</td>
<td>14</td>
<td>C</td>
</tr>
<tr>
<td>Training in reading, writing and calculation31</td>
<td>25</td>
<td>B</td>
</tr>
<tr>
<td>Training in sensory awareness and spatial organization30</td>
<td>24</td>
<td>B</td>
</tr>
<tr>
<td>Head movement, scanning and feedback39</td>
<td>22</td>
<td>B</td>
</tr>
<tr>
<td>Spatial-motor assembly and scanning82</td>
<td>18</td>
<td>B</td>
</tr>
</tbody>
</table>

A = adequate, B = unclear, C = inadequate
Comparison: 01 Cognitive rehabilitation versus control treatment of spatial neglect: immediate effects
Outcome: 06 Attentional skills (WAIS–R ‘Digit Span’ or FARS ‘Attention’)

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental n</th>
<th>mean (sd)</th>
<th>Control n</th>
<th>mean (sd)</th>
<th>SMD (95% CI Random)</th>
<th>Weight %</th>
<th>SMD (95% CI Random)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gordon 1985</td>
<td>42</td>
<td>4.50 (1.40)</td>
<td>21</td>
<td>4.10 (1.30)</td>
<td>40.3</td>
<td>0.29</td>
<td>[-0.24, 0.82]</td>
<td>C</td>
</tr>
<tr>
<td>Niemeier, 1988</td>
<td>16</td>
<td>4.50 (0.89)</td>
<td>15</td>
<td>4.67 (0.98)</td>
<td>24.0</td>
<td>-0.18</td>
<td>[-0.88, 0.53]</td>
<td>C</td>
</tr>
<tr>
<td>Weinberg 1977</td>
<td>14</td>
<td>11.14 (2.41)</td>
<td>11</td>
<td>10.38 (2.45)</td>
<td>19.3</td>
<td>0.30</td>
<td>[-0.49, 1.10]</td>
<td>B</td>
</tr>
<tr>
<td>Weinberg 1979</td>
<td>15</td>
<td>11.67 (1.92)</td>
<td>9</td>
<td>10.11 (1.43)</td>
<td>16.4</td>
<td>0.85</td>
<td>[-0.01, 1.72]</td>
<td>B</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>87</td>
<td></td>
<td>56</td>
<td></td>
<td>100.0</td>
<td>0.27</td>
<td>[-0.09, 0.63]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=3.29 df=3 p=0.35
Test for overall effect z=1.47 p=0.14

Figure 2. The effect of cognitive rehabilitation at the impairment level of functioning: general attentional tasks.
Comparison: 01 Cognitive rehabilitation versus control treatment of spatial neglect: immediate effects
Outcome: 01 Activities of daily living

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight % (95% CI Random)</th>
<th>SMD (95% CI Random)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean (sd)</td>
<td>n</td>
<td>mean (sd) (95% CI Random)</td>
<td></td>
</tr>
<tr>
<td>01 Barthel Index at (discharge)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kalra 1997</td>
<td>24</td>
<td>14.20 (3.70)</td>
<td>23</td>
<td>11.70 (4.20)</td>
<td>20.2</td>
</tr>
<tr>
<td>Loverro 1988</td>
<td>10</td>
<td>57.00 (31.00)</td>
<td>10</td>
<td>77.00 (12.00)</td>
<td>15.2</td>
</tr>
<tr>
<td>Paolucci 1996</td>
<td>12</td>
<td>47.50 (10.55)</td>
<td>11</td>
<td>35.91 (13.93)</td>
<td>16.0</td>
</tr>
<tr>
<td>Rossi 1990</td>
<td>18</td>
<td>50.00 (21.20)</td>
<td>21</td>
<td>54.00 (22.91)</td>
<td>19.5</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>64</td>
<td>65</td>
<td>70.9</td>
<td>0.16 [-0.53, 0.85]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=10.60 df=3 p=0.014
Test for overall effect z=0.45 p=0.7

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight % (95% CI Random)</th>
<th>SMD (95% CI Random)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean (sd)</td>
<td>n</td>
<td>mean (sd) (95% CI Random)</td>
<td></td>
</tr>
<tr>
<td>02 FIM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beis 1999</td>
<td>7</td>
<td>101.20 (19.80)</td>
<td>8</td>
<td>97.30 (14.30)</td>
<td>13.9</td>
</tr>
<tr>
<td>Wärt 1997</td>
<td>11</td>
<td>86.00 (23.00)</td>
<td>11</td>
<td>62.00 (14.00)</td>
<td>15.2</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>18</td>
<td>19</td>
<td>29.1</td>
<td>0.74 [-0.24, 1.71]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=2.02 df=1 p=0.16
Test for overall effect z=1.48 p=0.14

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental</th>
<th>Control</th>
<th>Weight % (95% CI Random)</th>
<th>SMD (95% CI Random)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean (sd)</td>
<td>n</td>
<td>mean (sd) (95% CI Random)</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>82</td>
<td>84</td>
<td>100.0</td>
<td>0.33 [-0.23, 0.88]</td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=14.64 df=5 p=0.012
Test for overall effect z=1.15 p=0.3

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**Figure 3.** The effect of cognitive rehabilitation at the activity level of functioning.

Comparison: 01 Cognitive rehabilitation versus control treatment of spatial neglect: immediate effects
Outcome: 09 A-rated studies only – Cancellation number correct (single letter task)

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental</th>
<th>Control</th>
<th>SMD (95% CI Random)</th>
<th>Weight</th>
<th>SMD (95% CI Random)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean (sd)</td>
<td>n</td>
<td>mean (sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fanthome 1995</td>
<td>9</td>
<td>24.00 (12.90)</td>
<td>8</td>
<td>22.90 (14.30)</td>
<td>27.0</td>
<td>0.08 [-0.88, 1.03]</td>
</tr>
<tr>
<td>Kalra 1997</td>
<td>24</td>
<td>37.20 (13.10)</td>
<td>23</td>
<td>30.10 (18.50)</td>
<td>73.0</td>
<td>0.44 [-0.14, 1.02]</td>
</tr>
<tr>
<td>Total (95%CI)</td>
<td>33</td>
<td>31</td>
<td>100.00</td>
<td>0.34 [-0.16, 0.83]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity chi-square=0.40 df=1 p=0.53
Test for overall effect z=1.35 p=0.18

Figure 4. The effect of cognitive rehabilitation at the impairment level of functioning: A-rated studies only.
A selection of the results will be discussed here. This varied depending on the particular outcome measure selected out of the many used. For example, Figures 1 and 2 show the effects of therapy at the impairment level of functioning of line-bisection and general attentional tasks respectively. Analysis of the five studies which collected bisection outcome data (Figure 1) suggest a small effect in favour of those assigned to the experimental group \(-0.54 \, [-0.95, -0.14]\). However, none of these studies were A-rated. In contrast, analysis of the four studies measuring attention (Figure 2) did not suggest a difference between experimental and control groups \(0.27 \, [-0.09, 0.63]\). Again, none were A rated. Two of these four ‘attention’ studies also contributed data to the analysis of bisection data.

There was insufficient evidence to confirm or exclude an effect of rehabilitation at the activity level (Figure 3) or on destination following discharge from hospital. There was some evidence that the experimental groups made fewer errors on cancellation tasks when reassessed for persisting effects of therapy \(-0.76 \, [-1.39, -0.13]\). Furthermore, there was limited opportunity for sensitivity analyses of only the A-rated studies. In the one area where this could be performed (cancellation correct – single letter) the results contradicted the earlier positive finding (Figure 4).

Conclusions

Neither single-case designs nor the Cochrane review currently provide strong evidence that neglect therapy improves patients’ ability to perform everyday activities or increases their odds of living independently. Much of the existing research has serious design flaws, which devalue their findings. As such, there is no justification to implement any approach into current practice, unless on a trial basis. However, several approaches show promise (e.g. prisms) and the way forward may be to evaluate a combined therapy approach including cueing, feedback and active (rather than passive) involvement of the participant. The findings to date suggest that further RCTs (of higher quality and appropriate size) are warranted. A detailed epidemiological study, based on the theoretical understanding of the different types of neglect, would greatly support the development of appropriate RCTs. Neglect type-specific therapy approaches should be developed and tested. Future studies need to include activity-level outcome measures that are sufficient to detect changes in neglect behaviour. The apparent failure to demonstrate the effectiveness of therapy may be due to insensitive outcome measures, e.g. the Barthel index. A cost-effectiveness evaluation also needs to be addressed in neglect research. The Cochrane review will be updated next year and the authors would be grateful to receive information about current trials.

Acknowledgements

We are grateful to Nadina Lincoln for her support with our research in this area.

Update Software kindly approved the inclusion of Figures 1–4, which were taken from Bowen A, Lincoln NB, Dewey M. Cognitive rehabilitation for spatial neglect following stroke (Cochrane review). In: The Cochrane Library, 2002; Issue 2. Oxford: Update Software.

Cochrane reviews are regularly updated as new information becomes available and in response to comments or criticisms. The reader should consult the Cochrane Library for the latest version of a Cochrane review. Information on the Cochrane Library can be found at www.update-software.com.

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The rehabilitation of unilateral neglect: a review of the evidence


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