



Is successful rehabilitation of complex regional pain syndrome due to sustained attention to the affected limb? A randomised clinical trial

G. Lorimer Moseley*

School of Physiotherapy, The University of Sydney, P.O. Box 170, East St, Lidcombe, Sydney, NSW 1825, Australia

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Abstract

In complex regional pain syndrome (CRPS1) initiated by wrist fracture, a motor imagery program (MIP), consisting of hand laterality recognition followed by imagined movements and then mirror movements, reduces pain and disability, but the mechanism of effect is unclear. Possibilities include sustained attention to the affected limb, in which case the order of MIP components would not alter the effect, and sequential activation of cortical motor networks, in which case it would. Twenty subjects with chronic CRPS1 initiated by wrist fracture and who satisfied stringent inclusion criteria, were randomly allocated to one of three groups: hand laterality recognition, imagined movements, mirror movements (RecImMir, MIP); imagined movements, recognition, imagined movements (ImRecIm); recognition, mirror movements, recognition (RecMirRec). At 6 and 18 weeks, reduced pain and disability were greater for the RecImMir group than for the other groups ($P < 0.05$). Hand laterality recognition imparted a consistent reduction in pain and disability across groups, however, this effect was limited in magnitude. Imagined movements imparted a further reduction in pain and disability, but only if they followed hand laterality recognition. Mirror movements also imparted a reduction in pain and disability, but only when they followed imagined movements. The effect of the MIP seems to be dependent on the order of components, which suggests that it is not due to sustained attention to the affected limb, but is consistent with sequential activation of cortical motor networks.

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1. Introduction

Several chronic pain conditions are associated with reorganisation of the primary somatosensory cortex (S1), for example, phantom limb pain (Flor et al., 1995), chronic back pain (Flor et al., 1997) and complex regional pain syndrome type 1 (CRPS1) (Juottonen et al., 2002). S1 representation of the affected body part is larger in many chronic pain states for example chronic back pain (Flor et al., 1995). However, S1 representation is smaller in CRPS1 (Juottonen et al., 2002; Maihofner et al., 2003; Pleger et al., 2004a), which is similar to that observed

post-amputation and after stroke, where the representation of the deafferented part is effectively smaller because of expansion of representation of territory adjacent to the deafferented zone (Flor et al., 1995; Pineiro et al., 2001).

The extent of S1 reorganisation correlates with the magnitude of pain in both phantom pain (Flor et al., 1995) and CRPS1 (Pleger et al., 2004b). In amputees, 'training the brain', for example via sensory discrimination training, reduces both pain and cortical reorganisation (Flor et al., 2001; Huse et al., 2001). There is also anecdotal evidence that mirror movements reduce phantom limb pain, supposedly training the brain via reconciliation of motor output and sensory feedback (Ramachandran et al., 1995).

Mirror movements have also reduced pain in acute CRPS1 (McCabe et al., 2003) and a motor imagery program (MIP), which consisted of 2 weeks each of hand laterality recognition, imagined hand movements and then mirror movements, reduced pain and swelling in chronic CRPS1

Abbreviations: NRS, numerical rating scale; MIP, motor imagery program; CRPS1, complex regional pain syndrome type I; NPS, neuropathic pain scale.

* Tel.: +61 2 9351 9312; fax: +61 2 9351 9601.

E-mail address: l.moseley@fhs.usyd.edu.au.

(Moseley, 2004a). The order of treatments in the MIP was based on previous findings that mirror movements alone do not reduce pain in people with chronic CRPS1 (McCabe et al., 2003) and the observation that patients with chronic CRPS1 commonly find that even imagined movements of the affected limb can exacerbate pain and swelling (Moseley, 2004b).

The mechanisms underpinning the MIP are not clear. One possible explanation is that the MIP provides sustained attention to the affected limb. Patients with CRPS1 have characteristics of neglect; they focus mental and visual attention in order to move the limb (Galer and Jensen, 1999) and often describe the affected limb as ‘not belonging to me’. Thus, perhaps the MIP simply reverses a learned disuse of the affected limb by making the patient attend to it for a substantial proportion of their waking day (~20%). Alternatively, perhaps the MIP sequentially activates cortical mechanisms associated with movement without evoking pain. Separate brain imaging studies show activation of motor networks during both hand laterality recognition (Parsons and Fox, 1998) and imagined hand movements (Grezes and Decety, 2001), although the tasks have not been compared directly.

We hypothesised that if the MIP simply provides sustained attention to the affected limb, then the order of components of the MIP should be unimportant. Conversely, if the MIP sequentially activates cortical motor networks, then the order of components will be important. To test these hypotheses, we undertook a clinical trial in which patients with chronic CRPS1 of one hand were randomly allocated to undertake the components of the MIP in different orders.

2. Methods

2.1. Design

Single blind randomised trial with 12-week follow-up, using repeated measures comparison of means.

2.2. Subjects

A sample of 38 patients (22F) who had sustained a non-complicated wrist fracture more than 6 months prior and, as a result, had developed CRPS1, were contacted. CRPS1 diagnosis was based on Breuhl et al. (1999). Patients were contacted through the hospital physiotherapy department, the neurological and orthopaedic clinics and via local general practitioners. Patients were excluded if they had: previously obtained pain relief from an intravenous regional sympathetic blockade; received any invasive analgesic procedure (e.g. spinal cord stimulator, sympathectomy); been diagnosed with any other neurological, psychopathology or motor disorder or dyslexia; had difficulty performing a rapid naming task; were visually impaired; had any other upper limb pathology or pain, or lived outside the immediate metropolitan area of the host department. Eighteen patients were excluded according to these criteria. Written informed consent was obtained from

the remaining 20 subjects (14F) (Table 1). Fig. 1A shows the experimental plan. All procedures were approved by the institutional research ethics committee and conformed to the Declaration of Helsinki.

2.3. Protocol

2.3.1. MIP component treatments (Moseley, 2004a).

- (i) Recognition of hand laterality. Using Matlab 6.5 (release 13, Mathworks, Natic, MA, USA), 56 photographs of left and right hands were randomly selected from a bank of 80 pictures and presented in random order on a monitor in front of the sitting subject. Patients responded by pressing either the left or right mouse button, as quickly as possible, according to whether they recognised the pictured hand to be a left hand or a right hand. Speed and accuracy of performance were emphasised. Patients borrowed a notebook computer and were advised to perform the task three times (total time ~10 min) each waking hour. The software program recorded the time of each trial and speed and accuracy of performance, which permitted evaluation of participation and any changes in performance over time.
- (ii) Imagined hand movements. Twenty-eight pictures of the affected hand were randomly selected from the picture bank and presented in random order. With the affected hand resting comfortably, patients were advised to imagine moving their own hand to adopt the posture shown in the picture, to then imagine returning the hand to its resting position and to repeat that process twice for each picture. Patients were advised to perform the task twice every waking hour (total time ~10 min). Smooth and pain-free imagined movements were emphasised. The software program recorded the time at which each trial was performed to provide an estimate of participation.
- (iii) Mirror movements. The patient placed both hands into a cardboard mirror box (two compartments each 300 mm × 300 mm × 300 mm and separated by a vertical mirror) with the affected hand concealed (behind the mirror). Emphasis was placed on watching the reflection of the unaffected hand in the mirror while the patient moved both hands. Paper copies of 20 pictures of the unaffected hand in postures that involved simpler movements were selected from the picture bank. The patient was advised to, every waking hour, slowly and smoothly adopt the posture shown in each picture with both hands, five times (total time ~10 min). The patient was advised to stop if they experienced an increase in pain either during or directly after mirror movements. A training diary was completed for this component to estimate participation.

The treatment in each component was modified from previous work (Moseley, 2004a) to ensure similar exposure across components (i.e. ~10 min each waking hour). Patients were advised to avoid changing medication or seeking alternative treatment during the course of the trial up to and including the 12-week follow-up. Patients were permitted to attend physiotherapy during the 12-week follow-up, but no criteria about physiotherapy were set.

Prior to randomisation, patients completed the Neuropathic pain scale (NPS) (Galer and Jensen, 1997) and responded in

Table 1
Mean and SD for each group is shown

| M/F (dom) | Aff. Hand | Prescribed medication (other medication) | Dur. (mths) | Age (yr) | NPS intensity | NPS total | Task NRS |
|--------------------------|-----------|--|-------------|----------|---------------|------------|-----------|
| F (r) | l | Gabapentin, amitriptyline (paracetamol, codeine ¹) | 17 | 23 | 6 | 46 | 1 |
| F (r) | r | Morphine, tramadol, codeine, vitamin C | 15 | 45 | 5 | 42 | 1 |
| F (r) | l | Gabapentin, amitriptyline (paracetamol and codeine ²) | 21 | 34 | 7 | 63 | 1 |
| F (r) | l | Amytrityline, zoloft ⁴ | 6 | 41 | 6 | 38 | 1 |
| M (r) | r | Morphine, amitriptyline, tramadol (act3, aspirin ⁴) | 9 | 27 | 7 | 53 | 0 |
| F (r) | l | Gabapentin, Zoloft | 10 | 44 | 7 | 59 | 0 |
| M (r) | l | Morphine, amitriptyline ⁴ , gabapentin (neurofen, topical voltaren ³) | 6 | 36 | 5 | 43 | 1 |
| <i>Group 1 mean (SD)</i> | | | 12 (6) | 36 (8) | 6.1 (0.9) | 49.2 (9.4) | 0.7 (1.4) |
| F (r) | l | Gabapentin, tramadol | 12 | 32 | 4 | 45 | 1 |
| M (l) | r | Gabapentin amitriptyline (paracetamol ¹ , cerebex, aspirin, naprogesic ²) | 12 | 19 | 7 | 58 | 0 |
| M (l) | l | Morphine (cannabis, paracetamol, codeine) | 15 | 26 | 5 | 42 | 0 |
| F (r) | r | Morphine, amitriptyline ⁵ | 21 | 23 | 6 | 43 | 1 |
| F (r) | r | Gabapentin, zoloft (cannabis) | 23 | 22 | 6 | 54 | 2 |
| F (r) | l | Morphine, amitriptyline, tramadol | 14 | 37 | 7 | 44 | 1 |
| <i>Group 2 mean (SD)</i> | | | 16 (5) | 27 (7) | 5.8 (1.2) | 46.7 (6.7) | 0.8 (1.5) |
| M (r) | l | Gabapentin, amitriptyline (paracetamol ¹ , codeine) | 18 | 38 | 6 | 45 | 0 |
| F (r) | l | Gabapentin, naprogesic6T12 | 44 | 5 | 43 | 1 | |
| F (l) | r | Gabapentin zoloft ⁶ | 6 | 25 | 8 | 59 | 1 |
| F (r) | r | Morphine, amitriptyline, tramadol (paracetamol) | 17 | 51 | 5 | 43 | 0 |
| M (r) | l | Morphine, tramadol (neurofen ^{1,7} , digesic ^{1,7}) | 21 | 42 | 5 | 39 | 2 |
| F (l) | r | Oxycontin ¹ , amitriptyline, gabapentin | 14 | 37 | 7 | 42 | 1 |
| F (r) | l | Oxycontin, gabapentin (paracetamol) | 9 | 41 | 5 | 37 | 1 |
| <i>Group 3 mean (SD)</i> | | | 14 (5) | 39 (8) | 5.6 (1.1) | 44.1 (7.3) | 0.9 (1.4) |

Dom, dominant hand; Aff, affected hand; Dur (mths), duration since fracture in months; NPS, neuropathic pain scale. Superscript numbers indicate medication reduced >25% during ¹recognition of hand laterality component, ²imagined movements component, ³mirror movements component, ⁴follow-up period; medication commenced during ⁵first imagined movement component, ⁶mirror movement component; ⁷medication recommenced during mirror movement component.

reference to pain over the two previous days. The properties of the NPS are maintained when used with people with CRPS1 (Galer and Jensen, 1997).

Patients were also asked to select five activities or tasks that they regularly performed prior to their fracture, but now found difficult to perform. Using an 11-point numerical rating scale (NRS) anchored with '0, completely unable to perform' and '10, able to perform normally' they were asked 'How well can you perform that task now?' This Task-specific NRS is based on similar measures validated in patients with neck pain (Westaway et al., 1998) and knee pain (Chatman et al., 1997) and is reliable in people with CRPS1 (Moseley, unpublished data). Questionnaire scores were entered into a datasheet by an independent investigator who was blind to group and assessment occasion.

Using a random numbers table, an independent investigator allocated consenting patients into one of three treatment groups: RecImMir (MIP, group 1), ImRecIm (group2) and RecMirRec (group 3) (Fig. 1B).

2.4. Statistical analysis

All statistics were performed using SPSS 11.0.0 (SPSS, Chicago, IL, USA). Pre-treatment differences between groups

were assessed with a series of *t*-tests. Separate two-way repeated measures MANOVAs were used to compare the total NPS score and the total Task-specific NRS score (dependent variables) between groups and assessment occasions (independent variables). Scheffé tests were used for post hoc analyses. Significance was set at $\alpha=0.05$.

3. Results

There were no pre-treatment differences between groups ($P>0.19$ for all) (Table 1). Between 8.00 am and 8.00 pm, mean \pm SD participation rate was $75 \pm 7\%$ and training occupied $14 \pm 2\%$ of the wakeful day (Table 2). Participation was similar across components and across groups. There was a main effect on NPS score of time ($F(14,4)=6.9$, $P<0.01$) and a time by group interaction ($F(14,8)=2.4$, $P=0.02$). There was a main effect on Task-specific NRS score of time ($F(14,4)=81.5$, $P<0.01$) and group ($F(14,2)=58.5$, $P<0.01$) and a time by group interaction ($F(14,8)=13.7$, $P<0.01$). Those results mean that patients

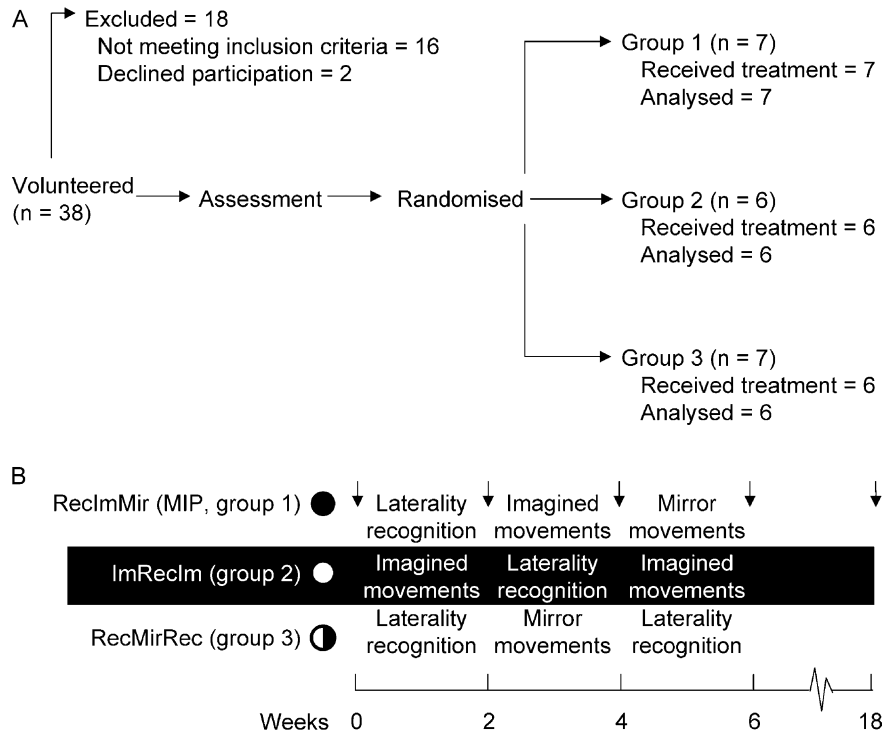


Fig. 1. (A) Treatment plan. (B) Order of component treatments for RecImMir (MIP, group 1; filled circles), ImRecIm (group 2; open circles) and RecMirRec (group 3; half-filled circles). Neuropathic pain scale was assessed on three occasions and then at 18 weeks (12-week follow-up). Assessment times marked by vertical arrows.

improved and the effect on pain and disability was different between groups.

3.1. Effects of treatment group

At 6 weeks, reduction in total NPS score was greater for the RecImMir (MIP, group 1) than it was for RecMirRec (group 3) ($P < 0.05$) and increase in Task-specific NRS was greater for the RecImMir (MIP, group 1) than it was for ImRecIm (group 2) or RecMirRec (group 3) ($P < 0.05$ for both). At 12-week follow-up, reduction in total NPS score and increase in Task-specific NRS were greater for RecImMir (MIP, group 1) than for

ImRecIm (group 2) or RecMirRec (group 3) ($P < 0.05$ for all) (Figs. 2 and 3).

Two other results were drawn from the experimental data. First, although many studies regard statistical significance the criterion for a positive outcome, that criterion is misleading if the magnitude of the effect is minimal. For example, recent work suggests that a positive

Table 2
Mean (SD) compliance with treatment and percentage of time between 8.00 am and 8.00 pm spent doing treatment exercises

| | | Compliance (%) | Time (% of 8.00 am–8.00 pm) |
|---------|-------------|----------------|-----------------------------|
| Group 1 | Recognition | 83 ± 7 | 14 ± 8 |
| | Imagined | 76 ± 10 | 12 ± 8 |
| | Mirror | 66 ± 18 | 10 ± 8 |
| Group 2 | Imagined | 68 ± 28 | 15 ± 12 |
| | Recognition | 79 ± 10 | 15 ± 9 |
| Group 3 | Recog | 80 ± 8 | 13 ± 8 |
| | Mirror | 68 ± 14 | 13 ± 10 |
| Total | Recog | 84 ± 7 | 16 ± 8 |
| | | 75 ± 7 | 14 ± 2 |

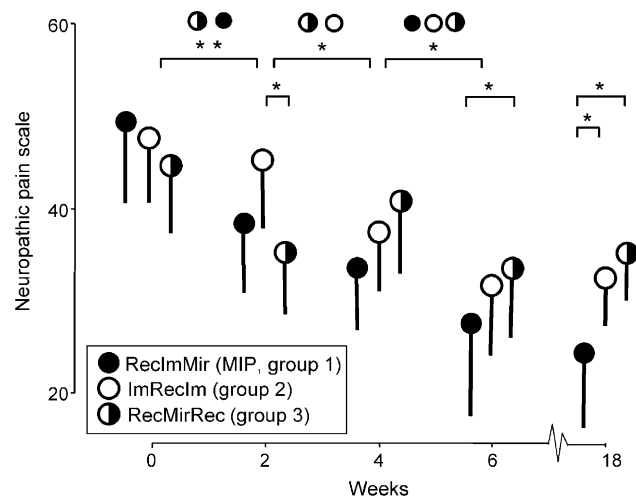


Fig. 2. Mean (circles) and SD (error bars) total Neuropathic pain scale score (possible range 0–100) for RecImMir (MIP, group 1; filled circles), ImRecIm (group 2; open circles) and RecMirRec (group 3; half-filled circles) at each assessment occasion. Horizontal bars indicate significant difference ($*P < 0.05$, $**P < 0.01$) between measurement occasions (top bars) and between groups (bottom bars).

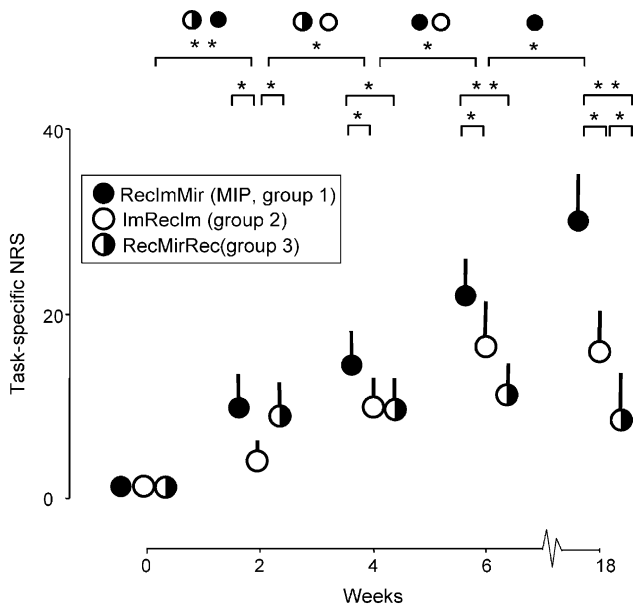


Fig. 3. Mean (circles) and SD (error bars) task-specific NRS score for RecImMir (MIP, group 1; filled circles), ImRecIm (group 2; open circles) and RecMirRec (group 3; half-filled circles) at each assessment occasion. Horizontal bars indicate significant difference (* $P < 0.05$, ** $P < 0.01$) between measurement occasions (top bars) and between groups (bottom bars).

outcome of treatment for CRPS1 is a 50% reduction in NPS score (see Forouzanfar et al., 2003 for review). We calculated the proportion of each group for whom there was a 25 and a 50% reduction in NPS score at 6 weeks and at 12-week follow-up. At 12-week follow-up, ~70% of the RecImMir (MIP, group 1) group and ~20% of the ImRecIm (group 3) group had a 50% reduction in NPS score (Fig. 4A).

Second, because each group showed improvement, we calculated the effect size, which can be thought of as a measure of how much one treatment is better than another. Fig. 4B shows mean effect size in NPS points for RecImMir (MIP, group 1) when compared to the other two groups at

6 weeks and at 12-week follow-up. At 12-week follow-up, the mean reduction in NPS score for RecImMir (MIP, group 1) was ~7 points greater than the mean reduction for ImRecIm (group 2) and ~18 points greater than the mean reduction for RecMirRec (group 3).

3.2. Effect of each component—comparison of 2, 4 and 6 week assessments (Figs. 2 and 3)

Regardless of the order in which it is was performed, recognition of hand laterality imparted a decrease in NPS score (~8 points) and an increase in Task-specific NRS (~7 points) ($P < 0.05$ for all). When imagined movements directly followed hand laterality recognition (group 1, weeks 2–4 and group 2, weeks 4–6), there was a further reduction in NPS (~8 points) and a further increase in Task-specific NRS (~8 points, $P < 0.05$ for both). However, when imagined movements were performed before hand laterality recognition (group 2, weeks 0–2), there was no effect ($P = 0.32$). Similarly, when mirror movements followed imagined movements (group 1), there was a further reduction in NPS (~6 points) and a further increase in Task-specific NRS (~12 points, $P < 0.05$ for both). However, when mirror movements directly followed hand laterality recognition (group 3, weeks 2–4), there was no effect on Task-specific NRS ($P > 0.39$), but an increase in NPS ($P = 0.04$). Those results mean that a positive effect of imagined movements and mirror movements was dependent on the order of components and that when mirror movements were performed straight after hand laterality recognition, symptoms appeared to worsen.

During the follow-up period, ~60% of patients in each group attended physiotherapy consisting of mirror movements (patients in the MIP group), hand laterality recognition, imagined movements (groups 2 and 3 only), active movements of the affected limb (13/13), hydrotherapy (10/13), fine motor control training (13/13), neural mobilisation techniques (5/13) and functional training

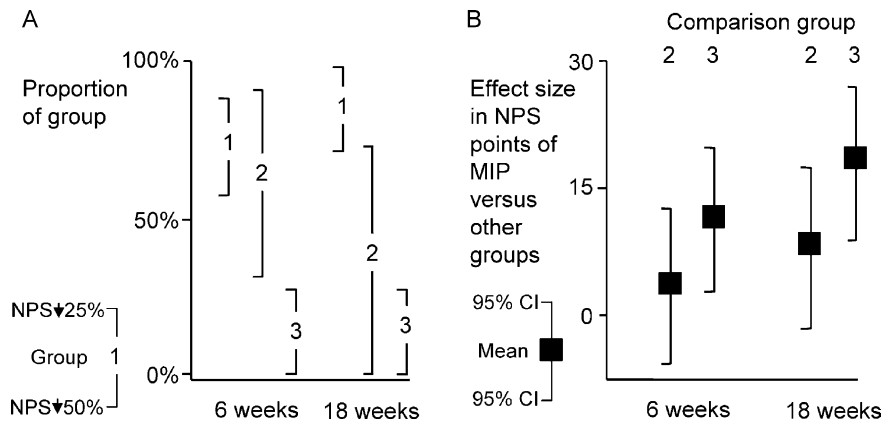


Fig. 4. (A) Proportion of each group who achieved 25% (upper limit) and 50% (lower limit) reduction in neuropathic pain scale (NPS) at 6 weeks and at 12-week follow-up (18 weeks) for each group. (B) Effect size in NPS points attributable to MIP when compared to groups 2 and 3. Mean and 95% confidence interval (CI) are shown.

(13/13). Apart from the components of the MIP, there was no systematic difference in the nature of physiotherapy interventions provided during the follow-up period between groups. Despite advice to the contrary, 11 patients decreased their medications and two patients commenced new medications during the experimental period. The nature of these changes are noted in Table 1.

4. Discussion

The results do not support the hypothesis that the effect of the MIP is imparted by sustained attention to the affected limb, but the results are consistent with sequential activation of cortical motor networks. Two main findings uphold this position. First, patients in the MIP group did better than patients in either of the other groups. Second, imagined movements only imparted an effect when they followed hand laterality recognition and mirror movements only imparted an effect when they followed imagined movements. Notably, participation rate was similar between groups and between components within each group. Taken together with available neuroimaging data, the current results suggest that in patients with CRPS1 of the hand after wrist fracture, it may be important to sequentially activate pre-motor and motor networks prior to reconciliation of sensory feedback and motor output via mirror movements. These results add to a growing body of literature that supports the efficacy of training the brain in patient groups characterised by cortical reorganisation.

The current results corroborate previous work in chronic CRPS1 patients that found reduced pain and swelling with a MIP (Moseley, 2004a) and are comparable with a trial of mirror therapy alone in people with acute CRPS1 (McCabe et al., 2003). The current results also demonstrate via the Task-specific NRS, clear gains in perceived functional status. Functional improvement is implied in previous studies, but not directly estimated and although the Task-specific NRS is not a behavioural measure, such self-report tools are thought to be valid indicators of functional status in other groups (Chatman et al., 1997; Westaway et al., 1998). Therefore, the current data strengthen previous proposals that advocate training the brain in people with chronic pain syndromes, for example via sensory discrimination training (Flor et al., 2001) or mirror movements (Ramachandran et al., 1995) in people with phantom limb pain.

We proposed that the order of MIP components may be important because it achieves sequential activation of pre-motor and then motor networks. The proposal is based on neuroanatomical data drawn from independent studies of hand laterality recognition tasks and imagined movements. Using positron emission tomography (PET) during hand laterality recognition in healthy volunteers, Parsons and Fox (1998) reported increased regional blood flow in limb-specific supplementary motor area (SMA), inferior pre-motor cortex (BA 44/46), dominant left SMA, and superior

pre-motor (BA 6). Importantly, that work did not find blood flow changes in primary motor (M1) or primary somatosensory (S1) cortices. This is in contrast to a number of studies that have shown activation of M1 and S1 during imagined movements (Binkofski et al., 2000; Decety, 1996; Lotze et al., 1999, 2001). Taken together and in light of the current results, those neuroanatomical data suggest that in people with chronic CRPS1, the poor effect on symptoms of imagined or mirror movements not preceded by hand laterality recognition may be because imagined and mirror movements activate M1 or S1, or both. Perhaps cortical neurons involved in execution of hand movements activate a highly sensitised cortical network for pain, the so-called 'pain neurosignature' (Melzack, 1990). Findings of disinhibition (Schwenkreis et al., 2003) of the motor cortex in patients with CRPS1 appear consistent with that possibility. Another possibility is that, in a chronically active and sensitised nociceptive system, descending facilitatory projections from the rostroventral medulla to spinal nociceptive neurones are activated by executive motor commands (Porreca et al., 2002). In this sense, it is possible that commencing training with imagined or mirror movements is simply too great a load on the sensitised system. Perhaps a more conservative progression, via tasks that activate cortical neurones associated with movement preparation, but not neurones associated with movement execution, is prerequisite. Activation of pre-motor cortex primes M1 and this initial priming may be important in imparting an effect. That would be broadly consistent with the proposal that activation of the pre-motor cortex is an important prerequisite for primary motor cortex reorganisation and recovery after stroke (Seitz et al., 1998). Breaking down the motor task to tasks that activate only pre-motor mechanisms, is in line with established principles of physical and psychological rehabilitation that advocate graduated exposure to a pertinent input with prevention of the unwanted response. Although it is not possible to make conclusions about brain activity during each component of the MIP, the current results confirm that the established principles of graduated exposure can be applied to training the brain.

The effect of the MIP may be mediated in part by cortical reorganisation. In amputees with phantom limb pain, regional anaesthesia at the stump causes both rapid reduction in cortical reorganisation and elimination of phantom limb pain, although phantom limb pain returns as the anaesthesia subsides (Birbaumer et al., 1997). Attempts in that group to train the brain have shown a similar relationship between reduced symptoms and reduced S1 reorganisation (Flor et al., 2001; Huse et al., 2001). Those findings suggest that reversal of cortical reorganisation may explain the positive therapeutic effects of the MIP. Further research is currently underway to verify this possibility. Although mirror movements are thought to be effective because they reconcile sensory feedback with motor output (Altschuler et al., 1999; Ramachandran et al., 1995) this too

remains to be verified. Perhaps viewing a virtual image of the affected hand moving without making any attempt to move would impart the same therapeutic effect.

Finally, any interpretation of the current data should consider limitations of the experimental design. First, stringent exclusion criteria were used to define a relatively homogenous sample of CRPS1 patients, which simultaneously limits the external validity of the findings. Second, the follow-up period, although comparable to previous work (Gobelet, 1992; Zuurmond et al., 1996), may not have been sufficient to determine the long-term effects and did not permit evaluation of the treatment on work status, although for many patients, items on the Task-specific NRS were work-related. Also, it is possible that movements without a mirror would have imparted similar effects to that component of the MIP. Although previous research in this patient group would suggest limited response to conventional physical therapies including active movements (McCabe et al., 2003; Moseley, 2004a) this possibility cannot be excluded. Third, subjects for the current study were accessed via several sources and over several months. Although they were randomised to treatment group, there may have been a systematic effect of time or treatment pathway that affected results. Also relevant in this regard is the many treatment options that are offered to people with CRPS1. Although we attempted to monitor medication and treatment, it was not possible to control these factors and they may have had an effect on outcome. That said, there appeared to be clear reductions in medication intake in the MIP group that were not reported in the other groups, which means that this issue probably did not threaten the main outcome of the study. Finally, the sample size was small and more subtle effects may have remained undetected. Although this limitation raises the possibility that there were some undetected effects of the non-MIP treatments, this limitation also does not compromise the main finding of the study, namely that the order of the treatment components is important in imparting the treatment effects of the MIP.

In summary, the results do not support the hypothesis that, in patients with chronic CRPS1 of the hand, the therapeutic effect of the MIP is imparted by sustained attention to the affected limb. Patients in the MIP group did better than patients in either of the other groups and the treatment components were only effective when they followed the prerequisite component. The results add to a growing body of literature that supports the efficacy of training the brain in patient groups characterised by chronic pain and cortical reorganisation. Perhaps more importantly, the results suggest that in this particular group it may be appropriate to gradually expose the patient to activation of the cortical networks involved in movement in a manner that prevents the unwanted response. Mirror movements, which are thought to reconcile motor output and sensory feedback, appear to be an important final component in this regard.

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