doi:10.1093/brain/awr077 Brain 2011: 134; 1373–1386 | 1373

BRAIN
A JOURNAL OF NEUROLOGY

Mental practice with motor imagery in stroke recovery: randomized controlled trial of efficacy

Magdalena Ietswaart,[1] Marie Johnston,[2] H. Chris Dijkerman,[3] Sara Joice,[4] Clare L. Scott,[2] Ronald S. MacWalter[4] and Steven J.C. Hamilton[5]

1 Department of Psychology, School of Life Sciences, Northumbria University, Newcastle upon Tyne NE1 8ST, UK
2 College of Life Sciences and Medicine, University of Aberdeen, Health Sciences Building, Foresterhill, Aberdeen AB25 2ZD, UK
3 Helmholtz Institute, Experimental Psychology, Utrecht University, Heidelberglaan 2, 3584 CS Utrecht, The Netherlands
4 Ninewells Hospital and Medical School, University of Dundee, Dundee DD1 9SY, UK
5 Department of Medicine for the Elderly, Grampian University Hospital Trust, Aberdeen, AB15 6XS, UK

Correspondence to: Magdalena Ietswaart, PhD,
Department of Psychology,
School of Life Sciences,
Northumbria University,
Newcastle upon Tyne NE1 8ST,
UK
E-mail: magdalena.ietswaart@unn.ac.uk

This randomized controlled trial evaluated the therapeutic benefit of mental practice with motor imagery in stroke patients with persistent upper limb motor weakness. There is evidence to suggest that mental rehearsal of movement can produce effects normally attributed to practising the actual movements. Imagining hand movements could stimulate restitution and redistribution of brain activity, which accompanies recovery of hand function, thus resulting in a reduced motor deficit. Current efficacy evidence for mental practice with motor imagery in stroke is insufficient due to methodological limitations. This randomized controlled sequential cohort study included 121 stroke patients with a residual upper limb weakness within 6 months following stroke (on average <3 months post-stroke). Randomization was performed using an automated statistical minimizing procedure. The primary outcome measure was a blinded rating on the Action Research Arm test. The study analysed the outcome of 39 patients involved in 4 weeks of mental rehearsal of upper limb movements during 45-min supervised sessions three times a week and structured independent sessions twice a week, compared to 31 patients who performed equally intensive non-motor mental rehearsal, and 32 patients receiving normal care without additional training. No differences between the treatment groups were found at baseline or outcome on the Action Research Arm Test (ANCOVA statistical $P = 0.77$, and effect size partial $\eta^2 = 0.005$) or any of the secondary outcome measures. Results suggest that mental practice with motor imagery does not enhance motor recovery in patients early post-stroke. In light of the evidence, it remains to be seen whether mental practice with motor imagery is a valid rehabilitation technique in its own right.

Keywords: motor imagery; stroke; rehabilitation; motor recovery; plasticity; therapeutic benefit
Abbreviations: ARAT = Action Research Arm Test

Received November 17, 2010. Revised February 18, 2011. Accepted March 4, 2011. Advance Access publication April 22, 2011

Introduction

Much interest has been raised by the potential of mental practice of motor tasks, also called 'motor imagery', as a neuro-rehabilitation technique to enhance motor recovery following stroke (e.g. Jackson *et al*., 2001; Braun *et al*., 2006; Sharma *et al*., 2006; De Vries and Mulder, 2007; Zimmermann-Schlatter *et al*., 2008; Dijkerman *et al*., 2010). The appeal of motor imagery as a potentially effective neuro-rehabilitation technique is popular, which is reflected in multiple reviews of relatively few reported clinical evaluations. Moreover, the studies evaluating the clinical benefit of mental practice in stroke so far are mostly small feasibility studies, while the few randomized controlled trials reported had relatively small sample sizes. As such, the evidence for mental practice in the treatment of movement disorders following stroke, and other neurological conditions, remains somewhat anecdotal.

The idea of mental practice as a neuro-rehabilitation technique relies on sound and engaging evidence. Over the past decade, a wealth of data have demonstrated that the brain simulates action and other functions. For example, studies by Decety and colleagues (1996) have shown that imagery of movement activates largely the same brain areas that are activated when movements are actually executed. Furthermore, even passive observation of movement has been shown to activate cortical motor areas (Grezes and Decety, 2001). This fuelled an understanding that if mental simulation of action triggers neural activations of relevant motor areas then we can 'jog' the brain in the absence of movement execution. This potential is significant in light of evidence emerging over the last two decades demonstrating that brain plasticity has an intrinsic role to play in recovery following brain damage. In particular, recovery of motor function after stroke is accompanied by a redistribution of activity within a network of parallel-acting multiple cortical motor areas (Weiller, 1995; Marshall *et al*., 2000) and reinforcement of the spared area adjacent to the lesion (Nudo *et al*., 1996). The theoretical neuroscience basis for the potential clinical benefit of mental practice in the recovery of motor function is therefore generally described in neurophysiological terms—imagining movements could stimulate restitution and redistribution of brain activity, which accompanies recovery of motor function, thus resulting in reduced deficit.

A strong case to capitalize on brain plasticity processes in neuro-rehabilitation was made by Robertson and Murre (1999). They proposed that so-called 'guided-recovery' can 'rescue' lesioned circuits by activating the specific circuits through 'precise targeted bottom-up and top-down inputs'. These authors elegantly describe how a process based on the Hebbian-learning principle that 'cells that fire together, wire together' can induce recovery. They make an important distinction between the 'spontaneous' Hebbian-learning-based process of self-repair, and 'targeted stimulation', which they claim can induce restitution of function through the same Hebbian-learning-based reconnection of neural connectivity. They propose that by providing additional input to damaged networks, a degree of completion may be facilitated that would not be possible without such external, patterned input. Mental practice as a neuro-rehabilitation technique would be a prime example of such 'guided-recovery'.

Physical practice has been shown to induce reorganization of the areas adjacent to focal ischaemic infarction in the primary motor cortex in monkeys (Nudo *et al*., 1996). Furthermore, neuroimaging studies have demonstrated cortical functional reorganization associated with recovery of hand function after 3–4 weeks of physical training in acute (Nelles *et al*., 2001) and chronic stroke patients (Carey *et al*., 2002; Jang *et al*., 2003). Whether mental practice alone can promote the modulation of neural circuits, inducing the same plastic changes in the motor system as those following repeated physical practice, is still to be substantiated. Studies with healthy volunteers have provided evidence for functional redistribution following motor imagery training (Pascual-Leone *et al*., 1995; Jackson *et al*., 2003). Furthermore, there is some preliminary evidence for this effect in stroke from a single case study of a stroke patient showing reorganization within sensorimotor areas of the injured hemisphere following motor imagery training (Johnson-Frey, 2004). Some further tentative evidence comes from a case series reported by Butler and Page (2006) and a recent small group study by Page and colleagues (2009), the latter reporting changes in cortical activation in primary, premotor and superior parietal areas of 10 chronic stroke patients following 10 weeks of motor imagery training, although no control group was included. Functional reorganization following mirror therapy has also been demonstrated in the neurologically intact brain of phantom limb patients (Giraux and Sirigu, 2003).

Further to the neuroscientific argument for mental practice in stroke, we also see a health psychology argument related to perceived control. There is evidence that patients' beliefs that they have control over their recovery predicts the amount of motor recovery achieved, controlling for initial levels of cognitive and motor impairment (Partridge and Johnston, 1989; Johnston *et al*., 1999; Bonetti *et al*., 2008) and is predictive up to 3 years following stroke (Johnston *et al*., 2004). However, the process by which control beliefs determine outcome is unclear. Actual engagement in rehabilitation exercises has been hypothesized as a mechanism but the evidence does not offer support (Johnston *et al*., 1999). Alternatively, patients high in perceived control may spontaneously engage in mental practice, which might explain the effects of perceived control on recovery. Furthermore, mental practice offers an attractive clinical rehabilitation option, as it would allow patients to practice motor tasks frequently and safely.

Reported clinical evaluations of mental practice in stroke so far have mostly found at least some evidence to suggest a therapeutic benefit. However, it should be noted that possible publication bias may exist with regards to the effectiveness of mental practice, where similar small studies finding negative results would be dismissed as lacking in power. Positive findings are reported in case studies of both chronic stroke patients (Page *et al*., 2001*a*; Stevens and Stoykov, 2003; Johnson-Frey, 2004; Liu *et al*., 2004; Gaggioli *et al*., 2006) and a patient a few months post-stroke (Jackson *et al*, 2004). Evidence also came from a series of feasibility studies including 4–10 patients in the treatment group who were either years post-stroke (Page, 2000; Crosbie *et al*., 2004; Dijkerman *et al*., 2004; Page *et al*., 2005, 2009) or <1 year post-stroke (Page *et al*., 2001*b*; Butler and Page, 2006;

Mueller *et al*., 2007). To date, the results of three small randomized controlled trials have been reported. The randomized controlled trial by Liu and colleagues (2004) examined the effect of combined physical and mental practice of activities of daily living, such as folding laundry and going to the park, in patients 2 weeks post-stroke compared to the control group performing the same activities physically only. They found higher levels of independence on trained and untrained activities of daily living in the mental practice group; however, they failed to find enhanced recovery on the standard Fugl–Meyer Assessment of upper-limb motor function in this group. In a recent study (Liu *et al*., 2009) these training effects were further documented, but no reference was made to standardized measures of motor recovery. A second randomized controlled trial by Page and colleagues (2007) found improved upper limb function after combined physiotherapy and motor imagery training in chronic stroke patients. Yet the study sample size was only 16 patients per group, and the therapeutic benefit they found was associated with a high effect size. Bovend'Eerdt *et al*. (2010) published the findings of a randomized controlled trial involving 15 (mostly stroke) patients planned to receive motor imagery training embedded in usual physical therapy, compared to 15 patients receiving standard therapy only. The authors of the study report to be unable to draw conclusions about the effectiveness of their embedded motor imagery programme due to low therapist and patient treatment compliance. The authors furthermore deemed their sample size insufficient.

The fact that these studies included a self-selecting sample from a small pool of volunteers recruited through advertising in rehabilitation centres, and the fact that these patients were often years post-stroke, is potentially problematic, as these patients may not be representative of the clinical population set to benefit from this technique. In addition, the studies reported to date may also suggest that the effect of mental practice may be no more than consolidation of particular movements in those patients that can cope with the cognitive demands of mental practice and for whom motor imagery ability is not compromised by sustained brain damage. We found some evidence for this in a feasibility study we conducted (Dijkerman *et al*., 2004) when we observed that mental practice gave rise to enhanced motor performance on the trained task but not on other motor tasks. In this earlier work, we combined physical and mental practice and found that the enhanced performance in the experimental motor imagery group, compared with the group that engaged in physical but not mental practice of this task, was limited to the actual trained task, and was not associated with a more generalized recovery. To exclude the possibility that mental practice does nothing but consolidate particular movement patterns, it is necessary to demonstrate the benefit of mental practice offered separate from a programme of physical practice. Only when mental practice is shown to work independently of physical practice, can claims about mechanisms of brain plasticity be sustained (as also suggested by Sharma *et al*., 2006). Furthermore, if the underlying mechanism of the benefit of mental practice is related to the process of brain plasticity, one would expect this to be most beneficial when the process of plasticity is most active in the first 6 months post-stroke (Robertson and Murre, 1999).

Finally, if mental practice is of general applied clinical value it is necessary to demonstrate the benefit in a sequential cohort study that is sufficiently powered. We sought to investigate whether any effects of mental practice observed were due to the specific effects of mental practice or simply due to the non-specific effects of additional therapist attention and encouragement. Here, we report a single-blind randomized controlled trial in which a large sample of unselected stroke patients within 6 months following stroke undertook a programme of either 4 weeks of motor imagery training, or a control training programme, or received normal care. The protocol for this study has been published (Ietswaart *et al*., 2006). Due to the fact that the intervention was developed on the basis of basic neuroscientific evidence (as suggested by Ian Robertson and colleagues, e.g. Robertson and Murre, 1999), it is necessary to provide further details with regards to the intervention rationale.

Intervention rationale

This mental practice with motor imagery intervention consists of a training programme that has been specifically developed to promote recovery of hand function through motor imagery by recruiting areas of the brain that could stimulate functional redistribution of brain activity (e.g. Annett, 1995; Decety and Grezes, 1999; Decety and Chaminade, 2003). As such, each task in the programme was chosen on the basis of evidence from cognitive neuroscience showing the task to activate motor areas in the brain. The nature of mental practice in this trial consistently emphasized the internal kinaesthetic image of movement, and task facilitation was geared towards this. At all times, patients were asked to imagine the movements from an internal, first person perspective and to employ kinaesthetic imagery, engaging the sensations of what it feels like to do the movements (Jeannerod, 1994). All tasks focused on the affected upper limb.

The idea is that conscious access to motor memories during motor imagery and mental training is achieved at the cortical level through a specific pattern of activation that closely resembles that of action execution, leaving the motor system in an active state of rehearsing the content of the motor representations (Jeannerod, 1995). Due to the cognitively demanding nature of mental practice with motor imagery, careful consideration in designing the intervention was given to ways of facilitating the motor imagery process, again drawing on the cognitive neuroscience evidence base. In the design, such means to facilitate were based on a rich emerging research literature, demonstrating that a wide range of sensory inputs can trigger action simulation in the brain (e.g. Grafton, 2009). For example, visual and auditory inputs can facilitate accessing the content of motor images. Therefore, verbal information was implemented because current motor cognition theories (e.g. Jeannerod, 2001), which suggests that language resonates with motor representations, and activation of motor areas can therefore be achieved through the verbal route (e.g. Barsalou, 2008). In the same way, the use of objects was implemented in motor imagery training, as it has been shown that visual perception of objects affords action (e.g. Grezes and Decety, 2001). Pictorial depiction of movement was implemented because this has also been shown to trigger action simulation (e.g. Handy *et al*., 2005). Finally, action observation was implemented throughout the intervention to facilitate motor imagery, because passive observation of movement has been shown to activate cortical motor areas (Grezes and Decety, 2001), as was discussed in the 'Introduction' section. Although action observation is sometimes considered a technique separate from motor imagery, the rationale to employ both arises from the perspective that the aim of the intervention is to evoke action simulation in the brain (Jeannerod and Decety, 1995). Action observation was implemented by asking patients to observe each movement that they were subsequently asked to imagine.

Following the rationale that verbal and visual information can facilitate the motor imagery process, verbal facilitation during active motor imagery was achieved through the use of scripts recited by the therapists training the patients. These detailed scripts described the muscular sensations of the movements. Face validity of the scripts for each movement was established through consultation with physiotherapists, and scripts were thought to maximize kinaesthetic imagery by referring to the correct muscle groups. Motor imagery was further maximized through action observation of the therapists making the actions. Verbal facilitation and action observation were emphasized during motor imagery of elementary movements. Training of goal-directed movements such as reaching and grasping was further facilitated by the presence of graspable objects. Training of activities of daily living made use of pictorial information or the presence of the objects involved in the movement.

As the intervention aims to evoke action simulation in the brain (Jeannerod and Decety, 1995), it may be justified to further incorporate other techniques that have been shown the evoke action simulation. Mirror therapy is one of these techniques, as is mental rotation of hands. Mirror therapy, as suggested by Ramachandran and Rogers-Ramachandran (1996), makes use of the so-called mirror box where patients look at the reflection of uncompromised movement made by the unaffected hand, which evokes the illusion of the impaired hand moving. This has been shown to improve recovery of hand weakness in stroke (Altschuler *et al*., 1999; Stevens and Stoykov, 2003; Yavuzer *et al*., 2008) as well as lift phantom limb pain in amputees (Ramachandran and Rogers-Ramachandran, 1996; Moseley, 2006). The underlying mechanism of mirror therapy is thought to be brain plasticity of motor areas induced by covert motor imagery (Giraux and Sirigu, 2003). Mirror therapy in the current intervention was a structured activity and included a range of elementary movements recruiting different muscle groups, as well as a few minutes where the patient could do any movements they liked. Patients were asked to imagine they were looking at their impaired hand making the movements, but to keep the impaired hand still. A second task similar to the mirror movement illusion was developed for the current training making use of video, utilizing the mechanisms of both action observation and illusion of movement. Akin to the rationale of using mirror therapy to evoke covert motor imagery, the video set-up aimed to maximize motor imagery processes and thus the potential effects of this training. During this task, the patient placed their hand under a video display of a hand making elementary movements such as described above for mirror therapy. Because the display of the moving hand is in a proprioceptive location and visually close to that of the patient's own hand placed under the display, watching the video gives a strong illusion of the own hand moving. To maximize this illusion of movement, patients were asked to imagine it was their own hand making the movements. In the current intervention ~25% of training time involved the use of mirrors and video (see 'Materials and Methods' section for details on the organization of the intervention).

Certain task features further justify the use of mirrors and video in the aim to achieve optimal action simulation in the brain as part of this motor imagery intervention. Holmes and Collins (2001) draw on the evidence of motor imagery efficacy in sports when advocating that motor imagery intervention design should consider the different aspects that strengthen the motor memory trace according to their model. Holmes and Collins (2001) describe how the physical position of the patient should be active and compatible with the actions, as was the case in current intervention, and should not be relaxed or removed from the scene of action. They further stress the role of environment, which is why the intervention aimed to be meaningful, and multisensory. They suggest that to consider the role of task, which is why objects were present where possible in the intervention. Finally, Holmes and Collins (2001) demonstrate how timing needs consideration in optimizing mental practice, which is why the natural movement tempo in the use of mirrors and video was important in the current intervention.

Although the tasks using video and mirrors were believed to involve automatic recruitment of motor activation, they all required the patient to engage in active motor imagery of the internal kinaesthetic image of movement. To utilize a purely covert form of motor imagery, a final task of mental rotation of visual depictions of hands was included in the intervention. This task involved judging handedness through mentally simulated action, as suggested by Parsons (1994). Parsons and others have shown that mental rotation of hands recruits motor imagery and activates motor areas (Parsons 2001).

To control for non-specific effects of mental practice with motor imagery that may induce improvement through mechanisms unrelated to those under evaluation, it is necessary to compare this treatment to more than a simple placebo condition. A methodological weakness of previous mental practice evaluations is that they used placebo conditions such as relaxation which, while controlling for attention, do not control for other non-specific aspects of the intervention, i.e. parts of the intervention that are necessary to deliver the intervention, but are not the theoretically active components. Therefore, two control conditions were included in the design of this trial. An attention-placebo control condition was included to control for both cognitive and motivational non-specific effects. Cognitive non-specific aspects of mental practice were carefully mapped on a control treatment condition, again drawing on the cognitive neuroscience evidence base. This condition also served to control for motivational aspects such as therapist attention and a potentially significant efficacy belief. A second routine-care control condition was included to confirm that any differences between the experimental and placebo-control treatment would indicate clinical benefit of the experimental treatment, rather than a negative effect of the placebo-control.

Table 1 **Demographic and clinical characteristics at baseline for the experimental 'Motor Imagery Training' treatment group, the 'Attention-Placebo Control' group and the 'Normal Care Control' group**

	Motor Imagery Training (*n* = 41)	Attention-Placebo Control (*n* = 39)	Normal Care Control (*n* = 41)
Age in years (SD)	69.3 (10.8)	68.6 (16.3)	64.4 (15.9)
Gender (male/female)	23/18	22/17	25/16
Education in years (SD)	10.6 (1.7)	10.6 (1.4)	10.3 (1.7)
Hospitalization (in-patient/out-patient)	31/10	32/7	31/10
Lesion side (left/right/subcortical or bilateral/no data)	13/16/10/2	12/12/10/5	18/12/9/2
Side of weakness (left/right)	24/17	23/16	22/19
Time post-stroke in days (SD)	82.0 (55.0)	90.8 (63.4)	80.5 (62.7)
Spontaneous motor imagery use (yes/no/no data)	14/18/9	14/13/12	14/16/11
Receiving other rehab therapy (yes/no)	33/8	35/4	34/7
MSQ score out of 10 (SD)	8.9 (1.0)	8.7 (1.2)	9.1 (0.9)
HADS score out of 42 (SD)	13.4 (7.8)	13.7 (7.7)	13.2 (8.0)
Location baseline assessment (hospital/home/university)	27/9/5	29/7/3	28/9/4
Baseline and outcome at same location (yes/no)	38/3	34/5	41/0

HADS = Hospital Anxiety and Depression Scale; MSQ = Mental Status Questionnaire.

This trial evaluated the clinical benefit of mental practice with motor imagery compared to these two control conditions.

Materials and methods

Please refer to the published protocol (Ietswaart *et al*., 2006).

Participants

This multi-centre trial involved the cohort of patients with suspected stroke, admitted over a period of 2 years and 7 months, to three Scottish hospitals providing acute care. National Health Service Grampian and National Health Service Tayside ethical review boards governing each clinical centre approved the study protocol REC Number 0310299, and written informed consent was obtained from each participant. The Clinical Trial Registration for this study is NCT00355836.

Patients were not considered for participation in the trial if (i) they were discharged from hospital within 1 week; (ii) did not present with an upper limb motor weakness; or (iii) the medical team sought discharge to a nursing home rather than a stroke rehabilitation setting or home, which was taken as the exclusion criterion of a limited rehabilitation potential.

The following inclusion criteria were applied: (i) a history of stroke 1–6 months prior to participation in the project; (ii) Action Research Arm Test (ARAT) score of between 3 and 51 (maximum score 57; Lyle, 1981) indicating a persistent motor weakness with the preserved ability to make some movement with the affected arm; (iii) no alcohol dependency or evidence of substance abuse; (iv) no severe cognitive impairment (Mental Status Questionnaire score of 7 or more; Kahn *et al*., 1981); and (v) no severe aphasia [based on clinical notes and verified at baseline assessment using 10 representative items of the language comprehension Token Test (De Renzi and Faglioni, 1978; items 1.1–2; 2.1–2; 4.1–2; 6.1–2; 6.4–5, passing 8/10 trials or more)].

Recruitment and allocation procedures

Patient details of all stroke admissions were routinely recorded by stroke coordinators at the different acute hospitals. Using a detailed recruitment protocol, all stroke admissions were considered for inclusion in the study. Patients were approached about the study in the first month post-stroke or as soon as patients were medically stable thereafter. All eligible patients were given written information in person during their hospital stay or through a letter from the responsible clinician if the patient had already been discharged. Consenting participants were screened by members of the research team who also conducted the baseline assessment. Depending on patients' admission status, baseline assessment took place in a quiet room in the hospital in the case of in-patients, while out-patients were assessed at a university laboratory where possible, or at the patient's home if required (Table 1). Where possible, patients were assessed in the same situation at baseline and outcome assessment (Table 1).

Within 1 week after baseline assessment, randomization took place following a statistical minimization procedure (Pocock, 1983). Group allocation was based on five stratification factors: age, sex, severity of motor impairment (baseline ARAT score), side of brain damage (left hemisphere, right hemisphere, or bilateral damage) and the time post-stroke. The randomization process was automated and the data for randomization were entered by the research therapists. This research therapist also delivered the intervention, and was never the assessor at baseline or outcome. This ensured that assessors remained blinded to the patients' group allocations for the full duration of the trial. Any unblinding was recorded.

Patients were informed about group allocation by the research therapist, and intervention always commenced within one week after baseline assessment. The researchers involved in intervention delivery all had a psychology or occupational therapy qualification. They were researchers employed in an academic setting and were not part of the patients' clinical team. Based on detailed operational manuals devised for this study, extensive training was given by experienced members of the research team to ensure that all research therapists and assessors had a full grasp of the operational procedures of assessment or intervention. Several hours of cross-validation took place throughout the study involving each of the researchers, to ensure consistency in assessment and intervention delivery. Because research therapists were not part of the clinical team, they were a different person from the therapists providing standard care physical rehabilitation or any other normal care. The clinical team was not informed by the research team about treatment allocation of patients in their care.

All patients received standard treatment for stroke in terms of medical care and rehabilitation. Treatment as part of the intervention was additional to the patients' standard medical care and rehabilitation. Consenting patients entered the trial as soon as possible after the first month following stroke.

Eligible patients were randomly assigned to one of three groups: the experimental patient group and two control patient groups. The experimental group received training in motor imagery (the 'Motor Imagery Training' group). Patients in the first control group received equally intensive training involving other forms of mental rehearsal that were not related to motor control, such as visual imagery of objects ('Attention-Placebo Control' group). Patients in the second control group received normal care with no additional training ('Normal Care Control' group).

Outcome measures

Outcomes were evaluated by a blinded assessor 5 weeks after the baseline assessment, when any training had been completed. The primary outcome measure was the ARAT (Lyle, 1981), designed to assess recovery of the upper extremity function following cortical injury. The test included four subscales: grasp, grip, pinch and gross movement. Secondary outcome measures included motor recovery assessment of grip strength measuring the force applied with the affected hand compared to the unimpaired hand using a dynamometer (Heller *et al*., 1987), and hand function through timed manual dexterity performance (Dijkerman *et al*, 2004). The latter task formed an integrated part of the motor imagery- and attention-placebo control training programmes, as this timed manual dexterity task demonstrated the beneficial effect of motor imagery training in a preliminary study of this work (Dijkerman *et al*., 2004).

Levels of independence and functional limitations were evaluated with regards to Activities of Daily Living using the Barthel Index (Mahony and Barthel, 1965), and disability using the modified Functional Limitation Profile (Pollard and Johnston, 2001), covering items of ambulation, body care, mobility, alertness and communication.

Process measures

The ability to perform mental practice was evaluated as part of this trial by looking at individual differences between patients in motor imagery ability, as this ability may vary depending on lesion site (Sirigu *et al*., 1996) and hand function (Parsons *et al*., 1998, Nico *et al*., 2004). Motor imagery ability was assessed through a mental chronometry task assessing the ability to predict, through mental imagery, the time necessary to perform movements (Sirigu *et al*., 1995; Malouin *et al*., 2008). Imagined and executed finger thumb opposition with the unaffected hand was performed once, twice or three times in a row. As a measure of motor imagery ability we took the difference in the slope of the regression line through the data points of performing (actually executing) a particular movement once, twice and three times, and the slope of the estimated timing (predicted through engaging in motor imagery) of the same movements, with the unaffected hand and measured at baseline. To compare patients' performance on this measure with neurologically intact participants, 32 healthy age-matched controls were recruited. These control participants were volunteers recruited through local advertising, as approved by the ethics committee of Northumbria University's School of Psychology and Sports Sciences. They were 16 male and 16 female volunteers aged between 53 and 84 years (mean age 66.88; SD = 8.02) and were all right handed with no history of brain damage. All patients were also asked at baseline assessment whether they did motor imagery or mental practice of movements of their own accord (spontaneous motor imagery).

Perceived control was measured using the Recovery Locus of Control scale (Johnston *et al*., 1999). Emotional distress was assessed with the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983), and mental status was assessed with the Mental Status Questionnaire (Kahn *et al*., 1981).

Intervention and control group procedures

Research therapists worked with patients on a one-to-one basis during 45-min training sessions 3 days a week. Patients further engaged in 30-min previously instructed training sessions working independently twice a week. Training was provided for 4 weeks. Depending on patients' admission status, in-patients received supervised training in a quiet room in the hospital, while out-patients were visited at home (Table 1). The experimental and attention-placebo control groups had the same duration of therapist contact and each therapist trained an equal number of patients in each group.

Motor imagery intervention

Twelve highly structured 45-min sessions were developed for the purpose of supervised patient motor imagery training. All activities were standard tasks following a detailed operational manual that did not allow tasks to be individualized. Each session was organized to maximize the engagement of the patient by offering a range of shorter closely supervised tasks. Active motor imagery was structured to include verbal facilitation, the presence of objects, pictorial scenes, and action observation, as described in the above intervention rationale.

The mental practice with motor imagery sessions were structured as follows:

(i) The first 30 min of each session was reserved for mental practice actively imagining a variety of elementary movements (such as opening and closing of the hand, wrist rotation, arm elevation), goal directed movements (such as reaching, grasping and lifting household objects), and activities of daily living (such as ironing, washing under the arms or doing buttons on a shirt). Goal directed movements included mental performance of the timed manual dexterity task (Dijkerman *et al*., 2004), the physical performance of which was described as one of the outcome measures above.

(ii) A further 10 min per session was reserved for active motor imagery using mirrors and video, as described above in the intervention rationale. The use of mirrors or video was alternated between sessions.

(iii) The final 5 min of each session was reserved for a covert form of motor imagery activity of mentally rotating visual depiction of hands, judging handedness through mentally simulated action, as described in the above intervention rationale.

In addition to the above supervised sessions, the intervention included a further eight structured independent sessions. Patients had a bag with materials and were guided through each of the tasks through verbal instruction on an audio tape. These were 30-min audio-paced training sessions and incorporated the elements of active motor imagery with verbal and visual facilitation as described above. The motor imagery tasks during homework sessions were imagined movements including: (i) elementary movement sequences; (ii) reaching and grasping with objects present; (iii) tracing movements; and (iv) activities of daily living using pictorial flip books.

Independent sessions took place on the days between supervised sessions, and the research therapist would discuss the independent session with the patient during the supervised session before and after the day the patient worked independently. Patients were asked to keep a log book of these independent practice sessions, recording the time of day and ticking the activities included on the audio instructions. The log book entry was then discussed with the research therapist the following day, to address any problems patients may have had with independent practice.

Attention-placebo control intervention

For comparison of the effectiveness of the motor imagery training programme, a visual imagery control programme was developed to serve as the attention-placebo control training programme. This training programme was carefully devised to control effectively for the motor imagery intervention. This included controlling for therapist attention, as well as the cognitive functions indirectly recruited during motor imagery that could account for non-specific effects of motor imagery training. Therapist attention was controlled for by closely matching the intensity of the training to the experimental training programme, matching the frequency and duration of therapist and homework sessions, as well as matching the belief in the effectiveness of the training that the researcher may convey to the patient. Cognitive demands that were controlled for included sustained attention, visualization, memory demands, visual illusions, and inhibition. As in the experimental training, it was attempted to facilitate imagery through visual information and verbal description throughout.

Twelve highly structured 45-min sessions were developed for the purpose of supervised patient attention-placebo control training, and were structured as follows. The first 25 min of each session was reserved for active visual and sensory imagery using a variety of short tasks: (i) visualizations of static objects like fruit, flowers and buildings, based on pictures; (ii) visualization of static scenes, recalling visual and sensory information based on verbal description; (iii) imagery of sensory temperature sensation on the skin based on depictions of climate information, such as sunshine or blizzard; (iv) imagery of smell association based on pictures and verbal description, such as the smell of coffee or a bakery setting; and (v) scene recall of landscapes or static scenes based on video and pictures.

A further 10 min per session was reserved for tasks controlling for cognitive inhibition. The inhibition tasks performed were: (i) delayed answer, requiring giving the response to a previous question; and (ii) a so-called Stroop task, such as reading aloud the word green printed in red ink.

A further 5 min per session required patients to watch optical illusions of motion, such as the waterfall illusion. The final 5 min of each session was reserved for a visual imagery activity of mentally rotating visual depictions of objects, judging left and right orientation.

Each session was concluded with a movement familiarization and consolidation procedure of the timed manual dexterity task (Dijkerman *et al*., 2004) described as one of the outcome measures above. This was achieved performing the task with the unaffected arm. Mental practice of this task was integrated in the experimental training programme above.

In addition to the above supervised sessions, the intervention included a further eight structured independent sessions. Patients had a bag with materials and were guided through each of the tasks through verbal instruction on an audio tape. These were 30-min audio-paced training sessions and incorporated the elements of visual and sensory imagery described above. The organization of independent sessions was as described for the motor imagery intervention above.

Power and statistical analysis

A power analysis was conducted to estimate the different power values for a range of sample sizes at various nominated effect sizes (small, medium and large, according to Cohen, 1992) and is reported in Table 2. This analysis was applied to the ANCOVA model at a 5% significance level, entering anticipated means into the model based on previous studies that have examined the effect of intervention programmes using the same primary outcome measure (ARAT), reporting a difference in excess of eight units, which might be regarded as indicating a meaningful clinical benefit (Van der Lee *et al*., 1999; Dromerick *et al*. 2000; Page *et al*., 2001*b*).

Any statistical group differences at baseline were explored with one-way ANOVAs, while descriptive statistics were used to explore group differences on nominal measures such as gender. Overall recovery between baseline and outcome assessment was analysed as the factor 'time' in a repeated measurements ANOVA for each of the outcome variables. To examine the therapeutic benefit of mental practice with motor imagery, separate analyses of variance analysed the differences between the three treatment groups in the change from baseline to post-training assessment for both primary and secondary outcome measures, using analysis of covariance (ANCOVA) with pre-intervention assessment entered as a covariate (Dimitrov and Rumrill, 2003). Assuming that pre-intervention assessment will be highly correlated to post-intervention assessment, this analysis further increases the power of the study.

For completeness, an intention-to-treat analysis was also conducted, including all patients that had entered the study regardless of whether they completed the trial, using multiple regression methods for imputation of missing values. This analysis used a generalized linear model with simple contrasts comparing the experimental group with each of the two control groups, with as covariates the five stratification variables used in the minimization procedure and any variables with significant baseline differences between groups.

Table 2 Percentage power to detect differences between the three groups at error level (alpha) 0.05 for ANCOVA when there is a small, medium or large effect size according to Cohen (1992) for a range of sample sizes, including the recruited sample size (n = 121) and the number of completions (n = 102)

	n = 140	n = 121	n = 102	n = 80
Small, f = 0.1	17%	15%	13%	11%
Medium, f = 0.25	75%	68%	60%	49%
Large, f = 0.4	99%	98%	95%	89%

Group differences on motor imagery ability were analysed with a repeated measurements analysis of variance with 'mode' (predicted versus actual performance) as within subject factor and treatment group (motor imagery training, attention-placebo control, or normal care control) or healthy control group (patient versus healthy age-matched controls) as between-subject variable. The relationship between motor imagery ability and outcome was explored through correlations, taking as measure of motor imagery ability the difference in slope between predicted and actual performance expressed as a proportion of actual performance.

Results

Recruitment

Participants ($n = 121$) were recruited from a consecutive cohort and reported following the Consolidated Standards of Reporting Trials statement (Moher *et al*., 2001) summarized in Fig. 1.

Recruitment took place within two acute National Health Service Trusts in the North-East of Scotland over a period of 2 years and 7 months, considering 2521 in-patients for participation in this trial. Of these patients, 250 patients died, 624 were discharged from hospital within 1 week with suspected transient ischaemic attack, 248 patients were given a diagnosis other than stroke, in 12 patients stroke was not confirmed, 222 patients could not be followed up as part of the study because they lived >50 miles away, and 36 patients could not take part in the study because they were already recruited to a conflicting research study.

Of the 1129 patients with a confirmed diagnosis of stroke, 463 patients were excluded because they did not present with an upper limb motor weakness within the criteria of this study (including 353 patients with no or a very mild motor weakness and 10 patients with gross motor deficits), 170 patients were excluded because the medical team sought discharge to a nursing home rather than a stroke rehabilitation setting or home, which was taken as the exclusion criterion of a limited rehabilitation potential, 195 patients were excluded because of issues of comorbidity, and 11 patients were excluded because they were medically unwell. Seventy-nine patients were still under review at the close of the study.

In total, 211 patients were invited to take part in the study with 86 patients declining. A total of 125 patients consented to participate, completed the baseline assessment, and entered into the minimization procedure for randomization. Four patients were randomized in error, and were excluded because they had an ARAT score above the inclusion criterion of ARAT score 51. Therefore, 121 were assigned to one of the three treatment groups (see Table 1 for demographic and clinical data). From the patients assigned to the 'Motor Imagery Training' group one patient died, and one patient requested withdrawal from the trial. From the patients assigned to the 'Attention-Placebo Control' group one patient died, four patients requested withdrawal from the trial, and a further three patients dropped out because they became medically unwell. From the patients assigned to the 'Normal Care Control' group one patient died, six patients requested withdrawal from the trial, one further patient withdrew because he/she was medically unwell, and one patient did not complete the primary outcome measure during the outcome assessment. Therefore, in the experimental 'Motor Imagery Training' group 39 of 41 randomly allocated patients completed the trial, in the 'Attention-Placebo Control' group 31 out of 39 patients completed the trial, and in the 'Normal Care Control' group 32 out of 41 patients completed the trial.

All incidences where an assessor was unblinded to a patient's group allocation were recorded, and the achieved blinding success over the trial was 86% of patients.

Baseline differences

Randomization, using a statistical minimizing procedure, was successful and no group differences at baseline were found on the primary outcome measure or any of the other stratification factors (age, sex, side of brain damage and time post-stroke) as illustrated in Table 1. Neither were there baseline differences on any of the other demographic or clinical characteristics shown in Table 1. No group differences at baseline were found on any of the secondary outcome measures (Table 3).

Outcome

Recovery between baseline and outcome assessment was evident on all outcome variables, as is apparent from the means summarized in Table 3 (the main effect of time had $P < 0.001$ and effect sizes $0.170 < \eta_p^2 < 0.432$ for all outcome variables). However, no differences between the three groups were found on the primary outcome measure, the ARAT (Table 3). Neither were there differences between the groups on any of the secondary outcome measures: activities of daily living level of independence (activities of daily living Barthel Index), the Functional Limitation Profile or the more sensitive motor measures of grip strength or speed of performance on the timed manual dexterity task (Table 3). The very small effect sizes ($0.001 < \eta_p^2 < 0.019$; Table 3) demonstrate that the absence of group effects should not be viewed as a lack of power (Table 2). The additional intention-to-treat analysis rendered very similar results, showing no greater recovery on any of the outcome measures in the experimental 'Motor Imagery Training' group compared to either the 'Attention-Placebo Control' group (e.g. on ARAT primary outcome measure [$F(1,79) = 1.77$, $P = 0.39$ with confidence interval (CI) = (−2.26, 5.80)] or the 'Normal Care Control' group e.g. on ARAT [$F(1,82) = 0.76$, $P = 0.71$ with CI = (−3.21, 4.72)].

Improvement on the primary outcome measure, the ARAT score, correlated with improvement on the secondary outcome measures of activities of daily living level, ($r = 0.23$, $P < 0.05$), manual dexterity performance speed ($r = -0.60$, $P < 0.001$), and Function Limitation Profile ($r = -0.25$, $P < 0.01$), but not with grip strength ($r = 0.12$, n.s).

Mental status questionnaire score at baseline showed a significant relationship with improvement on activities of daily living level ($r = -0.26$, $P < 0.01$) but not with improvement on any of the other outcome measures ($P > 0.12$). Levels of depression and anxiety (Hospital Anxiety and Depression Scale score at baseline) did not demonstrate a significant relationship with improvement on any of the outcome measures ($P > 0.06$), and neither did

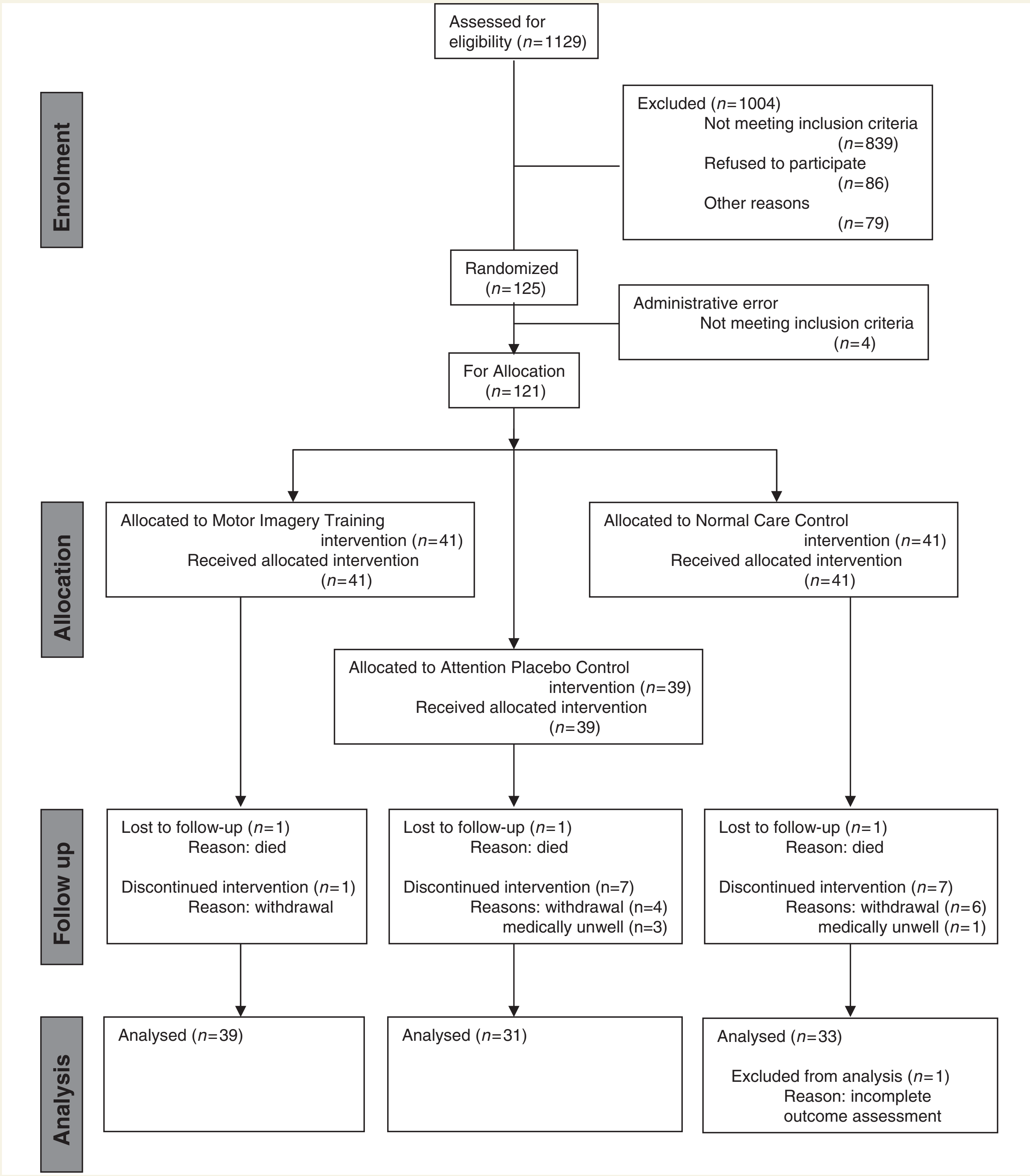

Figure 1 Flow diagram summarizing the passage of participants through the stages of the trial.

perceived control over recovery [Recovery Locus of Control scale score at baseline and change on the ARAT; $P > 0.73$; even when controlling for initial cognitive (Mental Status Questionnaire) and motor (ARAT) impairment; $P > 0.38$]. Therefore, as we did not find a relationship between the patients' beliefs that they have control over their recovery and the amount of motor recovery achieved, we excluded this measure from further analysis.

Motor imagery ability

There were no differences in motor imagery ability between the treatment groups [$F(2,97) = 0.65$, $P = 0.52$, $\eta_p^2 = 0.01$). Control data collected with age-matched neurologically intact healthy volunteers ($n = 32$) on the same measure with the right hand, suggests no difference in motor imagery ability between participants

Table 3 Mean performance and ANCOVA analysis group differences on primary and secondary outcome measures, for the experimental 'Motor Imagery Training' treatment group, the 'Attention-Placebo Control' and the 'Normal Care Control' group

Group	*n*	Baseline assessment	Outcome assessment	Between group difference	
		Mean (SD)	Mean (SD)	*P*-value	η_p^2
Upper limb impairment (ARAT)					
Motor Imagery Training	39	25.64 (18.10)	31.51 (20.68)	0.77	0.005
Attention-Placebo Control	31	26.23 (17.92)	32.87 (20.76)		
Normal Care Control	32	23.06 (17.66)	30.38 (20.53)		
Grip strength (force affected/unaffected hand, %)					
Motor Imagery Training	39	32.64 (34.17)	38.15 (36.07)	0.60	0.000
Attention-Placebo Control	31	27.90 (29.95)	34.55 (34.84)		
Normal Care Control	32	25.12 (27.97)	34.32 (33.80)		
Hand function (manual dexterity performance speed in s)					
Motor Imagery Training	39	121.46 (53.32)	104.44 (55.93)	0.98	0.000
Attention-Placebo Control	31	109.30 (54.17)	95.71 (57.59)		
Normal Care Control	32	124.02 (52.29)	107.28 (56.20)		
Activities of daily living level (Barthel Index)					
Motor Imagery Training	39	13.08 (4.81)	16.23 (4.13)	0.38	0.019
Attention-Placebo Control	31	14.87 (4.33)	16.84 (3.75)		
Normal Care Control	32	12.28 (5.41)	14.87 (4.79)		
Functional limitations profile					
Motor Imagery Training	38	58.40 (15.02)	50.28 (18.78)	0.98	0.000
Attention-Placebo Control	31	64.16 (14.04)	55.42 (15.81)		
Normal Care Control	31	62.50 (14.26)	53.49 (18.68)		

in the trial and healthy controls [$F(1,142) = 1.56$, $P = 0.21$, $\eta_p^2 = 0.01$]. Motor imagery ability of the participants in the trial correlated with mental status (Mental Status Questionnaire score, $r = -0.23$, $P = 0.011$, $n = 100$) and also with change between baseline and outcome assessments on the primary outcome measure, the ARAT difference score ($r = 0.28$, $P = 0.002$, $n = 100$). However, within the 'Motor Imagery Training' group, motor imagery ability was not correlated with ARAT change scores ($r = 0.12$, $P = 0.23$, $n = 38$).

Discussion

The results of this study showed no evidence of the benefit of mental practice with motor imagery in stroke. No enhanced improvement as a result of mental practice with motor imagery was found on any of the outcome measures. Furthermore, patients were not found to be impaired on motor imagery as a group and, while motor imagery ability was related to improvement on motor tasks, no relationship between motor imagery ability and the benefit of motor imagery practice was found. This trial demonstrates clear nil-findings with regards to the efficacy of mental practice with motor imagery in stroke rehabilitation, raising some important issues with regards to the clinical benefit of mental practice.

The aim of this study was to evaluate the therapeutic benefit of mental practice in sub-acute stroke patients with a moderate motor weakness. This study was different from preceding reports in that it was sufficiently powered, that it was a sequential cohort study selecting a representative sample, that it recruited patients early post-stroke, that it was carefully controlled for both intervention effects and for attention-placebo, that it evaluated individual differences in motor imagery ability using objective measures, and that it was the first study to test a plasticity account of mental practice by assessing mental practice of motor tasks separate from physical practice.

The rationale for the efficacy of mental practice in stroke, which is widely subscribed to by researchers and clinical practitioners generating a strong belief that this is a useful rehabilitation method, is that activation of motor brain areas through imagery will enhance brain plasticity. If the neural principle of 'firing is rewiring' applies to mental practice in stroke, than we would expect to find a clinical benefit in patients early post-stroke. Processes of functional redistribution have been demonstrated in early recovery and have been linked to physical practice (Nelles *et al*., 2001). If the underlying mechanisms of mental practice can be attributed to brain plasticity rather than motivational or cognitive factors, then we should see enhanced recovery in stroke patients participating in mental practice independent of physical practice of movements. In the design of this study a number of factors were carefully considered in order to provide a more direct evaluation of this plasticity account. The current intervention was designed as an intensive therapy programme including only those training tasks that have been demonstrated to activate the cortical motor network on the basis of neuroimaging studies. Furthermore, mental practice was not embedded in physical therapy (which was instead offered to all participants as part of normal care) in order to provide a more direct evaluation of the plasticity account.

The design of this study further considered the implications of the neuro-rehabilitation 'guided-recovery' account of Robertson and Murre (1999), calling for targeted stimulation of lesioned circuits to induce restitution of function through reconnection of neural connectivity. The success of guided-recovery, Robertson and Murre (1999) claim, depends on post-lesion states, including—among others—the extent of the loss of connectivity in a particular circuit and the time lapsed since injury. For this reason, the current study included patients with residual motor function (which coincidentally also allowed for reliable baseline assessment) and recruited patients at an early stage, where possible 1 month (and no more than 6 months) post-stroke. The principle of guided-recovery makes use of a critical period within which appropriate patterned stimulation must be given if the networks are to survive. Robertson and Murre (1999) suggest that 'timely and intensive application of patterned stimulation to accelerate self-repair of networks may be of crucial importance'. It would therefore not be helpful to dismiss the lack treatment effects in this study as being due to involving patients early post-stroke. It is an issue of concern that most previous studies evaluating the therapeutic benefit of mental practice in stroke involved chronic patients, including one of the few previous randomized controlled trials (Page *et al*., 2007). The patients in the study by Page and colleagues (2007) were on average 3.5 years post-stroke, and had fallen out of the habit of using their affected upper limb following discharge from their therapy regimes. Participation in the trial by Page *et al*. (2007) offered combined physical and mental practice. Self-referral to the trial, therefore, provided patients with physical practice of dormant motor processes. This scenario implies possible confounds and furthermore limits the relevance to the applied rehabilitation setting.

This relates to the issue of combined physical and mental practice. An important part of the rationale of the current trial was to exclude the possibility that mental practice merely provides prolonged opportunity to consolidate particular movement patterns, and find a more direct indication that mental practice works through processes of brain plasticity independent of the effects of physical movement. Since we previously found that combined mental and physical practice gave improvement on the trained task only (Dijkerman *et al*., 2004), we felt it was necessary to evaluate the benefit of mental practice when not combined with physical practice of the movements. The prudence of evaluating motor imagery training independent of motor performance was also pointed out by Sharma and colleagues (2006). Previous studies combined mental practice with physical practice. In their mental practice evaluations Page and colleagues (Page, 2000; Page *et al*., 2001*a*, *b*; Butler and Page, 2006) reported a clinical benefit for mental practice in a series of small studies and one randomized controlled trial (Page *et al*., 2007). The placebo condition was always audiotape-led relaxation. This means that patients in the treatment group had an opportunity during mental practice to consolidate movement patterns that they earlier had been practicing physically, while the control group did not have this advantage. The benefit of combined physical and mental practice can therefore be attributed to any of the following mechanisms. The mental practice extended engagement with motor processes, which may give rise to enhanced cognitive models of performed movements, or may even have a motivational effect. Alternatively, it is possible that an indirect effect of neuroplasticity accounts for the findings, where mental practice reactivates recently used motor representations allowing for an increased effect of the physical practice itself. However, all these explanations would imply that the benefit of mental practice is not independent of physical practice, and does not provide a 'backdoor to the motor systems after stroke' or form an alternative if physical practice is not possible (Sharma *et al*., 2006).

A second randomized controlled trial evaluating mental practice in stroke by Liu and colleagues (2004) did not show a generalized effect of mental practice. Like the study of Page and colleagues, the study by Liu *et al*. (2004) combined physical and mental practice and focused on activities of daily living only. They found a mixed result. No enhanced recovery of motor function was found following mental practice on standard measures of motor recovery, notably the Fugl–Meyer Assessment of upper-limb motor function. The study did demonstrate an increased level of competence in the experimental group performing activities of daily living, including 15 trained and five untrained tasks. However, mental practice in the study by Liu and colleagues (2004) had a strong cognitive emphasis, and it is questionable to what extent it can be considered mental motor practice. Furthermore, the nature of this particular treatment makes it especially likely that the findings of Liu and colleagues (2004), further documented in 16 new patients (Liu *et al*., 2009), relate to a cognitive or even practice effect. As part of the motor imagery training programme, patients were trained to analyse task sequences and engaged in so-called problem identification. They practiced 'rectified task performance using mental imagery and actual practice' (Liu *et al*., 2009, p. 1404), and mental rehearsal and actual practice were intertwined throughout the relearning process (Liu *et al*., 2004). In this respect, mental practice in the Liu *et al*. (2004) study was quite distinct from all other studies, including the current one.

On a theoretical point, if a scientifically informed programme of mental practice alone does not result in enhanced recovery in the patients in the current study, then there are possible implications for the neuroplasticity account of mental practice. The fact that intensive training on tasks, which neuroimaging studies have shown to activate motor regions, does not result in behavioural change, may question the functional relevance of cortical activation in mental simulation of action and possibly non-motor tasks demonstrated in numerous neuroimaging studies (Rizzolatti and Craighero, 2004; Pulvermuller, 2005). Moreover, the clinical implications of the apparent complex interaction between mental and physical practice would be, that at best, only patients with preserved motor ability stand to benefit from mental practice. Furthermore, patients with limited cognitive resources are also unlikely to gain from this treatment, which makes the unselected sample of the current study so relevant in the evaluation of mental practice efficacy. However, at the moment, even a motivational account of the positive evidence for a therapeutic benefit of mental practice cannot be dismissed.

Furthermore, as patients performed well on the objective motor imagery ability measure, it is also unlikely that patients were unable to benefit from mental practice due to impaired motor imagery. It is possible that spontaneous recovery in these sub-acute patients masked the subtle benefit of mental practice (motor recovery independent of treatment group was evident in this study, as mentioned above and illustrated in Table 3), but again the reported small effect sizes of the treatment effects in this study do not suggest this. Additionally, effects of non-invasive intervention have been shown early post-stroke, for example, in our randomized controlled trial of an intervention to enhance control beliefs, which resulted in improved motor performance (Johnston *et al*., 2007).

Although there is always the possibility that the devised intervention was inadequate, in comparison the current intervention nevertheless included the key elements used in previous studies and offered training of at least equal intensity. The current intervention was a daily activity comprising a total of 9 h supervised therapy plus 4 h independent training. This was a higher dosage than for example the intervention reported by Page *et al*. (2007) comprising of twice weekly activities at a total 6 h. We furthermore include in this article a detailed account of this scientifically based training programme. In the rationale, we have demonstrated that all tasks used in the intervention have been demonstrated to activate motor areas in healthy volunteers, and as no impairment on motor imagery ability was found in these patients, it is unlikely that the nature of the intervention can be dismissed as inadequate. A final possibility is that the patients did not adhere to the intervention. We feel confident that such an explanation is unlikely as the intervention was closely supervised, and the intervention largely comprised of intensive one-to-one sessions with research therapists.

Sufficient power was required in demonstrating the anticipated moderate to small effects of mental practice with motor imagery, and it was important to include a representative sample of stroke patients by conducting the first sequential cohort study. The current study included a far larger sample of patients than any mental practice evaluation to date. And although we did fall short of our patient trial completion target, with 13% less completers in the experimental group than planned (Ietswaart *et al*., 2006), we still had sufficient power to detect a clinically meaningful treatment effect (Table 2). Power problems are extremely unlikely to account for the fact that we did not find differences between the groups. As shown in Table 3, improvements in ARAT scores were similar for all three groups, with the 'Normal Care Control' group showing the largest improvement. The effect sizes on all outcome measures were extremely small (Table 3), suggesting very clean nil-results. In the evaluation of mental practice as a treatment technique, carefully controlled trials with a reasonable sample size are few. Although the reported evidence of smaller studies has been positive, we need to consider the role of publication bias where negative findings are not reported when they have an equally small sample size. This asymmetric funnel effect, where small trials report positive effects but large well-controlled trials include nil-findings, has been widely recognized as an evident mechanism with regards to clinical trials in general (Egger *et al.*, 1997). As such, the finding of the current carefully controlled powered trial, representative of the stroke population, is important in the evaluation of the therapeutic benefit of mental practice.

Future research will need to investigate the role of both chronic patient status and combined physical and mental practice in clarifying the therapeutic benefit of mental practice in stroke. Future studies should further focus on delineating the precise relation between motor imagery training content and mode of delivery, patient variables and motor improvement, using well-designed evaluation trials.

In conclusion, the nil-results of this study may challenge 'guided recovery' as described by Robertson and Murre (1999), notably only with regards to this particular technique of mental practice with motor imagery. The idea that brain plasticity is the underlying mechanism of the reported effects of mental practice with motor imagery may not be substantiated. The carefully controlled nature of this trial, offering intensive and closely supervised mental practice in isolation of physical practice, challenges this idea. This suggests that the benefit of mental practice as previously found by ourselves (Dijkerman *et al*., 2004) and others, is essentially due to combined physical and mental practice. It remains unclear whether the benefit of this combination is associated with enhanced cognitive models of performed movements, motivational mechanisms, or an indirect effect of neuroplasticity where mental practice reactivates recently used motor representations allowing for an increased effect of the physical practice itself. The latter account would suggest that only patients with preserved motor ability could benefit from mental practice that only works in combination with physical practice. Our account would also explain why the most compelling evidence for the efficacy of motor imagery in stroke comes from chronic patients. Chronic patients in particular, who over time have lost much of the affected limb's motor repertoire, would benefit from enhanced cognitive movement consolidation associated with mental rehearsal following physical practice. However, chronic patients do not form the target group of this rehabilitation technique in its applied setting. Furthermore, a cognitive consolidation mechanism underlying a cognitively demanding technique like mental practice would significantly diminish its applied value. These explanations of the potential underlying mechanisms of mental practice would therefore suggest that patients in the stroke rehabilitation population early post-stroke, and those with either limited cognitive resources or a dense weakness may not benefit from mental practice in their motor recovery.

Acknowledgements

We would like to thank all the patients and controls participating in this study. We further would like thank the researchers working on this project: Dimitra Anezoulaki, Linda Boyd, Heather Cassie, Andrea Collard, Tracy Davidson, Joanna Greer, Louise Mackie, Suzie Mahr, Charlotte Stockton and Pauline Stokman. For statistical advice, we would like to thank John Crawford, Mark Moss, Derek Johnston, Gladys McPherson and Jill Mollison. We would like to thank physiotherapists Carin Shroeder, Frederike van Wijck, Jacqui Morris and Ingrid Cole for advice and help with the validation of training and assessment tools. The authors are grateful to Nichola Callow for her input on earlier versions of the article.

Funding

This work was supported by the Chief Scientist Office of the Scottish Executive Health Department [CHZ/4/153].

References

Altschuler EL, Wisdom SB, Stone L, Foster C, Galasko D, Llewellyn DME, et al. Rehabilitation of hemiparesis after stroke with a mirror. Lancet 1999; 353: 2035–6.

Annett J. Motor imagery - perception or action. Neuropsychologia 1995; 33: 1395–417.

Barsalou LW. Grounded cognition. Ann Rev Psychol 2008; 59: 617–45.

Bonetti D, Johnston M. Perceived control predicting the recovery of individual-specific walking behaviours following stroke: testing psychological models and constructs. Br J Health Psychol 2008; 13: 463–78.

Bovend'Eerdt TJ, Dawes H, Sackley C, Izadi H, Wade DT. An integrated motor imagery program to improve functional task performance in neurorehabilitation: a single-blind randomized controlled trial. Arch Phys Med Rehab 2010; 91: 939–46.

Braun SM, Beurskens AJ, Borm PJ, Schack T, Wade DT. The effects of mental practice in stroke rehabilitation: a systematic review. Arch Phys Med Rehab 2006; 87: 842–52.

Butler AJ, Page SJ. Mental practice with motor imagery: evidence for motor recovery and cortical reorganization after stroke. Arch Phys Med Rehab 2006; 87: S2–11.

Carey JR, Kimberley TJ, Lewis SM, Auerbach EJ, Dorsey L, Rundquist P, et al. Analysis of fMRI and finger tracking training in subjects with chronic stroke. Brain 2002; 125: 773–88.

Cohen J. A power primer. Psychol Bull 1992; 112: 155–9.

Crosbie JH, McDonough SM, Gilmore DH, Wiggam MI. The adjunctive role of mental practice in the rehabilitation of the upper limb after hemiplegic stroke: a pilot study. Clin Rehab 2004; 18: 60–8.

de Vries S, Mulder T. Motor imagery and stroke rehabilitation: a critical discussion. J Rehab Med 2007; 39: 5–13.

Decety J. The neurophysiological basis of motor imagery. Behav Brain Res 1996; 77: 45–52.

Decety J, Chaminade T. When the self represents the other: a new cognitive neuroscience view on psychological identification. Consciousness Cogn 2003; 12: 577–96.

Decety J, Grezes J. Neural mechanisms subserving the perception of human actions. Trends Cogn Sci 1999; 3: 172–8.

De Renzi E, Faglioni P. Normative data and screening power of a shortened version of token test. Cortex 1978; 14: 41–9.

Dijkerman HC, Ietswaart M, Johnston M, MacWalter RS. Does motor imagery training improve hand function in chronic stroke patients? A pilot study. Clin Rehab 2004; 18: 538–49.

Dijkerman HC, Ietswaart M, Johnston M. Motor imagery and the rehabilitation of movement disorders: an overview. In: Guillot A, Collet C, editors. The neurophysiological foundations of mental and motor imagery. Oxford: Oxford University Press; 2010. p. 127–44.

Dimitrov DM, Rumrill PD. Pretest-posttest designs and measurement of change. Work 2003; 20: 159–65.

Dromerick AW, Edwards DF, Hahn M. Does the application of constraint-induced movement therapy during acute rehabilitation reduce arm impairment after ischemic stroke? Stroke 2000; 31: 2984–8.

Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Br Med J 1997; 13: 629–34.

Gaggioli A, Meneghini A, Morganti F, Alcaniz M, Riva G. A strategy for computer-assisted mental practice in stroke rehabilitation. Neurorehab Neural Repair 2006; 20: 503–7.

Giraux P, Sirigu A. Illusory movements of the paralyzed limb restore motor cortex activity. Neuroimage 2003; 20: S107–11.

Grafton ST. Embodied cognition and the simulation of action to understand others. Ann NY Acad Sci 2009; 1156: 97–117.

Grezes J, Decety J. Functional anatomy of execution, mental simulation, observation, and verb generation of actions: a meta-analysis. Hum Brain Map 2001; 12: 1–19.

Handy TC, Borg JS, Turk DJ, Tipper CM, Grafton ST, Gazzaniga MS. Placing a tool in the spotlight: spatial attention modulates visuomotor responses in cortex. Neuroimage 2005; 26: 266–76.

Heller A, Wade DT, Wood VA, Sunderland A, Hewer RL, Ward E. Arm function after stroke - measurement and recovery over the 1st 3 months. J Neurol Neurosurg Psychiat 1987; 50: 714–9.

Holmes PS, Collins DJ. The PETTLEP approach to motor imagery: a functional equivalence model for sport psychologists. J Appl Sport Psychol 2001; 13: 60–83.

Ietswaart M, Johnston M, Dijkerman HC, Scott CL, Joice SA, Hamilton S, et al. Recovery of hand function through mental practice: A study protocol. BMC Neurol 2006; 6: 39.

Jackson PL, Doyon J, Richards CL, Malouin F. The efficacy of combined physical and mental practice in the learning of a foot-sequence task after stroke: a case report. Neurorehab Neural Repair 2004; 18: 106–11.

Jackson PL, Lafleur MF, Malouin F, Richards CL, Doyon J. Functional cerebral reorganization following motor sequence learning through mental practice with motor imagery. Neuroimage 2003; 20: 1171–80.

Jackson PL, Lafleur AF, Malouin F, Richards C, Doyon J. Potential role of mental practice using motor imagery in neurologic rehabilitation. Arch Phys Med Rehab 2001; 82: 1133–41.

Jang SH, Kim YH, Cho SH, Lee JH, Park JW, Kwon YH. Cortical reorganization induced by task-oriented training in chronic hemiplegic stroke patients. Neuroreport 2003; 14: 137–41.

Jeannerod M. The representing brain - neural correlates of motor intention and imagery. Behav Brain Sci 1994; 17: 187–202.

Jeannerod M. Mental-imagery in the motor context. Neuropsychologia 1995; 33: 1419–32.

Jeannerod M. Neural simulation of action: a unifying mechanism for motor cognition. Neuroimage 2001; 14: S103–9.

Jeannerod M, Decety J. Mental motor imagery: a window into the representational stages of action. Curr Opin Neurobiol 1995; 5: 727–32.

Johnson-Frey SH. Stimulation through simulation? Motor imagery and functional reorganization in hemiplegic stroke patients. Brain Cogn 2004; 55: 328–31.

Johnston M, Bonetti D, Joice S, Pollard B, Morrison V, Francis JJ, MacWalter R. Recovery from disability after stroke as a target for a behavioural intervention: results of a randomized controlled trial. Disabil Rehab 2007; 29: 1117–27.

Johnston M, Pollard B, Morrison V, Macwalter R. Functional limitations and survival following stroke: psychological and clinical predictors of 3-year outcome. Int J Behav Med 2004; 11: 187–96.

Johnston M, Morrison V, Macwalter R, Partridge C. Perceived control, coping and recovery from disability following stroke. Psychol Health 1999; 14: 181–92.

Kahn RL, Goldfarb AI, Pollack KM, Peck A. Mental status questionnaire [MSQ]. In: Kane RA, Kane RL, editors. Assessing the elderly: a practical guide to measurement. Lexington, MA: Lexington Books; 1981. p. 92–94.

Liu KP, Chan CC, Lee TM, Hui-Chan CW. Mental imagery for promoting relearning for people after stroke: a randomized controlled trial. Arch Phys Med Rehab 2004; 85: 1403–8.

Liu KP, Chan CC, Wong RS, Kwan IW, Yau CS, Li LS, Lee TM. A randomized controlled trial of mental imagery augment generalization of learning in acute poststroke patients. Stroke 2009; 40: 2222–5.

Lyle RC. A performance-test for assessment of upper limb function in physical rehabilitation treatment and research. Int J Rehab Res 1981; 4: 483–92.

Mahony FL, Barthel DW. Functional evaluation. The Barthel Index. Maryland State Med J 1965; 14: 61–5.

Malouin F, Richards CL, Durand A, Doyon J. Reliability of mental chronometry for assessing motor imagery ability after stroke. Arch Phys Med Rehab 2008; 89: 311–9.

Marshall RS, Perera GM, Lazar RM, Krakauer JW, Constantine RC, DeLaPaz RL. Evolution of cortical activation during recovery from corticospinal tract infarction. Stroke 2000; 31: 656–61.

Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel group randomized trials. BMC Med Res Methodol 2001; 1: 2.

Moseley GL. Graded motor imagery for pathologic pain - a randomized controlled trial. Neurology 2006; 67: 2129–34.

Mueller K, Butefisch CM, Seitz RJ, Homberg V. Mental practice improves hand function after hemiparetic stroke. Restor Neurol Neurosci 2007; 25: 501–11.

Nelles G, Jentzen W, Jueptner M, Muller S, Diener HC. Arm training induced brain plasticity in stroke studied with serial positron emission tomography. Neuroimage 2001; 13: 1146–54.

Nico D, Daprati E, Rigal F, Parsons L, Sirigu A. Left and right hand recognition in upper limb amputees. Brain 2004; 127: 120–32.

Nudo RJ, Wise BM, SiFuentes F, Milliken GW. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. Science 1996; 272: 1791–4.

Page SJ. Imagery improves upper extremity motor function in chronic stroke patients: a pilot study. Occupat Ther J Res 2000; 20: 200–15.

Page SJ, Levine P, Khoury JC. Modified constraint-induced therapy combined with mental practice thinking through better motor outcomes. Stroke 2009; 40: 551–4.

Page SJ, Levine P, Leonard A. Mental practice in chronic stroke - results of a randomized, placebo-controlled trial. Stroke 2007; 38: 1293–7.

Page SJ, Levine P, Leonard AC. Effects of mental practice on affected limb use and function in chronic stroke. Arch Phys Med Rehab 2005; 86: 399–402.

Page SJ, Levine P, Sisto SA, Johnston MV. Mental practice combined with physical practice for upper-limb motor deficit in subacute stroke. Phys Ther 2001a; 81: 1455–62.

Page SJ, Levine P, Sisto S, Johnston MV. A randomized efficacy and feasibility study of imagery in acute stroke. Clin Rehab 2001b; 15: 233–40.

Page SJ, Szaflarski JP, Eliassen JC, Pan H, Cramer SC. Cortical plasticity following motor skill learning during mental practice in stroke. Neurorehab Neural Repair 2009; 23: 382–8.

Parsons LM. Temporal and kinematic properties of motor behavior reflected in mentally simulated action. J Exp Psychol Hum Percep Perf 1994; 20: 709–30.

Parsons LM. Integrating cognitive psychology, neurology and neuroimaging. Acta Psychol 2001; 107: 155–81.

Parsons LM, Gabrieli JDE, Phelps EA, Gazzaniga MS. Cerebrally lateralized mental representations of hand shape and movement. J Neurosci 1998; 18: 6539–48.

Partridge C, Johnston M. Perceived control and recovery from stroke. Br J Clin Psychol 1989; 28: 53–9.

Pascual-Leone A, Dang N, Cohen LG, Brasilneto JP, Cammarota A, Hallett M. Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor-skills. J Neurophysiol 1995; 74: 1037–45.

Pocock ST. Clinical trials: a practical guide. Chichester: Wiley; 1983.

Pollard B, Johnston M. Problems with the sickness impact profile: a theoretically based analysis and a proposal for a new method of implementation and scoring. Soc Sci Med 2001; 52: 921–35.

Pulvermuller F. Brain mechanisms linking language and action. Nat Rev Neurosci 2005; 6: 576–82.

Ramachandran VS, Rogers-Ramachandran D. Synaesthesia in phantom limbs induced with mirrors. Proc Roy Soc Lond Ser B Biol Sci 1996; 263: 377–86.

Rizzolatti G, Craighero L. The mirror-neuron system. Annu Rev Neurosci 2004; 27: 169–92.

Robertson IH, Murre JMJ. Rehabilitation of brain damage: brain plasticity and principles of guided recovery. Psychol Bull 1999; 125: 544–75.

Sharma N, Pomeroy VM, Baron JC. Motor imagery: a backdoor to the motor system after stroke? Stroke 2006; 37: 1941–52.

Sirigu A, Cohen L, Duhamel JR, Pillon B, Dubois B, Agid Y, et al. Congruent unilateral impairments for real and imagined hand movements. Neuroreport 1995; 6: 997–1001.

Sirigu A, Duhamel JR, Cohen L, Pillon B, Dubois B, Agid Y. The mental representation of hand movements after parietal cortex damage. Science 1996; 273: 1564–8.

Stevens JA, Stoykov MEP. Using motor imagery in the rehabilitation of hemiparesis. Arch Phys Med Rehab 2003; 84: 1090–2.

van der Lee JH, Wagenaar RC, Lankhorst GJ, Vogelaar TW, Deville WL, Bouter LM. Forced use of the upper extremity in chronic stroke patients - results from a single-blind randomized clinical trial. Stroke 1999; 30: 2369–75.

Weiller C. Recovery from motor stroke - human positron emission tomography studies. Cerebrovasc Dis 1995; 5: 282–91.

Yavuzer G, Selles R, Sezer N, Sutbeyaz S, Bussmann JB, Koseoglu F, et al. Mirror therapy improves hand function in subacute stroke: A randomized controlled trial. Arch Phys Med Rehab 2008; 89: 393–8.

Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiat Scand 1983; 67: 361–70.

Zimmermann-Schlatter A, Schuster C, Puhan MA, Siekierka E, Steurer J. Efficacy of motor imagery in post-stroke rehabilitation: a systematic review. J Neuroeng Rehab 2008; 5: 8.