

A controlled pilot study of the utility of mirror visual feedback in the treatment of complex regional pain syndrome (type 1)

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Background. We assessed mirror visual feedback (MVF) to test the hypothesis that incongruence between motor output and sensory input produces complex regional pain syndrome (CRPS) (type 1) pain.

Methods. Eight subjects (disease duration ≥ 3 weeks to ≤ 3 yr) were studied over 6 weeks with assessments including two controls (no device and viewing a non-reflective surface) and the intervention (MVF). Pain severity and vasomotor changes were recorded.

Results. The control stages had no analgesic effect. MVF in early CRPS (≤ 8 weeks) had an immediate analgesic effect and in intermediate disease (≤ 1 yr) led to a reduction in stiffness. At 6 weeks, normalization of function and thermal differences had occurred (early and intermediate disease). No change was found in chronic CRPS.

Conclusions. In early CRPS (type 1), visual input from a moving, unaffected limb re-establishes the pain-free relationship between sensory feedback and motor execution. Trophic changes and a less plastic neural pathway preclude this in chronic disease.

KEY WORDS: Complex regional pain syndrome, Mirror visual feedback.

Complex regional pain syndrome (CRPS) is a painful, debilitating condition. This diagnostic term embraces several syndromes, including reflex sympathetic dystrophy, causalgia and algodystrophy. Characteristic clinical features include sensory disturbances, such as burning pain with allodynia and hyperalgesia; motor disturbances, such as weakness, tremor and muscle spasms; and changes in vascular tone, temperature and oedema [1]. Over time, functional loss and trophic changes may occur. The syndrome can occur spontaneously or following trauma (CRPS type 1) or in association with peripheral nerve damage (CRPS type 2). This paper addresses patients presenting with CRPS type 1.

A characteristic feature of CRPS is that signs and symptoms spread beyond the site of initial insult. Severe pain may occur seemingly out of proportion to the original pathology. It may persist over long periods and

is frequently resistant to a wide range of treatments. Traditionally, interrupting the sympathetic supply to the painful area was thought to treat such pain. However, the effectiveness of this approach is not supported by randomized controlled trials [2]. Recent studies on other intractable pain conditions have reported the analgesic benefits of mirror visual feedback therapy [3]. Phantom limb pain, relieved by this therapy, has many characteristics similar to CRPS pain (burning, cramping, and mislocalized). We therefore investigated the effect of mirror visual feedback in CRPS.

The classical picture of a pain mechanism as a single hard-wired, dedicated pathway is no longer widely held [4, 5]. Instead, converging evidence from physiological and functional imaging studies suggests a much more diffuse and plastic system involving the cord, brainstem, thalamus and cortex [6]. In addition, psychological

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Submitted 20 March 2002; revised version accepted 7 June 2002.

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states such as attention, anticipation and preparation for action may be inherent, essential components modulating the experience of pain. Abnormal plastic changes in the CNS have been associated with a number of pain syndromes [7, 8] including phantom limb pain [9]. For example, using non-invasive neuromagnetic imaging, Flor *et al.* [10] found a strong relationship between the amount of plastic change in primary somatosensory cortex and the extent of phantom pain experienced.

Ramachandran and Roger-Ramachandran [3] proposed that phantom limb pain results from disruption of the normal interaction between motor intention to move the limb and the absence of appropriate sensory (proprioceptive) feedback. They speculated that visual feedback might interrupt this pathological cycle. Using a mirror that enabled amputees to superimpose the visual image of their normal limb on the location where they felt their phantom limb to exist, Ramachandran and Roger-Ramachandran [3] found that the phantom spasms and their associated pain were rapidly relieved during exercises involving the 'virtual limb' in six out of 12 cases. Harris subsequently hypothesized, on the basis of clinical observation and functional imaging studies [11], that disorganized cortical representations may lead to the experience of peripheral pain. He proposed that a mismatch between motor intention and predicted proprioceptive or visual feedback of the affected limb may drive this process [12].

We hypothesized that the pain of CRPS is a consequence of disruption of central sensory processing and that congruent visual feedback from the moving unaffected limb, as provided by a mirror, would restore the integrity of cortical processing, thereby relieving pain and restoring function in the affected limb.

Method

Participants

Adult subjects who conformed to the diagnostic criteria for CRPS type 1 [1] in a single limb were recruited consecutively from the out-patient clinics at the Royal National Hospital for Rheumatic Diseases, Bath over an 18-month period. We excluded patients with CRPS type 2, for example those with peripheral nerve lesions.

Clinical method

Subjects were assessed at two time points: on presentation and 6 weeks later. The assessment protocol was divided into three distinct stages: two control phases (using no device and viewing a non-reflective surface) and an intervention phase (viewing a mirror). An additional daily diary was used to record frequency of mirror use and pain severity between assessments. Visual analogue scales (VAS) were used to assess pain intensity, with 0=no pain and 10=pain as bad as it could be. Infrared thermography (IRT) was used to quantify vasomotor changes that influenced temperature in the affected and unaffected limbs [13]. Images were taken on presentation and at week 6.

Subjects were seated and initially asked to visualize both limbs (affected and unaffected). Pain at rest and on movement was recorded (control phase 1). A non-reflective board was

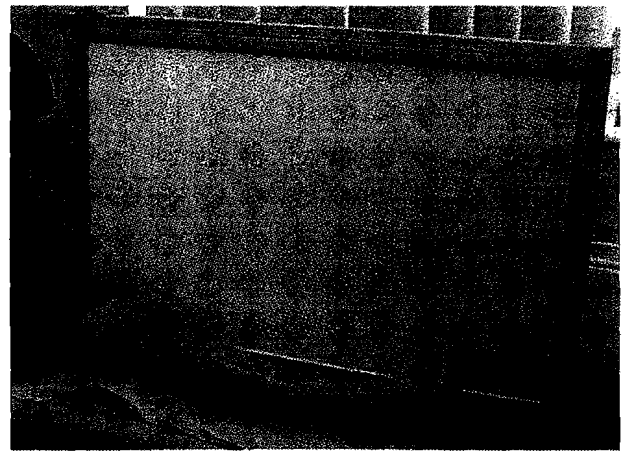


FIG. 1. Subject viewing non-reflective surface with painful limb hidden.

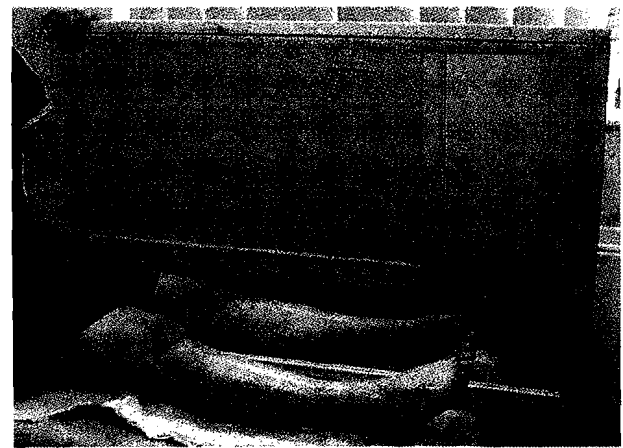


FIG. 2. Subject viewing non-painful limb in mirror with painful limb hidden.

then positioned perpendicular to the subject's midline, with the unaffected limb facing the non-reflective surface and the affected limb hidden (control phase 2). Subjects were asked to attend to the non-reflective surface for a period of 5 min and exercise their non-painful limb and, if possible, their painful limb in a congruent manner (Fig. 1). All subjects were asked to attempt to perform similar exercises: flexion-extension cycles of the relevant body parts. The range of movement and speed of these exercises was dictated by the subject's pain. Following the control stages, a mirror of similar size to the control device was positioned so that only the unaffected limb, and its reflected image in the mirror, could now be seen (Fig. 2). Subjects attended to the reflection now occupying the space of their painful limb. Again, subjects were requested to exercise both limbs (flexion-extension cycles as described above) for 5 min in a congruent manner. Pain on movement was recorded after each control and intervention stage.

Following the initial procedures, subjects were directed to use the mirror as frequently as they wished. A maximum time limit of 10 min was set for each period of mirror therapy to ensure concentration was maintained. Subjects were also advised to conduct the treatment protocol in a quiet environment, where

concentration would not be interrupted. Subjects recorded daily the frequency of mirror use and their movement-related pain score.

Results

(Table 1) Eight subjects were recruited, aged 24–40 yr (mean 33 yr) with disease duration of 3 weeks to 3 yr. Three subjects had early disease (≤ 8 weeks), two had disease of intermediate duration (5 months and 1 yr) and the remaining three had long-standing disease (≥ 2 yr). CRPS was precipitated by trauma in four of the eight subjects (cases 3, 5, 7 and 8); no obvious precipitant was identified in the remaining four. Case 6 had a concurrent diagnosis of ankylosing spondylitis but there was no clinical or imaging evidence of synovitis or enthesopathy in the painful region. Case 7 had extensive ulcers on the affected limb and all three chronic cases (cases 6–8) had contracture deformities in the CRPS-affected limb due to prolonged immobility.

All presented with a single limb affected by allodynia, hyperalgesia, reduced movement with related pain and stiffness and vasomotor disturbances. The only exception to this was case 4, who reported severe stiffness of the limb with little pain on movement but met all other criteria.

All subjects had had previous interventions that did not relieve pain, including analgesia, physiotherapy modalities, sympathetic blocks, immobilization, transcutaneous electrical nerve stimulation, osteopathy and acupuncture (Table 2). The more chronic cases had received the greater number of interventions, which included sympathetic blocks and immobilization. Standard physiotherapy treatment was continued throughout the study period (Table 3) for all subjects except case 5, who had discontinued treatment prior to the start of the study due to lack of benefit. The analgesic type, dose and frequency remained constant during the pre-study period and throughout the study period for those with chronic disease (cases 6–8). However, cases 1–5 reduced their analgesic requirements as the study progressed and at the 6-week follow up only case 5 still required any form of analgesia, and this only intermittently.

Control stages

All subjects reported no relief of pain on movement when both limbs were visualized without a device or when the non-reflective surface was viewed. Indeed, movement exacerbated pain. Control phase 2 of the protocol (using a whiteboard in place of the mirror) was only performed at the initial assessment. The reason for this was that the participants who experienced an immediate analgesic response with the mirror were aware that the whiteboard trials were purely for control purposes. It therefore no longer worked as a fair control, and as the mirror was so clearly beneficial to these participants they were reluctant to continue with the whiteboard. In order to keep the protocol uniform across the study participants, this phase was dropped for the 6-week intervention stage.

TABLE 1. Patient characteristics and the effect of the control and intervention phases on their pain at presentation; the frequency of mirror use on follow-up and final pain scores at 6 weeks with infra-red thermal temperature differences between affected and unaffected limbs

Subject, painful limb, age (yr), sex	Symptom duration	Mean temp difference: painful – non-painful limb (°C) ^a	At presentation				Follow-up									
			Control phase 1 ^b		Control phase 2 ^c		Intervention ^d		Frequency of mirror use (times per day) (duration of each treatment 10 min)						At 6 weeks	
			Pain VAS at rest	Pain VAS on movement	Pain VAS on movement	Pain VAS on movement	Pain VAS on movement	Pain VAS on movement	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Pain VAS	Mean temp. diff. (°C)
1, LL, 38, F	6 weeks	1.1	9	9	9	2	8	3	3	3	2	0	0	0	0.2	6
2, LA, 28 F	3 weeks	2.0	7	8	8	3	4	4	3	3	2	0	0	0	0.4	6
3, LL, 34, F	8 weeks	2.7	6	8	8	2	9	4	3	0	0	0	0	0	0.8	4
4, RA, 35, F	5 months	1.9	0	5 ^e	5 ^e	3 ^e	5	4	5	4	5	4	2 ^e	0.3	6	
5, RA, 40, M	1 yr	0.5	4	6	6	6	5	4	5	4	4	3	1	0.4	6	
6, LL, 24, M	2 yr	1.4	7	8	8	8	5	5	5	0	0	0	8	1.3	Unresolved	
7, LL, 38, F	3 yr	n.d. ^f	4	5	5	5	4	4	0	0	0	0	5	n.d.	Unresolved	
8, LL, 27, M	2 yr	2.1	7	8	8	8	4	4	0	0	0	0	8	2.6	Unresolved	

LA, left arm; LL, left leg; RA, right arm; F, female; M, male; n.d., not done.

^aRegion of interest constant significant difference if $> 0.4^{\circ}\text{C}$; ^bboth limbs (no device); ^cpainful limb hidden; ^dmirror visual feedback; ^estiffness; ^fcase 7 had widespread ulceration on her left leg, which made thermal imaging impossible.

TABLE 2. Therapeutic interventions before mirror visual feedback

Subject	Analgesia	IRSB (G)	Physiotherapy modalities	Occupational therapy	Immobilization	TENS	Osteopathy	Acupuncture
1	NSAID, simple		+					
2	NSAID, compound		+	+				
3	Compound		+					
4	NSAID		+				+	
5	Compound		+		+			
6	Opioid	+	+					+
7	Opioid	+	+		+	+		
8	NSAID	+	+		+			

IRSB (G), intravenous regional sympathetic blockade (guanethidine); TENS, transcutaneous electrical nerve stimulation; NSAID, non-steroidal anti-inflammatory drug.

Intervention stage

All three subjects with early CRPS (≤ 8 weeks) reported a striking reduction in their pain VAS during and after visual feedback of their moving, unaffected limb as provided by the mirror. A marked analgesic effect was observed within a few minutes of mirror use, followed by an abrupt return of pain when the mirror was removed initially. With repeated use (four to nine times daily, week 1), the period of analgesia extended progressively from a few minutes to hours, requiring less mirror use over the 6-week study period. At 6 weeks there was a reversal of vasomotor changes as measured by IRT, a return to normal function and no pain at rest or on movement. All three subjects felt they no longer required analgesic relief from the mirror and had stopped prior to assessment at 6 weeks (case 3, week 4; cases 1 and 2, week 6).

The two subjects with intermediate disease duration (5 months and 1 year; cases 4 and 5) reported that the mirror immediately eased their movement-related stiffness but there was no analgesic effect in case 5. They both reported that this reduction in stiffness facilitated movement and the effect lasted for increasing periods after use of the mirror. Although no objective data were collected on function, both subjects felt that by 6 weeks function had improved to such an extent that they were able to return to their usual manual occupations. Interestingly, despite the lack of analgesic effect during the mirror visual feedback procedure, case 5 reported reduced pain at the 6-week follow-up (VAS 6/10 at presentation and 1/10 at 6 weeks). Reversal of IRT temperature differences was recorded in case 4 at 6 weeks, and case 5 remained with no significant difference between the two affected limbs.

No subjective relief of pain and stiffness or reversal of IRT temperature differences was observed in the three subjects with chronic disease (≥ 2 yr) and they had all discontinued mirror use by the end of week 3 due to lack of effect.

Comment

Our observations, the first of their kind in CRPS, suggest that congruent visual feedback of the moving unaffected

TABLE 3. Treatment received during study protocol in addition to mirror visual feedback

Subject	Analgesia	Physiotherapy modalities	Occupational therapy	Osteopathy
1	Simple	+		
2	NSAID	+	+	
3	Compound	+		
4	None	+		+
5	Compound			
6	Opioid	+		
7	Opioid	+		
8	NSAID	+		

NSAID, non-steroidal anti-inflammatory drug.

limb, via a mirror, significantly reduces the perception of pain in early CRPS (type 1) and stiffness in the intermediate stages of the disease. The extent of the analgesic effect surprised both patients and investigators. The abrupt return of pain and stiffness when the mirror was removed supports the view that we were reliably able to influence these sensations. The two internal control stages excluded an analgesic effect from (i) moving the affected limb with normal visual feedback alone and (ii) the influence of selective attention when the limb was hidden. A placebo response is therefore highly unlikely, given the above control stages and the lack of benefit in chronic CRPS subjects. The effect was consistent between the five less chronic subjects and repeatable within subjects. Extended use of the mirror provided increasing periods of analgesia, which aided compliance with exercise regimens. Whilst early CRPS can resolve spontaneously, we are unaware of any therapeutic manoeuvres or drug effects that can achieve such an immediate analgesic effect. In addition, when the intervention is stopped there is an abrupt return of pain. Mirror visual feedback is a simple, inexpensive and, most importantly, a patient-directed treatment.

Our results support the hypothesis that the CNS is capable of generating a feedback-dependent state that can produce pathological levels of pain. In CRPS, this might involve a mismatch between different interdependent modalities, such as a disruption of normal interaction between motor intention and sensory feedback. In those

with inherent vulnerability to this incongruence it can lead, in some, to referred, intractable pain following trauma, and in others it can promote CRPS with a CNS origin. This might explain why some types of CRPS occur without discrete peripheral injury.

Our subjects' pain and stiffness, signalled by this incongruence, can be corrected by the use of false but nevertheless congruent visual feedback of the unaffected limb. The mirror reflection permits the subject to rehearse and practice movements of the affected limb without having to directly activate those parts of maladaptive central processes that typically produce pain. The centrally processed visual input, which appears to originate from the dysfunctional and painful side, acts to re-establish the normal pain-free relationship between sensory feedback and motor intention and consequently results in the rapid resolution of the pain state. In the absence of mirror feedback, movement exacerbates the pain, as was demonstrated in our control stages. In our subjects with long-standing disease there are two possible reasons why mirror visual feedback was ineffective. The first was that trophic changes, such as contractures, limited movement, and the second was that neural pathways may be more established over time. The effect in the two intermediate cases, in whom the easing of stiffness was more apparent than an analgesic response, provides further evidence that time plays a part in this process. Interestingly, single photon emission computed tomography studies [14] have shown that the early stages of the illness are associated with increased blood flow in the thalamus while in the later stages this region shows hypoperfusion. These changes and the peripheral changes that occur over time may explain the lack of treatment effect in subjects with chronic CRPS and the more limited effect in the intermediate cases.

Notwithstanding the therapeutic implications, our results provide an important insight into the pathogenesis of CRPS and possibly other conditions presenting with 'inappropriate' pain. Larger studies, supported ideally by functional imaging, are required.

During the final preparation of this manuscript, Professor Patrick Wall died (8 August 2001) and the other authors would like to dedicate this paper to his memory.

Acknowledgements

We are grateful to the patients who assisted in this study. We thank the physicians at The Royal National Hospital for Rheumatic Diseases for allowing us to study their patients and Mr D. Elvins and Miss R. Edwards for

technical assistance. This work was financed by an Arthritis Research Campaign Integrated Clinical Arthritis Centre Award. CSM is supported as an Arthritis Research Campaign Lecturer in Rheumatological Nursing. RCH is supported as an Arthritis Research Campaign Clinical Research Fellow. PWH is funded by the Medical Research Council.

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