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Review Article

Efficacy of mirror therapy, motor imagery, and visual feedback in the treatment of phantom limb pain after amputation: an updated systematic review

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ABSTRACT

Introduction: Phantom limb pain affects 50 percent to 85 percent of patients who have had their limbs amputated, lowering their quality of life. Clinical therapies for central pain, such as mirror therapy, motor imagery, or visual feedback, might help amputee patients suffering from phantom limb pain.

Objectives: To provide a general review of the efficacy of various approaches for treating phantom limb discomfort in amputee patients.

Methods: The following databases were used for a computerized literature search up to March 2022: PubMed, ScienceDirect, and Google Scholar. The modified Jadad score is utilized to measure study quality in this research. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines were followed while conducting this systematic review.

Results: In all, 15 papers matched our inclusion criteria, with 5 receiving a low study quality rating and 10 receiving a good study quality rating. All the studies revealed a considerable decrease in pain; however, the patients and techniques varied.

Conclusion: Mirror therapy, motor imagery, and visual feedback can alleviate phantom limb pain. However, there is a lack of scientific data to support their efficacy. Future studies should use more powerful research methodologies to investigate these medicines' short- and long-term advantages.

Keywords: mirror therapy, motor imagery, virtual feedback, phantom limb pain

INTRODUCTION

Phantom limb pain is experienced when the brain sends pain signals to limbs that are not there. The pain can differ in type and range in intensity. For example, a mild form might be experienced as a sharp, intermittent stabbing pain that causes the limb to jerk in reaction. An example of a more severe type is the feeling that the missing limb is being crushed. The pain often diminishes in frequency and intensity with time. For a small number of amputees, however, phantom limb pain can become chronic and debilitating due to the frequency and severity of the pain. Phantom limb pain (PLP) affects 50% to 80% of limb amputees. PLP is generally categorized as a neuropathic pain since it is accompanied by deafferentation and cortical remodeling of the somatosensory system.[1]

Although the impact of cortical remodeling on PLP is unknown, clinical therapies targeting the central neural process may lead to promising strategies for symptomatic therapy of central pain sensitization. Visually portraying the return of the limb using mirror boxes has shown that PLP can be reduced and that the cortical reorganizations are significantly reduced or return to the pre-amputation state.[2,3]

Motor imagery might also be effective in those with phantom limb pain. After randomly seeing images of both limbs, subjects were instructed to imagine adopting the position depicted twice with a smooth and pain-free movement. Subjects were instructed to see themselves performing the maneuver rather than watching themselves perform it.[4]

One treatment for phantom limb pain is visual feedback. The idea is that visual feedback of a "virtual arm" increases awareness and controllability of a phantom limb and lessens phantom pain. It uses phantom limb representations, including postures and structures particular to each person's phantom limb.[2]

Colmenero et al. conducted a systematic review in 2017 to assess the effectiveness of mirror therapy, motor imagery, and virtual feedback on phantom limb pain following amputation. They reviewed 12 studies and found that mirror therapy, imaginary motor, and virtual visual feedback reduce phantom limb pain; however, limited scientific evidence supports their effectiveness.[5] In this study, we aim to update the systematic review to get better findings than earlier research by including the most recent studies and using different study quality assessments.

METHOD

This systematic review was undertaken by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statements.

Search strategy

We conducted a systematic search of PubMed, ScienceDirect, and Google Scholar using the medical subject headings terms and free keywords “mirror therapy”, “mirror exercise”, “motor imagery”, and “visual feedback” from January 2006 to March 2022 and identified all potentially relevant articles. When searched databases allowed limits, searches were restricted to clinical trials or randomized clinical trials and provided in English. We also searched the list of references for the full-text literature and reviewed all relevant publications for studies to determine any missing studies.

Inclusion & exclusion criteria

Inclusion criteria are: (1) having upper or lower extremity amputation; (2) having PLP or peripheral neuropathic pain;

Exclusion criteria are: (1) having a visual impairment or severe hearing loss; (2) having any condition that prevents movement of the opposite extremity (such as plaster cast, paralysis in the intact limb, etc.); (3) being diagnosed with a mental disorder that could diminish ability to concentrate during therapy; (4) had upper motor neuron lesion (stroke, traumatic brain injury, etc); (5) had bilateral amputation.

Outcome of interest

The severity or intensity of phantom limb pain was measured using the visual analog scale (VAS), numeric rating scale (NRS), McGill pain questionnaire, and other pain assessment tools.

Study Quality

This study uses the modified Jadad score to assess study quality. Modified Jadad score or the Oxford quality scoring system was used to assess a clinical trial's methodological quality independently.

Data selection and extraction

Each trial was identified by the above search and assigned to a review topic (or topics). A self-designed data extraction form was used to independently extract contents by researchers, including lead author, year of publication, pain variable, intervention group, control group, technique, intervention, and outcome measures or results. Three reviewers conducted literature screening, quality evaluation, and data extraction process.

RESULTS

Study selection

The electronic search in the different databases produced 3.248 items from 3 databases: 3.010 studies from Google Scholar and 238 studies from PubMed and ScienceDirect.

After reading the title, abstract, and full text, 28 studies met the criteria. The studies with a methodology of case study/series, literature review, and qualitative studies were eliminated, resulting in 15 studies. Figure 1 shows the flowchart of the process of selection and exclusion of studies.

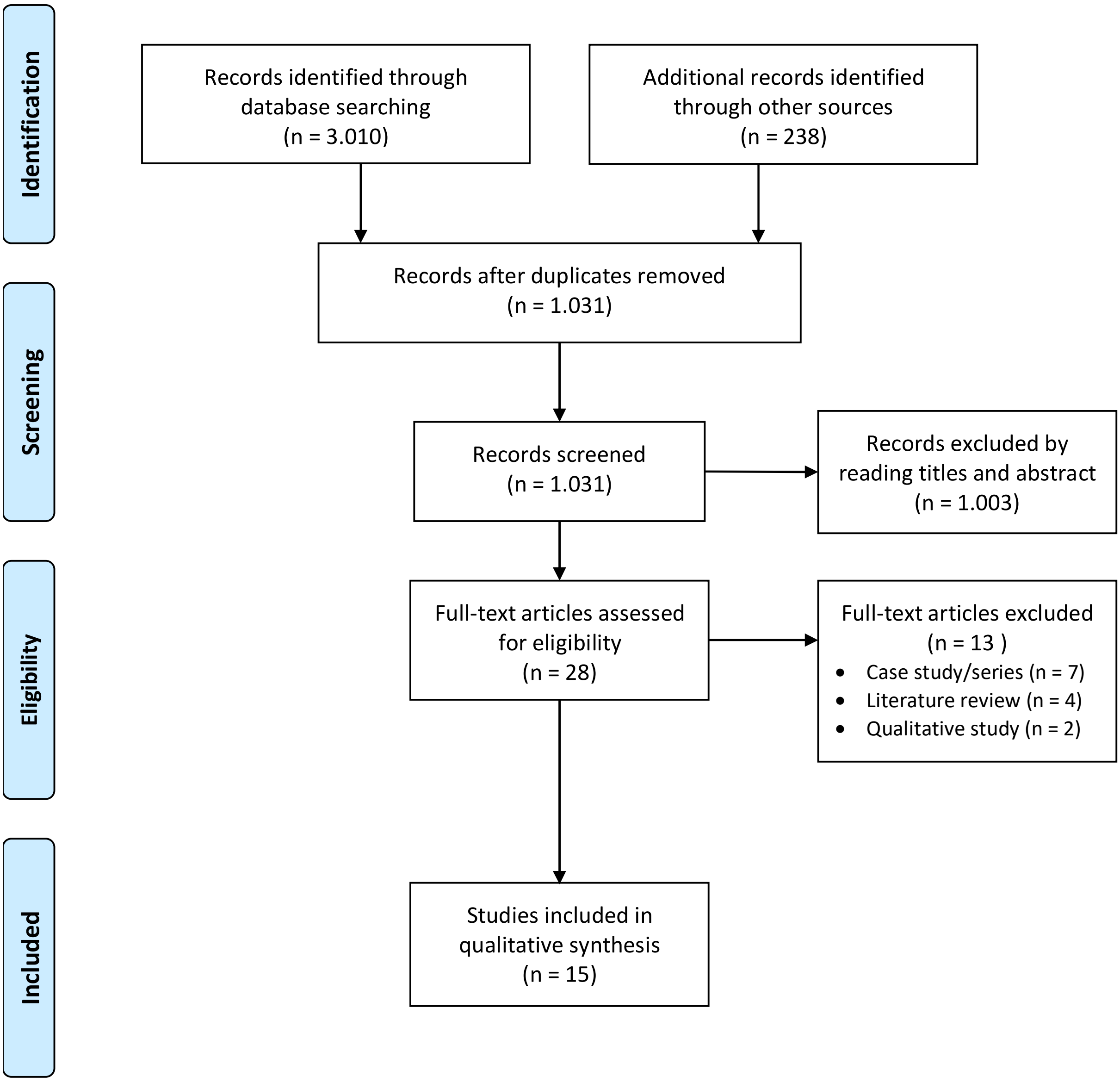

Figure 1. PRISMA flow diagram.

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Study characteristic

Table 1 summarizes the main information of the selected studies. The studies included in this review used 12 different measures of pain: Numerical Rating Scale (NRS),[6,7] Nuclear Magnetic Resonance Imaging (NMRI),[6,8] PLP Questionnaire,[5] Visual Analog Scale (VAS),[3,4,9–13] McGill Pain Questionnaire,[4,9,14,15] West Haven–Yale Multidimensional PLP Inventory,[16] Universal Pain Score (UPS),[11] Brief Pain Inventory (BPI),[17] Patient Information Form,[18] Mirror Therapy Practice Follow-Up Booklet,[18] Pain Rating Index,[15] and Weighted Pain Distribution Scale.[15]

The largest sample of amputees in the experimental group was 41 patients[14], and the lowest five patients.[4] Four papers presented a sample of upper limb amputees,[6,13,15,16] Five studies used lower limb amputees,[3,8,12,14,17] and six used a mixed upper and lower limb.[4,7,9–11,18].

Study quality

Ten of the 15 papers included in this review had a modified Jadad score of 4 or above. About five studies had a score of less than four, indicating that they are of low quality. The methodological quality of the research examined is shown in Table 2.

Table 2. The methodological quality of the study using modified Jadad scoring

Author	**(1)**	**(2)**	**(3)**	**(4)**	**(5)**	**(6)**	**(7)**	**(8)**	**Total score**	**Study Quality**
Brodie et al. (2007)[14]	1	1	0	0	0	0	0	1	3	Low
Brunelli et al (2015)[17]	1	1	0.5	1	0	1	0	1	5.5	Good
Chan et al. (2007)[3]	1	1	0	0	0	0	0	1	3	Low
Cole et al. (2009)[9]	0	0	0	0	0	1	1	1	3	Low
Diers et al. (2010)[16]	1	1	0	0	0	1	0	1	4	Good
Finn et al (2017)[13]	1	1	0	0	1	1	1	1	6	Good
Maciver et al (2008)[6]	0	0	0	0	0	1	0	1	2	Low
Moseley (2006)[4]	1	1	0.5	1	1	1	0	1	6.5	Good
Ol et al. (2018)[12]	1	1	0	0	1	1	1	1	6	Good
Ortiz-Catalan et al (2016)[15]	0	1	0	0	0	1	1	1	4	Good
Rothgangel et al (2018)[8]	1	1	0.5	1	1	1	1	1	7.5	Good
Sumitani et al. (2008)[7]	0	0	0	0	0	0	0	1	1	Low
Tilak et al. (2015)[11]	1	1	0.5	1	1	1	1	1	7.5	Good
Ulger et al. (2009)[10]	1	1	0	0	0	1	0	1	4	Good
Yildirim and Kanan (2016)[18]	0	0	0	0	1	1	1	1	4	Good

(1) The study described as randomized. (2) The method of randomization is appropriate. (3) The study was described as blinding (double-blind got one score, and single-blind got a 0.5 score). (4) The method of blinding is appropriate. (5) There is a description of withdrawals and dropouts. (6) There is a description of the inclusion/exclusion criteria. (7) The method used to assess adverse effects described. (8) The methods of

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statistical analysis described. A total score < 4 is considered a low-quality study. A score of 4 or more is classified as good quality.

Descriptions of mirror, motor imagery, and virtual visual treatment

In terms of treatment session progress, the research revealed various features. They differed in previous training, treatment, session time, and approach. Furthermore, some writers made choices on the medication given to the individuals throughout the therapy time.

Before the sessions, participants in nine research were taught to experience or envision their phantom limb motions.[4,6,10,12–16,18] Except for two research based on a single session [9,14] and another study with an unclear training time,[11] the training period in all 15 trials was at least four weeks. During therapy, the technique sessions differed from one trial to the next. Only three researchers employed repetitious exercises,10,13,14, while most were based on real-time work.[3,4,6–8,8,9,15,16,18] Five studies also performed therapy sessions at home after the therapist had received prior training.[6,8,12,16,18]

Four studies removed pain medication throughout the treatment period,[4,6,10,16], five studies did not modify medication or possibly conventional physiotherapy approaches, and the other studies did not describe this medical component,[8,9,13,15,16] and the other studies did not specify this medical feature.

DISCUSSION

The efficacy of mirror treatment, motor imagery, and visual feedback in amputees with PLP was studied in this study. Although all trials demonstrated that these treatments helped lower PLP, there was minimal evidence for their utility in reducing PLP.[19] Due to a variety of factors, we were able to pick 15 papers for our analysis. First, subjects with phantom sensation but no phantom pain were excluded from the study; second, bilateral amputees were excluded because the presence of an intact limb is required for the treatment process and for the therapies to have an effect; and third, a study that included multiple therapeutic interventions in addition to the therapies studied was also excluded.

In a systematic review study conducted by Colmenero in 2017, 12 studies were assessed, 9 of which were classified as having low methodological quality and 3 of which were rated as having moderate methodological quality. They are evaluating the methodological quality of the included studies using the PEDro scale, with only publications earning above 3 points being chosen.[5] In this study, we have applied the modified Jadad score to evaluate the study's quality, particularly the RCT study. We found 15 papers that matched our inclusion criteria, with 5 receiving a low study quality rating and 10 receiving a good study quality rating.

Some studies in this review did not discriminate between upper and lower limb amputations, the reason for amputation, or the gender of the patients. As a result, gender balance was not always achieved in certain groups. The lack of consistency in patients and techniques between research might result in large variances in the magnitude of the impact of post-amputation PLP. Previous research has shown that the likelihood of presenting PLP is lower in males than in women and that the risk of presenting PLP decreases with time in lower limb amputees compared to upper limb amputees.

The age range of the subjects in the investigations ranged from 19 to 82 years old. Neuronal plasticity is age-related, resulting in sensory and perceptual distortion and loss later in life. Changes in psychomotor performance are caused by the chemical events of neuronal aging, which include increased response time and decreased speed and accuracy of motions and activities.[20] As a consequence, the age discrepancy between the groups may contribute to the disparities in the findings.

Early rehabilitation has been identified as a good predictive factor; thus, the post-surgical period should be documented and studied.[2,19] To our knowledge, no research has revealed the period after the amputation and the ideal time to use these treatments.

Within and within trials, there has been heterogeneity in the kind and degree of PLP, particularly before therapy. PLP, on the other hand, was shown to be significantly reduced in all investigations. Four trials found that treatment effects at the motor and cortical sensory levels might explain the decrease in pain. According to Maciver et al., the right insula, posterior cingulate cortex, and premotor cortex were the key sensory and motor structures implicated in those interventions.[6] According to Diers et al., attempting to reactivate the cortical representation of the severed leg might stimulate brain plasticity in those regions, resulting in a decrease in PLP.[16] The activation of mirror neurons in the contralateral hemisphere of the brain to the amputated leg might potentially explain pain alleviation in mirror/virtual treatment, according to Chan et al.[3] This occurs when a person performs an action or simply sees another person doing a movement, resulting in a reduction in the activity of protopathic pain-perceiving systems. Ulger et al., on the other hand, showed that phantom limb workouts changed muscular tension.[10] They also discovered that the intensity of PLP is affected by the residual limb's location. As a result, bilateral exercises should be performed to reduce muscular tension and relax the remaining section of the severed limbs.

Primary motor cortex reactivation by visuomotor training plays a key role in lowering PLP in these treatments.[21] Conversely, Moseley claims that imagined motions may stimulate brain regions such as the premotor and primary motor cortex, impacting pain relief by changing hand laterality recognition, imagined, and mirror movements.[4] Brodie et al., on the other hand, found that repetitive motions of the contralateral limb decreased PLP by lowering cortical activity in the somatosensory and anterior cingulate cortex.[14]

A strategically positioned mirror may provide the appearance that the severed limb has been restored and can be moved on purpose, resulting in the intentional activation of visual motor imagery of the phantom limb. Furthermore, the patient may view the illusion or virtual movement as non-painful, making treatment enjoyable and enjoyable. Virtual reality may help reduce situational stress in the healthcare context, particularly in kinesiophobic patients, reducing PLP aggravation during therapy.[3,16,19]

There is an interesting finding in Ol et al. in 2018. Combined mirror-tactile treatment significantly improved PLP and stump pain compared to mirror or tactile therapy alone. However, the difference between the three treatment arms was slight and hardly clinically relevant.[12] And there is a tele-treatment approach of mirror therapy conducted by Rothgangel in 2018. It showed that the effects of mirror therapy on PLP at four weeks were insignificant. MT significantly reduced the duration of PLP at six months compared to the tele treatment and control group.[8]

There are some implications for these techniques in clinical practice and research. There is evidence that programs incorporating mirror therapy, motor imagery, and virtual reality may be helpful for patients with PLP. This research topic needs more research and models of interpretation. Research should focus on the influence of sequential activation of premotor and motor cortical networks and the effectiveness of attention resources as a treatment for the affected limb.

The review's key strength is its focus on the efficacy of relevant and novel intervention strategies on amputees with PLP from Prosthetics and Orthotics International. This review, however, contains several flaws. To begin with, the investigations included a wide range of themes and approaches. Second, accessing full-text versions of some papers proved problematic. Third, since a single investigator conducted the search, the search's inter-observer reliability could not be determined.

CONCLUSION

To establish efficacy in lowering PLP, further research with better methodological quality trials is required. However, there is a lack of scientific data to support their efficacy, but mirror therapy, motor imagery, and visual feedback can alleviate phantom limb pain.

REFERENCES

1. Richardson C, Kulkarni J. A review of the management of phantom limb pain: challenges and solutions. *JPR*. 2017;Volume 10:1861-1870. doi:10.2147/JPR.S124664
2. Murray C, ed. *Amputation, Prosthesis Use, and Phantom Limb Pain*. Springer New York; 2010. doi:10.1007/978-0-387-87462-3
3. Sh H, Da B, Jb W, Jj C, Jt H. Mirror Therapy for Phantom Limb Pain. *The New England Journal of Medicine*. Published online 2007:2.
4. Moseley GL. Graded motor imagery for pathologic pain: A randomized controlled trial. *Neurology*. 2006;67(12):2129-2134. doi:10.1212/01.wnl.0000249112.56935.32
5. Colmenero LH, Marmol JMP, Martí-García C. Effectiveness of mirror therapy, motor imagery, and virtual feedback on phantom limb pain following amputation: A systematic review. *Prosthetics and Orthotics International*.:11.
6. MacIver K, Lloyd DM, Kelly S, Roberts N, Nurmikko T. Phantom limb pain, cortical reorganization and the therapeutic effect of mental imagery. *Brain*. 2008;131(8):2181-2191. doi:10.1093/brain/awn124
7. Sumitani M, Miyauchi S, McCabe CS, et al. Mirror visual feedback alleviates deafferentation pain, depending on qualitative aspects of the pain: a preliminary report. *Rheumatology*. 2008;47(7):1038-1043. doi:10.1093/rheumatology/ken170
8. Rothgangel A, Braun S, Winkens B, Beurskens A, Smeets R. Traditional and augmented reality mirror therapy for patients with chronic phantom limb pain (PACT study): results of a three-group, multicentre single-blind randomized controlled trial. *Clin Rehabil*. 2018;32(12):1591-1608. doi:10.1177/0269215518785948
9. Cole J, Crowle S, Austwick G, Henderson Slater D. Exploratory findings with virtual reality for phantom limb pain; from stump motion to agency and analgesia. *Disability and Rehabilitation*. 2009;31(10):846-854. doi:10.1080/09638280802355197
10. Ülger, Topuz S, Bayramlar K, Şener G, Erbahçeci F. Effectiveness of phantom exercises for phantom limb pain: A pilot study. *J Rehabil Med*. 2009;41(7):582-584. doi:10.2340/16501977-0380
11. Tilak M, Isaac SA, Fletcher J, et al. Mirror Therapy and Transcutaneous Electrical Nerve Stimulation for Management of Phantom Limb Pain in Amputees - A Single Blinded Randomized Controlled Trial: Mirror Therapy Versus TENS for Phantom Limb Pain. *Physiother Res Int*. 2016;21(2):109-115. doi:10.1002/pri.1626
12. Ol HS, Van Heng Y, Danielsson L, Husum H. Mirror therapy for phantom limb and stump pain: a randomized controlled clinical trial in landmine amputees in Cambodia. *Scandinavian Journal of Pain*. 2018;18(4):603-610. doi:10.1515/sjpain-2018-0042

13. Finn SB, Perry BN, Clasing JE, et al. A Randomized, Controlled Trial of Mirror Therapy for Upper Extremity Phantom Limb Pain in Male Amputees. *Front Neurol*. 2017;8:267. doi:10.3389/fneur.2017.00267
14. Brodie EE, Whyte A, Niven CA. Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a 'virtual' limb upon phantom limb pain, sensation and movement. *European Journal of Pain*. 2007;11(4):428-436. doi:10.1016/j.ejpain.2006.06.002
15. Ortiz-Catalan M, Guðmundsdóttir RA, Kristoffersen MB, et al. Phantom motor execution facilitated by machine learning and augmented reality as treatment for phantom limb pain: a single group, clinical trial in patients with chronic intractable phantom limb pain. *The Lancet*. 2016;388(10062):2885-2894. doi:10.1016/S0140-6736(16)31598-7
16. Diers M, Christmann C, Koeppe C, Ruf M, Flor H. Mirrored, imagined and executed movements differentially activate sensorimotor cortex in amputees with and without phantom limb pain. *Pain*. 2010;149(2):296-304. doi:10.1016/j.pain.2010.02.020
17. Brunelli S, Morone G, Iosa M, et al. Efficacy of Progressive Muscle Relaxation, Mental Imagery, and Phantom Exercise Training on Phantom Limb: A Randomized Controlled Trial. *Archives of Physical Medicine and Rehabilitation*. 2015;96(2):181-187. doi:10.1016/j.apmr.2014.09.035
18. Yıldırım M. The Effect of Mirror Therapy on the Management of Phantom Limb Pain. *Agri*. Published online 2016. doi:10.5505/agri.2016.48343
19. Rothgangel A, Smeets R, Braun S, Beurskens S. *Treating Phantom Limb Pain Following Amputation The Potential Role of a Traditional and Teletreatment Approach to Mirror Therapy*. Gildeprint; 2019.
20. Mahncke HW, Bronstone A, Merzenich MM. Brain plasticity and functional losses in the aged: scientific bases for a novel intervention. In: *Progress in Brain Research*. Vol 157. Elsevier; 2006:81-109. doi:10.1016/S0079-6123(06)57006-2
21. Giraux P, Sirigu A. Illusory movements of the paralyzed limb restore motor cortex activity. *NeuroImage*. 2003;20:S107-S111. doi:10.1016/j.neuroimage.2003.09.024

Table 1. Efficacy of mirror therapy, motor imagery, and virtual feedback in the treatment of phantom limb pain after amputation: a systematic review

No	Author	Pain Assessment Tool	Intervention group	Control group	Technique	Intervention	Outcome measures/results
1	Brodie et al. (2007)[14]	VAS was used to record the intensity of PLS and PLP. MPQ	n = 41 amputees reporting that they had experienced phantom limb awareness, but the presence and strength of the phantom leg fluctuated as is normal in this population	n = 39 amputees reporting the same characteristics as the intervention group	Mirror therapy	Mirror therapy group: Subjects were asked to place their intact limb into the mirror box, direct their gaze onto the mirror image of their intact limb and align their phantom limb with this image. Control condition group: Participants aligned their intact leg and phantom leg to either side of the mirror while it was obscured, allowing the subject to view the intact limb but not its mirror image	Three subjects in both groups reported the abolition of PLP following the intervention. Significant main effects for time were found for MPQ total score ($F(1, 13) = 7.195$; $p < 0.05$) and MPQ sensory score ($F(1, 13) = 8.374$; $p < 0.05$). Subjects in both conditions reported a significant decrease in pain intensity, but statistical power was less than 80%
2	Brunelli et al (2015)[17]	BPI	n = 27 subjects with unilateral lower limb amputation with PLP and PLS	n = 24 subjects with unilateral lower limb amputation with PLP and PLS	Progressive muscle relaxation, Mental imagery, Phantom exercises	Experimental group: combined training of progressive muscle relaxation, mental imagery, and phantom exercises two times/week for four weeks; Control group: the same amount of physical therapy dedicated to the residual limb; No pharmacological intervention was initiated during the trial period	Experimental group: showed a significant decrease over time in the BPI ($p < 0.03$); Changes were statistically significant only for intensity of the worst pain and intensity of the average pain in the control group
3	Chan et al. (2007)[3]	Number and duration of pain episodes and the intensity of pain, using a 100-mm VAS; Number and duration of pain episodes; Severity of pain	n = 6 patients with PLP after the amputation of a leg or foot; mirror group who viewed a reflected image of their intact foot in a mirror	n = 6 patients with PLP after the amputation of a leg or foot; group that viewed a covered mirror (covered mirror group); n = 6 patients with PLP after	Mirror therapy. Covered mirror. Mental visualization	Under direct observation, patients performed their assigned therapy for 15 minutes daily during four weeks of therapy	Mirror group: Pain intensity decreased, as did the number and duration of pain episodes. After four weeks of treatment, 100% of patients reported decreased pain (median change on the VAS, –24 mm; range, −54 to −13). In comparing changes in the score on the VAS at four weeks, the mirror group differed significantly from the covered mirror group ($p = 0.04$) and the mental-visualization group ($p = 0.002$).

				the amputation of a leg or foot; group trained in mental visualization (mental-visualization group)			
4	Cole et al (2009)[9]	VAS ; MPQ	Group 1 (n = 7): leg amputation ; Age range: 27–72 years ; Mean age: 49 years ; Group 2 (n = 7): arm amputation ; Age range: 36–82 years ; Mean age: 56 years	n = 9 patients with lower limb amputation and intermittent PLP; pain free at the test time ; Age range: 29–78 years ; Mean age: 64 years	Virtual reality	Virtual reality (motion capture technology/ virtual prototype arm–leg) 60–90 min session	The percentages of reduction in pain through VAS were 22%–100% (with a mean of 64%) during the virtual reality test.
5	Diers et al. (2010)[16]	The modified German version of "West Haven–Yale Multidimensional Phantom Limb Pain Inventory"; Evaluation separately of PLP and residual limb pain	n = 14 unilateral upper limb amputees ; Group 1 (n = 7): with PLP ; Age range: 36–62 years ; Mean age: 54.3 ± 8.6 years ; Group 2 (n = 7): without PLP ; Age range: 41–60 years ; Mean age: 50.3 ± 7.2 years	n = 9 healthy control ; Range age: 39–61 years ; Mean age: 51.9 ± 6.9 years	Mirror therapy and motor imagery	NMRI during mirror therapy. NMRI measurements are separated by about 3 minutes each and pauses of about 5 minutes. Training to imagine movement during EMG of 1 h; Three treatment blocks (movements executed in the mirror and imagined)	The PLP and residual limb pain differed significantly between the three groups ($p < 0.05$) ; $p < 0.05$ for all variables of mirror therapy.
6	Finn et al (2017)[13]	VAS	PLP in unilateral, upper extremity	Group II (n = 3): covered mirror therapy;	Mirror therapy; covered	Each participant received 15 min of the assigned therapy daily for five days/week for four weeks	Group I had a significant decrease in pain scores, from a mean of 44.1 (SD = 17.0) to 27.5 (SD = 17.2) mm (p =

			amputees. Age range 18 - 70. Group I (n =9): mirror therapy group	Group III (n = 3): mental visualization therapy.	mirror therapy; mental visualization therapy		0.002). In addition, there was a significant decrease in daily time experiencing pain, from a mean of 1,022 (SD = 673) to 448 (SD = 565) minutes (p = 0.003). By contrast, the control group had neither diminished pain (p = 0.65) nor decreased overall time experiencing pain (p = 0.49)
7	Maciver et al (2008)[6]	Evaluation before and after training with NRS NMRI (variables: NRS constant pain, constant discomfort, NRS pain exacerbation, exacerbation of discomfort sensation) "Phantom limb pain questionnaire"	n = 13 (11 men and two women); Age range: 32–75 years; Mean age: 52.92 ± 13.6 years; Unilateral upper limb amputation above the wrist PLP lasting at least one year	n = 6 healthy volunteers; Age range: 30–56; Mean age: 43 years; Evaluated to determine the normal cortical responses to the set of tasks	Motor imagery	NMRI: before and after therapy, 30 s of movements, 30 s of rest, 6.5 min total; Experimental group: combining the exercise of "body-scan" and imagination of movement and the sensation in the phantom limb; Six individual therapy sessions with a therapist (once a week or every 15 days) for 60 min each. Daily home therapy of 40 minutes with a Compact Disc (CD) of the meditation and imagery exercises. Control group: healthy volunteers received no intervention but were scanned twice	Significant reduction in pain intensity (p < 0.0005) and reduced discomfort and pain unpleasantness (p < 0.01); Significant reduction of the intensity of daily discomfort exacerbations (p < 0.03) and discomfort of exacerbations (p < 0.005)
8	Moseley (2006)[4]	MPQ Pain VAS NRS	n = 5 amputees with PLP and complex regional pain syndrome	n = 4 amputees with PLP and complex regional pain syndrome	motor imagery	Experimental group (motor imagery): the first two weeks were the limb laterality recognition phase. The next two weeks were the imagined movement phase. The next Two weeks were the mirror movement phase. Control group (medical/physiotherapy management or standard care): participants undertook a 6-week physiotherapy treatment program and maintained the usual medical care	There was an improvement in the experimental group for pain VAS at post-program and follow-up. Then, graded motor imagery reduced pain in amputees with PLP and complex regional pain syndrome.

9	Ol et al. (2018)[12]	VAS (severe pain defined as VAS >6 cm, moderate pain as VAS 3–6 cm, and mild pain as VAS <3 cm)	n = 45. Traumatic transtibial amputation with PLP in low resources community. Mean age was 55.7 (SD 6.7) ; Group I (n = 15) : mirror therapy	Group II (n = 15) : Tactile Group ; Group III (n = 15): Combination	mirror therapy, tactile treatment, combined mirror, and tactile treatment	Group I: Mirror therapy (for 5 min every morning and night doing repeated movement of the foot while closely observing the reflected image of the uninjured limb); Group II: tactile treatment (for 5 min every morning and evening, patient concentrating on feeling the five different tactile stimuli that given by family); Group III: Combined mirror and tactile treatment (the mirror and the tactile treatments go on serially, with 5 min for each treatment). Four weeks practice period.	All three interventions were associated with a more than 50% reduction in visual analog scale (VAS)-rated PLP and stump pain. Combined mirror-tactile treatment had a significantly better effect on PLP and stump pain than mirror or tactile therapy alone. The difference between the three treatment arms was, however, slight, And hardly of clinical relevance. After treatment, the pain reduction remained unchanged for an observation period of 3 months.
10	Ortiz-Catalan et al (2016)[15]	NRS; The pain rating index formed by the summed contribution of 15 qualities of pain as in the short-form; MPQ; The weighted pain distribution scale	n = 14 patients with upper limb amputation afflicted by refractory chronic PLP	Uncontrolled clinical trial	Virtual reality	12 sessions of 2 hours per session. All patients received an intervention twice per week except for one who had it daily. Each session consisted of (1) pain evaluation, (2) placement of the electrodes and fiducial marker, (3) practice motor execution in augmented reality, (4) gaming by racing a car using phantom movements, and (5) matching random target postures of a virtual arm in virtual reality. Steps 3–5 were repeated for different movements following three difficulty levels.	All patients had a reduction in intensity and quality of pain (pain rating index, relative mean improvement of 51%; p = 0.0001); 12 patients had a positive change in the time-intensity profile (weighted pain distribution, relative mean improvement 56%; p = 0.001); 9 patients had a reduction of present pain intensity (NRS, relative mean improvement 55%; p = 0.004); 8 patients had a reduction in Numeric Rating Scale of at least 2 points.

11	Rothgangel et al (2018)[8]	0-10 Numeric Pain Rating Scale	unilateral lower limb amputation with PLP. Group A (n=26) and age 59.7: traditional mirror therapy followed by treatment group; group B (n=25) mean age 62.5: traditional mirror therapy followed by self-delivered mirror therapy group ;	Group C (n=24) mean age 61.0: sensorimotor exercise without mirror followed by self-delivered sensorimotor exercise group	traditional mirror therapy followed by the treatment group, traditional mirror therapy followed by the self-delivered mirror therapy group, sensorimotor exercise without mirror followed by the self-delivered sensorimotor exercise group	four weeks of traditional MT followed by six weeks of tile treatment using augmented reality MT (group A), four weeks of traditional MT followed by six weeks of self-delivered MT (group B), and four weeks of sensorimotor exercises to the intact limb followed by six weeks of self-delivered exercises (group C)	The effects of MT on PLP at four weeks were not significant. MT significantly reduced the duration of PLP at six months compared to the teletreatment (P = 0.050) and control group (P = 0.019). Subgroup analyses suggested significant effects on PLP in women, patients with telescoping, and patients with a motor component in PLP. The tile treatment had no additional effects compared to self-delivered MT at ten weeks and six months.
12	Sumitani et al. (2008)[7]	NRS	n = 22 patients with PLP or pain related to spinal cord or nerve injury (11 with single limb amputation, 2 with partial spinal cord injury, 7 with a brachial plexus lesion, and 2 with traumatic peripheral nerve	Uncontrolled clinical trial	Mirror therapy	Mirror therapy 10 min once daily for four weeks; Participants moved the intact limb, looking in the mirror and imagining limb motion with phantom sensation	All groups showed a decrease in pain (p = 0.002)

			lesions) ; Age range: 32–74 years				
13	Tilak et al. (2015)[11]	VAS ; UPS	n = 26 subjects with unilateral upper limb or lower limb amputation and PLP of any duration; Age range: 18–60 years of any gender; Group I (n = 13): mirror therapy group ; Mean age: 42.62 ± 10.69 years ;	Group II (n = 13): TENS group ; Mean age: 36.38 ± 9.55 years	Mirror therapy; TENS	Group I: Mirror therapy; Group II: Contralateral limb TENS; The treatment was given for four days. An initial assessment of pain was performed by a therapist blinded to the treatment given. After four days of treatment, the pain was re-assessed by the same therapist; Random allocation into Group I-mirror therapy and Group II-TENS was carried out.	Group I had a significant decrease in pain (VAS ($p = 0.003$) and UPS ($p = 0.001$)); Group II also showed a significant reduction in pain (VAS ($p = 0.003$) and UPS ($p = 0.002$)) ; No difference was observed between ; the two groups (VAS ($p = 0.223$ and UPS ($p = 0.956$))
14	Ulger et al. (2009)[10]	VAS	n = 10. Traumatic amputation of upper and lower limbs with PLP; Age range: 30–45 years	n = 10. Traumatic amputation of upper and lower limbs with PLP Age range: 30–45 years	motor imagery	Experimental group: instructed to move and feel the healthy and phantom limbs (motor imagery). 15 repetitions or until the pain went away for Four weeks. Control group: general exercises (strengthening, dynamic stretching, isometric exercises by level of amputation) and prosthetic exercises. Ten times twice a day for four weeks	Pain intensity decreased in all subjects after four weeks of treatment in both groups ($p < 0.05$). There were significant differences after treatment between experimental and control groups ($p < 0.05$) finding better scores for the group of motor imagery

15	Yildirim and Kanan (2016)[18]	Patient Information Form; Mirror Therapy; Practice Follow-Up Booklet	n = 19 amputee patients who had PLP	Uncontrolled clinical trial	mirror therapy	Teaching mirror therapy: The mirror therapy practical training (40 min). Continuation of mirror therapy practice at home: patients were called by phone Two times a week to encourage them; 4-week practice period	There was a statistically significant decrease in average PLP scores every week of the study period and for 1-month total score ($p < 0.01$)