Neurorehabilitation and Neural Repair
Volume XX Number X
Month XXXX xx-xx

10.1177/1545968309335977
http://nnr.sagepub.com

Mirror Therapy in Complex Regional Pain Syndrome Type 1 of the Upper Limb in Stroke Patients

Angelo Cacchio, MD, Elisabetta De Blasis, MD, Vincenzo De Blasis, MSc, Valter Santilli, MD, and Giorgio Spacca, MD

Background. Complex regional pain syndrome type 1 (CRPSt1) of the upper limb is a painful and debilitating condition, frequent after stroke, and interferes with the rehabilitative process and outcome. However, treatments used for CRPSt1 of the upper limb are limited. *Objective*. This randomized controlled study was conducted to compare the effectiveness on pain and upper limb function of mirror therapy on CRPSt1 of upper limb in patients with acute stroke. *Methods*. Of 208 patients with first episode of unilateral stroke admitted to the authors' rehabilitation center, 48 patients with CRPSt1 of the affected upper limb were enrolled in a randomized controlled study, with a 6-month follow-up, and assigned to either a mirror therapy group or placebo control group. The primary end points were a reduction in the visual analogue scale score of pain at rest, on movement, and brush-induced tactile allodynia. The secondary end points were improvement in motor function as assessed by the Wolf Motor Function Test and Motor Activity Log. *Results*. The mean scores of both the primary and secondary end points significantly improved in the mirror group ($P < .001$). No statistically significant improvement was observed in any of the control group values ($P > .001$). Moreover, statistically significant differences after treatment ($P < .001$) and at the 6-month follow-up were found between the 2 groups. *Conclusions*. The results indicate that mirror therapy effectively reduces pain and enhances upper limb motor function in stroke patients with upper limb CRPSt1.

Keywords: *Stroke; Complex regional pain syndrome; Mirror therapy; Poststroke shoulder pain; Pain; Rehabilitation*

Complex regional pain syndrome type 1 (CRPSt1) is a painful condition commonly observed after stroke that can hamper the functional recovery required to perform motor tasks, such as activities of daily living, and that consequently leads to disability.[1] CRPSt1 is characterized by (*a*) sensory disturbances, such as a burning pain with allodynia and hyperalgesia; (*b*) motor disturbances, such as weakness, tremor, and muscle spasms; and (*c*) dystrophic changes of the skin and bone that are not proportionate to the initiating event.[2] CPRSt1 is differentiated from CPRSt2 by the absence of neural trauma.[3] The etiology and pathogenesis of CPRSt1 are still unclear. Generally, the onset of CPRSt1 has been attributed to local ongoing changes in the peripheral parts of the body.[3] Consequently, the treatment of patients with CPRSt1 has focused on peripheral structures and thus includes oral analgesics, local corticosteroid injections, physiotherapy, and sympathetic block, most of which have displayed but limited effectiveness.[4] Moreover, recent reports have expressed doubt on the underlying causes of pathologies such as CPRSt1, fibromyalgia, focal hand dystonia, and phantom limb pain, suggesting that peripheral alterations may not be implicated in the genesis and maintenance of these conditions. Indeed, studies have shown that plastic changes within the brain, such as the disruption of sensory cortical processing, disinhibition of the motor cortex, and disrupted body schema, may generate a feedback-dependent state, which produces pain or other pathological sensations in patients with no evident peripheral damage.[5-12] Neuroscience-based rehabilitation is gaining support as a way to improve outcome in numerous pathologies, even in those in which the deficit appears to be due to cortical abnormalities.[13,14] Mirror therapy is a neurorehabilitation technique designed to remodulate cortical mechanisms of pain and has proved successful in phantom pain,[15] stroke,[16-18] and CRPSt1.[10] In mirror therapy, patients perform movements of the unaffected limb while watching its mirror reflection superimposed over the (unseen) affected limb, thus creating a visual illusion (and therefore positive feedback for the motor cortex) of the affected limb movement.[17] The visual illusion of the affected limb movement generates positive feedback to the motor cortex, which might in turn interrupts the pain cycle. We hypothesized that upper limb CRPSt1 in stroke patients is a consequence of the disruption of these cortical mechanisms and that congruent visual feedback from the moving, unaffected upper limb, as provided by a mirror, would restore the

From the Department of Physical Medicine and Rehabilitation, "San Salvatore" Hospital of L'Aquila, L'Aquila (AC, GS); Department of Emergency, Intensive Cardiology Division, "SS Filippo e Nicola" Hospital of Avezzano, L'Aquila (EDB); International Activities Service, Abruzzo Region Offices, L'Aquila (VDB); Department of Physical Medicine and Rehabilitation, University of Roma ''La Sapienza", Roma (AC, VS), Italy. Address correspondence to: Angelo Cacchio, MD, Dipartimento di Medicina Fisica e Riabilitazione, Ospedale "San Salvatore" di L'Aquila, Via L Natali 1, 67100 L'Aquila, Italy. E-mail: angelo.cacchio@tin.it.

integrity of cortical mechanisms, thereby relieving pain and restoring function in the affected limb.

Although mirror therapy has been used in the management of various clinical disorders,[5-12,15-19] no randomized placebo-controlled study has yet been conducted to assess its effectiveness in the management of upper limb CRPSt1 in stroke patients. To verify this effectiveness, we undertook a randomized placebo-controlled study in which stroke patients with upper limb CRPSt1 were randomly allocated to undertake the conventional stroke rehabilitation program plus mirror therapy or conventional stroke rehabilitation program alone.

Patients and Methods

Patients

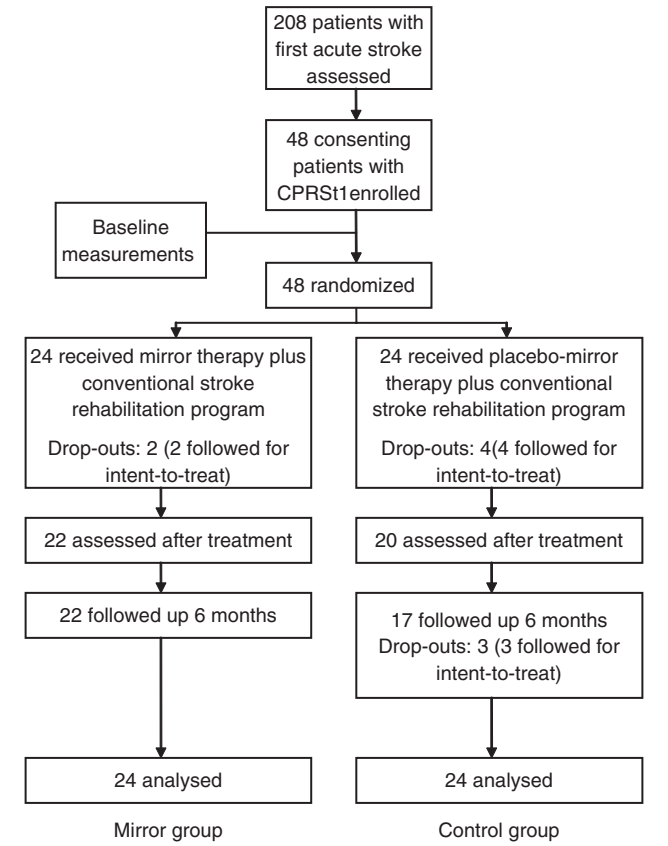
From October 2000 to December 2006, a total of 208 patients (81 women and 127 men, mean age 62.7 ± 13.1 years, ranging from 36 to 83 years) with hemiparesis following a first episode of unilateral ischemic or hemorrhagic stroke and admitted to our inpatient and outpatient rehabilitation center were evaluated for the presence of CRPSt1 (Figure 1). [AQ: 1] Of these 208 patients, 48 (23%), consisting of 26 women and 22 men with a mean age of 58.3 ± 10.5 years (range 40-78), were enrolled in this randomized placebo-controlled study on the basis of the following inclusion criteria: (*a*) first episode of unilateral stroke with hemiparesis during the previous 6 months and (*b*) diagnosis of CRPSt1 based on diagnostic criteria of Bruehl et al,[20] visual analogue scale (VAS, 0-10 cm) pain score >4 cm. Exclusion criteria were the following: (*a*) an intraarticular injection into the affected shoulder during the previous 6 months or use of systemic corticosteroids during the previous 4 months; (*b*) the presence of another obvious explanation for the pain (eg, fracture, radiculopathy); (*c*) prior surgery to either the shoulder or neck region; (*d*) serious uncontrolled medical conditions; (*e*) global aphasia and cognitive impairments that might interfere with understanding instructions for VAS, motor testing, and treatment; (*f*) visual impairments that might interfere with the aims of the study; (*g*) evidence of recent alcohol or drug abuse or severe depression.

Written informed consent was obtained from all the patients before enrolment in the study, and the procedures followed in the study were in accordance with the ethical standards of the local ethics committee and conformed to the Declaration of Helsinki.

Outcome Measures

All the patients were examined 3 times by an investigator who was blinded to the nature of treatment performed: before treatment (pretreatment), 1 week after treatment (posttreatment), and at 6 months (follow-up). The decision to set the follow-up at 6 months is based on the hypothesis that pain improves spontaneously over a long period of time. Outcomes were measured in terms of pain (primary end point) and motor recovery (secondary end point).

Figure 1
Flow Diagram of the Study



Primary End Points. The primary end points were a decrease, at the end of the therapy program compared with the baseline scores, of 2 points in the mean self-rated pain intensity score at rest and on shoulder movement (forward flexion) and of 2 points in the mean self-rated intensity score of tactile allodynia. Moreover, the maintenance of these results was assessed at the 6-month follow-up.

The self-rated pain intensity score, at rest and on shoulder movement(forward flexion), was measured on a 10-cm horizontal VAS,[21] with 0 cm labeled "no pain" and 10 cm labeled "worst pain I have ever had." We decided to measure pain both at rest and on movement because pain on movement may persist even when pain at rest disappears.[22] Tactile allodynia, which was assessed by means of a brush movement (3 movements) within the area of maximal pain, was considered to be present if stroking the skin evoked a sensation of pain, measured on a 10-cm horizontal VAS in the same way as pain at rest and on movement.

Secondary End Points. The secondary end points were a decrease, at the end of the therapy program compared with the baseline scores, of 1 point in the mean functional ability (FA) value and of 2 seconds in the mean performance time (PT) value, both of which are items in the Wolf Motor Function Test

(WMFT), and an increase of 2 points in the mean value of the Quality of Movement (QOM) item in the Motor Activity Log (MAL). Moreover, the maintenance of these results was assessed at the 6-month follow-up.

The WMFT is a 17-item functional limitation scale, used to assess upper limb functional limitations in stroke and other neurological disorders,[23,24] that evaluates strength (2 items) and timed-task performance (15 items). The tasks progress from joint-specific movements to multijoint movements. The WMFT yields 2 scores: a FA score, which assesses quality of performance, and a PT score, which assesses performance speed in seconds. The 15 timed tasks were filmed and later rated for FA on a 5-point scale. The reliability and validity of the WMFT have previously been established.[24]

The MAL is a disability scale structured as an interview that ascertains how much (6-point, range 0-5, Amount of Use scale) and how well (6-point, range 0-5, QOM scale) the patients use their affected upper limb in 30 activities of daily living performed outside the laboratory.[25] Adequate interrater reliability and internal consistency have been reported for chronic stroke patients.[26] We considered the QOM score alone for the statistical analyses because data in the literature suggest that the QOM scale is more internally consistent and reliable than the Amount of Use scale.[27]

Intervention

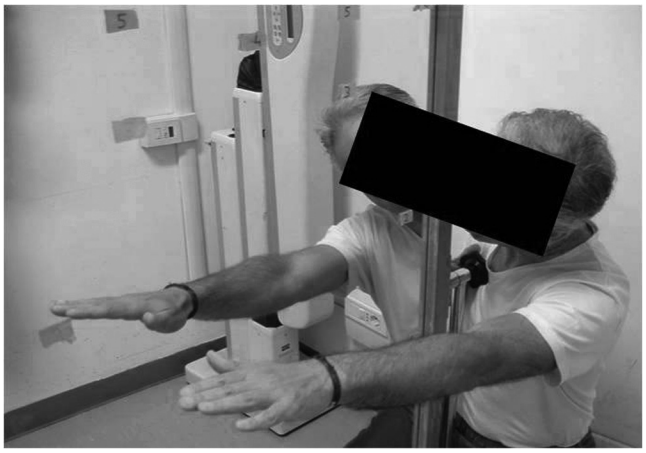
Both the mirror group and the control group received a 4-week conventional stroke rehabilitation program, consisting of five 1-hour sessions a week. The conventional program is patient specific and consists of neurorehabilitation techniques, occupational therapy, and speech therapy (the last, if required). The mirror group received an additional 30 minutes (for the first 2 weeks) and 1 hour (for the last 2 weeks) per session of a mirror therapy program consisting of unaffected upper limb movements. Patients were treated in isolation by a physiotherapist, so that no patient could view another's treatment. Physiotherapists were unaware of patients' assessment results. Patients were seated on a chair, with the mirror board (70 × 120 cm) positioned between the upper limbs perpendicular to the subject's midline and with the unaffected upper limb facing the reflective surface (Figure 2). Under the supervision of the physiotherapist, the patients observed the reflection of their unaffected upper limb while performing the following movements: flexion and extension of the shoulder, elbow, and wrist and prone-supination of the forearm. The speed of movements was self-selected and no additional verbal feedback was offered. The control group performed the same exercise for the same duration, but the reflecting part of the mirror was covered with paper. No analgesic drug for pain relief was administered to the patient during the study period.

Statistical Analysis

Statistical analyses were performed, using SAS 8.2 (SAS Institute Inc, Cary, NC), by one of us independent from the center involved in the study. Both the primary and secondary outcome analyses were performed according to the intention-to-treat (ITT) principle. In this study, subjects that provided baseline and at least 1 posttreatment measurement constituted the ITT population, whereas those who completed all tests from baseline to the 6-month follow-up constituted the per protocol population. For the ITT population, outcome measurements were analyzed using the last observation carried forward method.[28]

Assuming a reduction of 2 cm with a standard deviation of 1.5 for the primary outcome measures, obtained from the pilot data (n = 10), the required sample size for the study was estimated to be at least *36* patients for a power of *.9* and a significance level of .01. Anticipating that protocol violators and early discontinuations would amount to 30%, it was estimated that 48 patients should be enrolled. We tested normality by means of the Shapiro test and verified that the variables resulted normally distributed we have decided to apply parametric tests. [AQ: 2] Values are expressed as mean ± standard deviation. A 2-sample unpaired t test or χ^2 test, as appropriate, was applied to compare differences from the baseline data. Analysis of variance (ANOVA) for repeated measures with group (study versus control) as the between-patients factor and time (pretreatment, posttreatment, and follow-up) as the within-patients factor was used to assess significant differences between the study and control groups and within each group, before and after treatment and at the 6-month follow-up. We also carried out a separate ANOVA for each pain score. A Tukey post hoc comparison was used to assess significant differences between mean values when a significant main effect and interaction were found. Significance levels for multiple comparisons were adjusted with the Bonferroni procedure.

Figure 2
The Mirror Apparatus: Patient Viewing Unaffected Limb in Mirror With Affected Limb Hidden



Results

The baseline characteristics of the 48 participants (Table 1) were similar, with no statistically significant differences

Table 1
Baseline Characteristics of Both Groups

Characteristics	Mirror Group	Control Group	*P* Value
Patients, n	24	24	
Mean age ± SD, year	57.9 ± 9.9	58.8 ± 9.4	.772
Female/male, n (%)	13/11 (54.2/45.8)	13/11 (54.2/45.8)	.845
Lesion type, ischemic/hemorrhagic, n	18/6	17/7	.647
Mean time since stroke ± SD, months	5.1 ± 2.5	4.9 ± 2.8	.802
Mean time since CRPSt1 ± SD, months	2.8 ± 1.3	2.6 ± 1.5	.639
Treatment side, right/left (%)	16/8 (66.7/33.3)	18/6 (75/25)	.546
Mean WMFT			
Functional ability ± SD	3.5 ± 1.2	3.6 ± 0.7	.726
Performance time ± SD, seconds	5.6 ± 2.2	5.5 ± 2.1	.878
Mean MAL QOM ± SD	1.4 ± 0.4	1.3 ± 0.5	.468
Mean pain (VAS)			
At rest ± SD, cm	7.6 ± 1.2	7.5 ± 1.1	.775
On movement ± SD, cm	8.7 ± 0.6	8.3 ± 0.7	.134
Tactile allodynia ± SD, cm[a]	6.8 ± 2.1	6.5 ± 1.8	.598

Abbreviations: SD, standard deviation; CRPSt1, complex regional pain syndrome type 1; WMFT, Wolf Motor Function Test; MAL, Motor Activity Log; QOM, Quality of Movement; VAS, visual analogue scale.
[a]Only 14 patients in the mirror group and 13 in the control group.

between the groups. Both at the end of treatment period and at 6-month follow-up, there was suggestion of a positive effect in all outcomes assessed in the study group, but not in the control group.

None of the patients missed more than 2 scheduled sessions. Two patients (8%) in the mirror group and 7 patients (29%) in the control group dropped out of the study and thus did not attend the posttreatment and 6-month follow-up assessments. One of the 2 patients in the mirror group dropped out because he moved to another city, while the other decided to perform corticosteroid injection therapy in another center. Three of the 7 patients in the control group refused to complete the study, while 4 decided to perform corticosteroid injection therapy in another center.

Primary End Points

The ANOVA test of all the pain scores analyzed (at rest, on movement, and for tactile allodynia) revealed a significant effect of treatment ($F = .62$, $P < .001$ at rest; $F = .48$, $P < .001$ on movement; $F = .39$, $P < .001$ for tactile allodynia) and a significant treatment–time interaction ($F = .61$, $P < .001$ at rest; $F = .55$, $P < .001$ on movement; $F = .43$, $P < .001$ for tactile allodynia). Post hoc comparison demonstrated significant differences between the study and control groups after treatment ($P < .001$) and at the 6-month follow-up ($P < .001$). When the same parameter was compared before and after treatment within each group, a statistically significant reduction emerged in the mirror group both after treatment ($P < .001$ at rest; $P < .001$ on movement; $P < .001$ for tactile allodynia) and at the 6-month follow-up ($P < .001$ at rest; $P < .001$ on movement; $P < .001$ for tactile allodynia; Table 2).

Secondary End Points

The ANOVA test showed a significant effect of treatment ($F = .54$; $P < .001$) and a significant treatment–time interaction ($F = .66$; $P < .001$). Statistically significant improvements in the FA item score and in the PT item score were observed in the mirror group posttreatment ($P < .001$) and at the 6-month follow-up ($P < .001$; Table 3). Statistically significant worsening in the FA item score was observed in the control group at the 6-month follow-up ($P < .01$), though not posttreatment ($P = .415$; Table 3). The control group also displayed a worsening, which did not however reach statistical significance, in the PT item score posttreatment ($P = .04$) and at the 6-month follow-up ($P = .02$; Table 3). Statistically significant differences between groups were found posttreatment ($P < .001$) and at the 6-month follow-up ($P < .001$; Table 3).

The ANOVA test also revealed a significant effect of treatment ($F = .58$; $P < .001$) and a significant treatment–time interaction in the QOM item of the MAL ($F = .77$; $P < .001$), with statistically significant differences between groups being found posttreatment ($P < .001$) and at the 6-month follow-up ($P < .001$; Table 4). Statistically significant improvements in the QOM item score were also observed in the mirror group posttreatment ($P < .001$) and at the 6-month follow-up ($P < .001$; Table 4). No improvement was observed in the control group after treatment ($P = .606$) and at the 6-month follow-up ($P = .143$; Table 4).

Discussion

The aim of this study was to evaluate the response to mirror therapy in stroke patients affected by upper limb CRPSt1. To

Table 2
Pain Scores (VAS) in the Study and Control Groups

VAS Score (Range 0-10 cm)	Mirror Group (n = 24)	Control Group (n = 24)	*P* Value
Mean pain at rest ± SD, cm			
Pretreatment	7.6 ± 1.2	7.5 ± 1.1	.828[a]
Posttreatment	4.3 ± 2.5	7.2 ± 2.2	<.001[a]
Change (95% CI)	–3.3 ± 1.8 (2.1 to 4.4)	–0.3 ± 1.7 (–0.7 to 1.3)	
P value	<.001[b]	.553[b]	
Follow-up	4.7 ± 2.6	8.1 ± 2.0	<.001[c]
Change (95% CI)	–2.9 ± 1.9 (1.9 to 3.9)	0.6 ± 1.5 (–1.7 to 0.5)	
P value	<.001[d]	.292[d]	
Mean pain on movement ± SD, cm			
Pretreatment	8.7 ± 0.6	8.3 ± 0.7	.04[a]
Posttreatment	5.1 ± 2.6	8.2 ± 1.4	<.001[a]
Change (95% CI)	–3.6 ± 2.1 (2.5 to 4.7)	–0.1 ± 1.1 (–0.5 to 0.7)	
P value	<.001[b]	.756[b]	
Follow-up	4.8 ± 2.1	8.6 ± 2.0	<.001[c]
Change (95% CI)	–3.9 ± 1.8 (2.8 to 4.9)	0.3 ± 1.3 (–0.9 to 0.3)	
P value	<.001[d]	.491[d]	
Mean pain tactile allodynia[e] ± SD, cm			
Pretreatment	6.8 ± 2.1	6.5 ± 1.8	.598[a]
Posttreatment	3.8 ± 2.3	6.0 ± 2.1	<.001[a]
Change (95% CI)	–3.0 ± 2.2 (1.7 to 4.3)	–0.5 ± 1.9 (–0.6 to 1.6)	
P value	<.001[b]	.380[b]	
Follow-up	3.3 ± 2.6	6.8 ± 2.3	<.001[c]
Change (95% CI)	–3.3 ± 2.3 (1.9 to 4.4)	0.3 ± 2.0 (–1.5 to 0.9)	
P value	<.001[d]	.617[d]	

Abbreviations: SD, standard deviation; VAS, visual analogue scale; CI, confidence interval.
[a]Comparison between study and control groups both pretreatment and posttreatment.
[b]Comparison between pretreatment and posttreatment within each group.
[c]Comparison between study and control groups both pretreatment and at 6-month follow-up.
[d]Comparison between pretreatment and at 6-month follow-up within each group.
[e]Only 14 patients in the mirror group and 13 in the control group.

our knowledge, this is the first study that has been conducted to investigate the effects of mirror therapy on the treatment of upper limb CRPSt1 in stroke patients.

In our study, we found an incidence of the 23% of CRPSt1. Although the incidence of our series of patients could seem high, this is in agreement with the literature data that reports an incidence of the CRPSt1 after stroke ranging from 1.5% to 61%.[29-31] A recent study,[29] which specifically addressed the incidence of CPRSt1 after stroke, reported an incidence of 1.5% (1 of 64 patients). This conclusion is based on patients' positivity to the triple-phase bone scan. However, the authors also reported that 13 patients of 64 were clinically positive for CRPSt1. Therefore, their incidence based on clinical findings was 20.3%, which is almost equal to ours. Because our diagnosis of CRPSt1 was exclusively based on the clinical findings, this could explain our high incidence.

The wide range of variability in the incidence of CRPSt1 after stroke reflects the still nonuniform diagnostic criteria for CRPSt1,[32] and the frequency with which many symptoms considered typical of CRPSt1 are also transiently found in the paretic arm not affected by CRPSt1.[30]

Physiotherapy is widely recommended as the primary treatment for CPRS, though the physiotherapeutic treatment of choice is unclear, and controlled studies supporting the efficacy of physiotherapy are lacking.[33] Moreover, it has been postulated that pain in CRPSt1 is caused by a mismatch between motor intent and sensory feedback of real movement,[6,10] as occurs in phantom limb pain,[15] or by an involuntary neurological neglect-like condition.[34] Presuming that these hypotheses are correct, mirror therapy may be considered a good alternative to conventional physiotherapy in the treatment of CPRSt1.

Although the mechanism of action of mirror therapy is as yet unknown, some authors have successfully used this therapy in the management of CRPSt1 to relieve pain and other symptoms when conventional physical therapy has proved ineffective.[10,11] Moreover, previous studies have indicated that mirror therapy may be a promising tool in the treatment of hemiparetic upper[16,17,19] and lower limbs[18] in stroke patients.

In a randomized crossover design study with chronic stroke patients, Altschuler et al[16] reported an improved range of motion and speed and accuracy of arm movement in stroke patients who trained with mirror therapy. Sathian et al[19]

Table 3
The Mean Values of WMFT Functional Limitation Scale in the Study and Control Groups

	Mirror Group (n = 24)	Control Group (n = 24)	*P* Value
Mean functional ability (range 0-5) ± SD			
Pretreatment	3.5 ± 1.2	3.6 ± 0.7	.726[a]
Posttreatment	1.5 ± 0.7	3.4 ± 0.9	<.001[a]
Change (95% CI)	1.5 ± 0.9 (0.8 to 2.1)	–0.2 ± 0.8 (–0.3 to 0.7)	
P Value	<.001[b]	.415[b]	
Follow-up	1.9 ± 1.2	4.2 ± 0.8	<.001[c]
Change (95% CI)	–1.6 ± 0.7 (–2.2 to –0.9)	0.6 ± 0.7 (0.1 to 1.0)	
P Value	<.001[d]	.01[d]	
Mean performance time ± SD, seconds			
Pretreatment	5.6 ± 2.2	5.5 ± 2.1	.878[a]
Posttreatment	3.1 ± 2.7	6.7 ± 1.7	<.001[a]
Change (95% CI)	–2.5 ± 2.4 (–1.0 to –3.9)	1.2 ± 1.9 (–2.3 to 0.0)	
P Value	.002[b]	.04[b]	
Follow-up	3.6 ± 2.4	7.1 ± 2.4	<.001[c]
Change (95% CI)	–2.0 ± 2.3 (0.5 to –3.4)	1.6 – 2.2 (–2.9 to –0.2)	
P Value	.006[d]	.02[d]	

Abbreviations: WMFT, Wolf Motor Function Test; SD, standard deviation; CI, confidence interval.
[a]Comparison between study and control groups both pretreatment and posttreatment.
[b]Comparison between pretreatment and posttreatment within each group.
[c]Comparison between study and control groups both pretreatment and at 6-month follow-up.
[d]Comparison between pretreatment and at 6-month follow-up within each group.

Table 4
The Mean Values of MAL Disability Measures Scale in the Study and Control Groups

	Mirror Group (n = 24)	Control Group (n = 24)	P Value
Mean MAL, QOM ± SD (range 0-5)			
Pretreatment	1.4 ± 0.4	1.3 ± 0.5	.468[a]
Posttreatment	3.6 ± 1.5	1.2 ± 0.8	<.001[a]
Change (95% CI)	2.2 ± 1 (–2.8 to –1.5)	0.1 ± 0.6 (–0.3 to 0.5)	
P Value	<.001[b]	.606[b]	
Follow-up	3.4 ± 1.5	1.0 ± 0.8	<.001[c]
Change (95% CI)	2.3 ± 0.7 (–2.6 to –1.3)	0.3 ± 0.6 (–0.1 to 0.7)	
P Value	<.001[d]	.143[d]	

Abbreviations: MAL, Motor Activity Log; QOM, Quality of Movement; SD, standard deviation; CI, confidence interval.
[a]Comparison between study and control groups both pretreatment and posttreatment.
[b]Comparison between pretreatment and posttreatment within each group.
[c]Comparison between study and control groups both pretreatment and at 6-month follow-up.
[d]Comparison between pretreatment and at 6-month follow-up within each group.

reported a significant recovery of grip strength and hand movement of the paretic arm in chronic stroke patients after 2 weeks of intense mirror therapy program. Also, Stevens and Stoykov[17] found that 3 to 4 weeks of mirror therapy in stroke patients leads to a significant improvement of Fugl-Meyer Assessment scores, active range of motion, movement speed, and hand dexterity. Similarly, Sütbeyaz et al[18] reported an improvement of motor recover and motor functioning as measured by Brunnstrom stages and FIM, respectively. Our results corroborate these previous studies, also widening the intervention field of mirror therapy to stroke patients with CPRSt1.

The results of our study strongly support the hypothesis that mirror therapy significantly reduces the perception of pain and increases upper limb motor function in stroke patients with upper limb CRPSt1. Moreover, these results were maintained at the 6-month follow-up. The repetitive use of mirror therapy providing increasingly longer periods of analgesia should help improve patients' compliance with conventional neurorehabilitation exercises. Reduction in pain, as evaluated by the VAS scores, is comparable with that observed in other studies in which mirror therapy was used[10,11] for the treatment of CPRSt1. Our findings show that mirror reflection, generating a false

though congruent visual feedback of the unaffected limb movement, allows stroke patients with upper limb CPRSt1 to rehearse and practice movements of the affected upper limb without pain. The functional improvement observed in the upper limb of our patients, as evaluated by means of the WMFT and MAL, is also comparable with that obtained by other researchers by means of constraint-induced movement therapy.[35]

Mirror therapy appears to create a movement illusion of the affected arm within the brain in stroke patients. These mirror illusions, which have displayed marked effects on brain activity,[36] are believed to compensate for a reduced or absent proprioceptive input,[16] and reestablish the normal pain-free relationship between sensory feedback and motor intention, thus resulting in the rapid resolution of the pain state. Indeed, an increased inflow of inputs from sensory modalities via various pathways has been shown to enhance brain plasticity.[37]

The potential limitations of this study are the lack of direct evidence of brain reorganization after mirror therapy using imaging techniques (eg, functional magnetic resonance imaging), a follow-up period that was not sufficiently long to determine the long-term effect of mirror therapy and to assess its effects on the long-term quality of life in our stroke patients, and the limited size of our chronic CRPSt1 stroke patient population. Moreover, based on previous findings that mirror movements alone do not reduce pain in people with chronic CRPSt1[10] and the observation that patients with chronic CRPSt1 commonly find that even imagined movements of the affected limb can exacerbate pain and swelling,[11,38,39] our results require caution in their generalization due to the lack of patients with longer duration (>1 year) of CPRSt1 in our series. However, despite limited to a subacute group of stroke patients, the potential newness of our study, in comparison with many previous studies, is that it investigates the effectiveness of the mirror therapy in patients with upper limb CPRSt1 developed after a systemic (eg, stroke) and not peripheral (eg, wrist fractures) disease.

In conclusion, our results do indicate that mirror therapy effectively reduces pain (improvement in VAS scores) and increases upper limb function (improvement in WFMT and MAL) in stroke patients with upper limb CRPSt1 and that these results are maintained for 6 months. The fact that mirror therapy is easily applied combined with the results it yielded in our study suggest that mirror therapy may be an effective means of treating pain in stroke patients with upper limb CRPSt1. Although further studies supported by imaging (eg, functional magnetic resonance imaging) or neurophysiological (eg, transcranial magnetic stimulation) techniques are warranted to confirm these results, we suggest that mirror therapy be inserted into the conventional neurorehabilitation program.

References

1. Roy CW, Sands MR, Hill LD. Shoulder pain in acutely admitted hemiplegics. *Clin Rehabil*. 1994;8:334-340.
2. Wong GY, Wilson PR. Classification of complex regional pain syndromes. New concepts. *Hand Clin*. 1997;13:319-325.
3. Stanton-Hicks M, Janig W, Hassenbusch S, Haddox JD, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain*. 1995;63:127-133.
4. Forouzanfar T, Köke AJA, van Kleef M, Weber WE. Treatment of complex regional pain syndrome type I. *Eur J Pain*. 2002;6:105-122.
5. Ramachandran VS, Rogers-Ramachandran D, Stewart M. Perceptual correlates of massive cortical reorganization. *Science*. 1992;258:1159-1160.
6. Harris AJ. Cortical origin of pathological pain. *Lancet*. 1999;354: 1464-1466.
7. Juottonen K, Gockel M, Silen T, Hurri H, Hari R, Forss N. Altered central sensorimotor processing in patients with complex regional pain syndrome. *Pain*. 2002;98:315-323.
8. Jänig W, Baron R. Complex regional pain syndrome: mystery explained? *Lancet Neurol*. 2003;2:687-697.
9. Maihöfner C, Handwerker HO, Neundörfer B, Birklein F. Patterns of cortical reorganization in complex regional pain syndrome. *Neurology*. 2003;61:1707-1715.
10. McCabe CS, Haigh RC, Ring EF, Halligan PW, Wall PD, Blake DR. A controlled pilot study of the utility of mirror visual feedback in the treatment of complex regional pain syndrome (type 1). *Rheumatology (Oxford)*. 2003;42:97-101.
11. Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. *Pain*. 2004;108:192-198.
12. Turton AJ, McCabe CS, Harris N, Filipovic SR. Sensorimotor integration in complex regional pain syndrome: a transcranial magnetic stimulation study. *Pain*. 2007;127:151-160.
13. Liepert J, Bauder H, Miltner WHR, Miltner WH, Taub E, Weiller C. Treatment-induced cortical reorganization after stroke in humans. *Stroke*. 2000;31:1210-1216.
14. Sharma N, Pomeroy VM, Baron JC. Motor imagery. A backdoor to the motor system after stroke? *Stroke*. 2006;37:1941-1952.
15. Ramachandran VS, Roger-Ramachandran D. Synaesthesia in phantom limbs induced with mirrors. *Proc R Soc Lond B Biol Sci*. 1996;263: 377-386.
16. Altschuler EL, Wisdom SB, Stone L, et al. Rehabilitation of hemiparesis after stroke with a mirror. *Lancet*. 1999;353:2035-2036.
17. Stevens JA, Stoykov ME. Using motor imagery in the rehabilitation of hemiparesis. *Arch Phys Med Rehabil*. 2003;84:1090-1092.
18. Sütbeyaz S, Yavuzer G, Sezer N, Koseoglu BF. Mirror therapy enhances lower-extremity motor recovery and motor functioning after stroke: a randomized controlled trial. *Arch Phys Med Rehabil*. 2007;88:555-559.
19. Sathian K, Greenspan AI, Wolf SL. Doing it with mirrors: a case study of a novel approach to neurorehabilitation. *Neurorehabil Neural Repair*. 2000;14:73-76.
20. Bruehl S, Harden RN, Galer BS, et al. External validation of IASP diagnostic criteria for complex regional pain syndrome and proposed research diagnostic criteria. International Association for the Study of Pain. *Pain*. 1999;81:147-154.
21. Scott J, Huskisson EC. Graphic representation of pain. *Pain*. 1976;2: 175-184.
22. Fukui S, Morioka Y, Hayashi T. Objective evaluation of reflex sympathetic dystrophy of the limbs by means of a scoring system and three-phase bone scintigraphy. *Pain Clin*. 1994;7:117-124.
23. Wolf SL, Lecraw DE, Barton LA, Jann BB. Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. *Exp Neurol*. 1989;104:125-132.
24. Morris DM, Uswatte G, Crago JE, Cook EW, Taub E. The reliability of the Wolf Motor Function Test for assessing upper extremity function after stroke. *Arch Phys Med Rehabil*. 2001;82:750-755.
25. Taub E, Miller NE, Novack TA, et al. Technique to improve chronic motor deficit after stroke. *Arch Phys Med Rehabil*. 1993;74:347-354.
26. Miltner WH, Bauder H, Sommer M, Dettmers C, Taub E. Effects of constraint-induced movement therapy on patients with chronic motor deficits after stroke: a replication. *Stroke*. 1999;30:586-592.
27. Uswatte G, Taub E, Morris D, Vignolo M, McCulloch K. Reliability and validity of the upper-extremity Motor Activity Log-14 for measuring real-world arm use. *Stroke*. 2005;36:2493-2496.
28. Unnebrink K, Windeler J. Intention-to-treat: methods for dealing with missing values in clinical trials of progressively deteriorating diseases. *Stat Med*. 2001;20:3931-3946.

29. Petchkrua W, Weiss DJ, Patel RR. Reassessment of the incidence of complex regional pain syndrome type 1 following stroke. *Neurorehabil Neural Repair*. 2000;14:59-63.
30. Wasner G, Schattschneider J, Binder A, Baron R. Complex regional pain syndrome—diagnostic, mechanisms, CNS involvement and therapy. *Spinal Cord*. 2003;41:61-75.
31. Daviet JC, Preux PM, Salle JY, et al. Clinical factors in the prognosis of complex regional pain syndrome type I after stroke: a prospective study. *Am J Phys Med Rehabil*. 2002;8:34-39.
32. Baron R, Fields HL, Janig W, Kitt C, Levine JD. National Institutes of Health Workshop: reflex sympathetic dystrophy/complex regional pain syndromes—state-of-the-science. *Anesth Analg*. 2002;95:1812-1816.
33. Hollis S, Campbell F. What is meant by intention-to-treat analysis? Survey of a published randomised controlled trials. *BMJ*. 1999;319:670-674.
34. Kingery WS. A critical review of controlled clinical trials for peripheral neuropathic pain and complex regional pain syndromes. *Pain*. 1997;48: 171-175.
35. Galer BS, Jensen M. Neglect-like symptoms in complex regional pain syndrome: results of a self-administered survey. *J Pain Symptom Manage*. 1999;18:213-217.
36. Garry MI, Loftus A, Summers JJ. Mirror, mirror on the wall: viewing a mirror reflection of unilateral hand movements facilitates ipsilateral M1 excitability. *Exp Brain Res*. 2005;163:118-122.
37. Luft AR, Forrester L, Macko RF, et al. Brain activation of lower extremity movement in chronically impaired stroke survivors. *Neuroimage*. 2005;26:184-194.
38. Hamdy S, Rothwell JC, Aziz Q, Singh KD, Thompson DG. Long-term reorganization of human motor cortex driven by shortterm sensory stimulation. *Nat Neurosci*. 1998;1:64-68.
39. Moseley GL. Imagined movements cause pain and swelling in a patient with complex regional pain syndrome. *Neurology*. 2004;62:1644.