The Effectiveness of Mirror Therapy in the Treatment of Post-Amputation Phantom Limb Pain

Cassandra Wilson

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Abstract

Background: There are an estimated 1.6 million people living with a limb amputation in the U.S. Approximately 50-80% of amputees suffer phantom limb pain (PLP), which is pain felt in the absence of a limb that may manifest as stabbing, burning, throbbing or in some other fashion. Mirror therapy has been proposed as an alternative therapy for the treatment of PLP, but its efficacy as an intervention is yet to be elucidated. The purpose of this article is to review the literature to examine the use of mirror therapy to treat post-amputation PLP. Mirror therapy utilizes a mirror between the intact and non-intact limb to create an illusion of two intact limbs. The intact limb is then exercised while the patient watches the image of the two limbs in movement. Experimentation suggests this reconciliation of motor and visual feedback from the phantom may decrease phantom limb pain.

Method: An extensive literature search was performed using PubMed, CINAHL, Evidence Based Medicine Reviews Multifile and Medline using the keywords "phantom limb" and "mirror therapy," both individually and in combination. The search was limited to humans, English language, and full text articles available through Pacific University Library and that were published from 2000 to 2010. Two randomized controlled trials and two case reports were retrieved and included in the systematic review for final analysis.

Results: Of the four studies evaluated in this systematic review, all four showed some degree of success in using mirror therapy to reduce phantom limb pain. There were a number of limitations in the studies reviewed, including small sample size, observational study designs, and incomplete reporting of statistics.

Conclusion: The reviewed literature shows that mirror therapy reduces the severity of pain for patients experiencing phantom limb pain, however, using the GRADE approach the current evidence is considered to be of low to moderate quality. Additional large scale randomized controlled trials are needed to validate these findings. For the time being, the initiation of mirror therapy seems to safely provide short term relief for patients post-amputation suffering phantom limb pain.

Keywords: Phantom limb, mirror therapy

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First Advisor
Torry Cobb

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The Effectiveness of Mirror Therapy
In Treating Post-Amputation Phantom Limb Pain

Cassandra Wilson

A course paper presented to the College of Health Professions
in partial fulfillment of the requirements of the degree of
Master of Science

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Biography

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ABSTRACT

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INTRODUCTION

Background

There are an estimated 1.6 million people living with a limb amputation in the U.S. (Ziegler-Graham, MacKenzie, Ephraim, Travison, & Brookmeyer, 2008). Limb loss is primarily sequelae of vascular diseases, mainly diabetes mellitus (Ziegler-Graham et al., 2008). Diabetes mellitus may lead to elevated blood sugars which, over time, damages peripheral nerves and blood vessels. A limb with damaged nerves and vessels is more susceptible to infection, and an infection that is inadequately treated may develop gangrene and necessitate limb amputation.

The second most common cause of limb amputation is trauma (Ziegler-Graham et al., 2008). Trauma is the leading cause of limb amputation in individuals under 65 years of age (Ziegler-Graham et al., 2008). A unique and growing subset of amputees is those who sustained injury during the Iraq and Afghanistan conflicts. A reported 1,621 service members have sustained a partial (hand/foot/finger/toe) or major amputation during Operation Iraqi Freedom, Operation Enduring Freedom and/or other U.S. conflicts between 2001 and September 2010 (Fischer, 2010).

Subsequent to amputation, 50-80% of individuals suffer from phantom limb pain (PLP) in the region of their absent limb (Ramachandran & Altsuler, 2009). The pain may be experienced intermittently or constantly, and may be described as crushing, cramping, stabbing or throbbing, among other descriptors. The severity of phantom pain may be influenced by a variety of factors including stress, weather and sensation to the residual stump. For the individual, the pain may be so intense that it affects daily living. The National Guideline Clearinghouse (2007) recommends tricyclic antidepressants,
gabapentin and opioids to treat PLP. However, the recommendations are based on a limited number of randomized controlled trials with small sample sizes because much of the research on neurological pain has addressed painful polyneuropathy, trigeminal neuralgia, postherpetic neuralgia and central pain, rather than phantom limb pain. Alternative PLP treatments until this point have included regional nerve blocks, epidural treatments, calcitonin, transcutaneous electrical nerve stimulation, Farabloc (a metal threaded sock) and ketamine (Halbert, Crotty & Cameron, 2002). A systematic review by Halbert et al. (2002) dismissed the evidence for these treatments as inconsistent and insufficient to make any recommendations regarding the treatment of PLP.

Recently, mirror therapy has been proposed as an alternative treatment. With the use of a mirror, the patient places the non-intact limb on the non-reflective side of the mirror and the intact limb on the reflective side of the mirror. The patient views the reflective side so it looks as if there are two intact limbs. The patient proceeds to send motor commands to both limbs while watching both the intact limb and the reflection carry out the commands. This exercise provides reconciliation of motor and visual feedback from the phantom, which, in theory, may decrease phantom limb pain (Ramachandran & Altschuler, 2009).

The prevalence of limb amputation in the U.S. is increasing significantly, with rates projected to double from 1.6 to 3.6 million by the year 2050 (Ziegler-Graham et al., 2008). It is important to investigate mirror therapy because it is a low cost option that may be implemented in a variety of settings and for an extensive period of time with substantially low to no risk of harm or adverse effects. The therapy can also be self-
administered, which would allow the individual to get treatment without ever leaving the house.

Purpose of the Study

The purpose of this study is to explore mirror therapy as an alternative treatment for phantom limb pain. The outcomes in the reviewed studies will be evaluated using the GRADE approach. The intention is to perform a systematic review of the literature to determine the efficacy of mirror therapy in the treatment of post-amputation discomfort.

METHOD

An extensive literature search was performed using PubMed, CINAHL, Evidence Based Medicine Reviews Multifile and Medline. These databases were accessed through the Pacific University Library System. The keywords searched included “phantom limb” and “mirror therapy”, individually and in combination. The search was limited to human subjects, English language, and full text articles published between 2000 and 2010. The initial result included 22 articles, and after duplicates were removed, 17 articles remained. Articles were excluded if they addressed pre-amputation mirror therapy, treated exclusively stroke or complex regional pain syndrome, or explored treatments other than mirror therapy. Of the remaining 17 articles, four were chosen because they fulfilled the inclusion criteria of phantom limb pain, mirror therapy, post-amputation treatment, and amputation. Only randomized, controlled trials and case reports where full text was available through the Pacific library system were reviewed. Four trials were included in the final analysis: two case reports and two randomized controlled trials (Figure 1).
Inclusion/ Exclusion Criteria

Inclusion criteria consisted of phantom limb pain, mirror therapy, post-amputation treatment and amputation. Exclusion criteria consisted of pre-amputation therapy, therapy to treat conditions besides PLP and treatments besides mirror therapy.

RESULTS

In the first study Chan et al. (2007) conducted a randomized controlled trial (RCT) that included 22 lower limb amputee patients. Patients were randomly assigned to three groups identified as 1) mirror group, 2) covered-mirror (non-reflective) group, and 3) mental visualization group. Of the 22 subjects, 18 patients completed the study. Under direct observation, all groups performed 15 minutes of their exercise daily for 4 weeks. The primary end point of the study was severity of pain as measured with a 100 mm Visual Analogue Scale (VAS) at the end of 4 weeks. According to the VAS scale, 100 mm indicated the worst pain, and 0 mm indicated the least pain experienced by patients. Regarding treatment efficacy, the study revealed that 100% of the patients in the mirror group reported decreased phantom limb pain, with a median change of -24 mm, and range of -54 mm to -13 mm measured by VAS. In comparison, 17% of the covered-mirror group reported decreased pain, and 33% of the mental visualization group reported decreased pain. In contrast to decreased pain, 50% of subjects in the covered-mirror group and 67% of subjects in the mental visualization group reported increased pain. The study reported results between the mirror and covered mirror groups ($p=0.04$), and between the mirror and mental visualization groups ($p=0.002$).

The second study was an RCT by Moseley (2006) that included 51 patients who reported phantom limb pain after amputation, phantom limb pain after brachial plexus
avulsion, or had been diagnosed with complex regional pain syndrome 1. The participants were randomized into two groups: 1) a graded motor imagery group and 2) a standard medical and physiotherapy group. The graded motor imagery group (the experimental group) underwent three phases of treatment. The first two weeks were labeled the “limb laterality recognition phase.” This phase estimated task difficulty, and determined the increase in training load throughout the study. The following two weeks were labeled the “imagined movements phase,” and patients were instructed to imagine themselves performing movements and executing given postures. The final two weeks were labeled the “mirror movements phase” with the use of a mirror box, patients were again instructed to perform movements and execute given poses and were later evaluated using VAS. The standard medical and physiotherapy group (the control group) received standard medical care along with six weeks of physiotherapy. The medical care administered was not specifically described. The physiotherapy exercises were restricted from mimicking the experimental group’s exercises or incorporating mirror therapy or mental visualization.

The primary outcome evaluated by Moseley (2006) was pain measured through a 100 mm VAS and function measured through a numerical rating scale (NRS). The outcomes were assessed at baseline, at the end of the 6-week treatment period and again after a 6-month follow-up. After 6 weeks, the average decrease in pain was 23.4 mm (range of 16.2 - 30.4 mm) for the experimental group and 10.5 mm (range of 1.90 - 19.2 mm) for the control group. At the 6-month follow up, the average decrease in pain was 32.1 mm (range of 23.8 - 40.3 mm) for the experimental group and 11.6 mm (range of 2.40 - 20.7 mm) for the control group. During the follow up period, patients were allowed
to seek additional treatment. The number needed to treat to decrease pain was calculated to be less than 3.

The third study was a case report authored by Darnall (2009). The article describes treatment and results for a lower limb above-the-knee amputation patient. The 36 year-old male patient had tried numerous PLP treatments in the past including narcotics, physical therapy, relaxation techniques, anticonvulsants, and antidepressants. At the initiation of mirror therapy, his pain was rated at 4/10 while taking 3-4 vicodin 5/500 mg tablets daily. In addition, the patient was taking gabapentin 1200 mg and oxcarbazepine 600 mg, but reported that these medications did nothing to alleviate his pain. At the recommendation of Darnall, he decided to try home-based patient-delivered mirror therapy. The patient purchased a 4’ long mirror, which when reflecting his intact lower limb, provided the visual feedback identical to two intact limbs. While watching the reflection, he performed unstructured movements three times daily for 20-30 minutes per session. He also incorporated relaxation techniques to decrease anxiety. After one month of home-based treatment, the patient reported 0/10 phantom limb pain, and by three months his vicodin intake had decreased from 3-4 tablets daily to one tablet weekly on an as needed basis. Self-reported observation revealed that when his daily routine of mirror therapy was discontinued, he would remain pain-free for 1-2 days and then his PLP would recur. The recurring pain would only be alleviated by the reinstatement of mirror therapy. Darnall also noted that after experimenting with the mirror therapy and attaining PLP respite, the patient noticed a positive impact on other quality of life issues, such as mood, work and sex, with 100% improvement in all areas.
The fourth study by Sumitani et al. (2008) was a case report that observed 22 patients with deafferentation pain. Deafferentation pain is pain associated with the loss of sensory input from a region of the body. Eleven patients had PLP after sustaining either upper or lower limb amputation secondary to either malignant tumor surgery or trauma. The other eleven patients had pain as sequelae to nerve or spinal cord injury. For 10 minutes once a day, patients would exercise their intact limb while looking at the limb’s reflection. The duration of the daily exercises varied between patients (\(\bar{x} = 20.4\) weeks, S.D. ± 23.8 weeks) and patients were asked to assess their phantom limb pain before and after their mirror session. The study assessed four separate categories 1) the presence or absence of the phantom 2) the movement control of the phantom and whether the control was perceived to be willed, involuntary, immobilized, or absent, 3) the pain intensity via a NRS, and 4) a description of the sensations they were experiencing. The provided descriptions were categorized and counted. The words were divided into a superficial pain group (nociceptive pain, such as tingling, shooting, stabbing, and temperature associated pain, such as freezing and burning) and a deep pain group (pressure associated pain, such as crushing, throbbing, dullness, tightness, and movement or posture associated pain, such as twisting, clenching, cramping, tearing).

Patients were then evaluated in two groups: those who reported that they perceived control of their phantom and those who reported they did not perceive control of their phantom (including the involuntary, immobilized and absent reports). Post-treatment, the perceived control group reported decreased pain via NRS, where 0 = no pain and 10 = the worst pain ever felt (reported NRS: Pre 6.3 +/- 1.5, Post 3.2 +/- 2.4; p
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<0.001). However, the group without perceived control reported a much narrower decrease in pain intensity (reported NRS: Pre 7.3 ± 2.0, Post 6.4±2.4; \( p=0.50 \)).

The study also evaluated amelioration of superficial pain in comparison to deep pain. The study found that the group with perceived control reported a significant decrease in the total count of deep pain descriptors, but not in the total count of superficial pain descriptors (Superficial: Pre =28, Post = 22; \( P=0.43 \). Deep: Pre = 31, Post = 7; \( P <0.0001 \)). The group without perceived control reported no significant decrease of either deep or superficial pains (Superficial: Pre= 16, Post=15; \( P=0.72 \). Deep: Pre=11, Post=9; \( P=0.64 \)).

Out of the 11 amputation patients included in this study, four showed >50% pain relief, three showed 30-50% pain relief, and another four showed <30% pain relief attributable to mirror visual feedback. Of the four patients categorized into the <30% effect group, three were in the non-willed motor imagery group and one was in the willed motor imagery group.

DISCUSSION

In this systematic review, four articles were reviewed to evaluate the efficacy of mirror therapy for PLP treatment (Table 1). All four articles concluded that with mirror therapy there was some degree of success in eliminating PLP, however, the standards of measurement varied between studies.

Chan et al. (2007) and Moseley (2006) both used a 100 mm VAS to quantify reported changes in pain. Using this standard of measurement, Chan reported an average of 24% decrease in pain with mirror therapy. Similarly, Moseley reported an average
23% decrease in pain after 6 weeks of graded motor imagery and an average 32% decrease in pain at the 6 month follow-up.

The remaining two studies were case reports and used an NRS to rate the severity of pain from 0 to 10. On this scale, 0 indicated the least pain and 10 indicated the worst pain experienced by patients. In Darnall’s (2009) study, the patient reported a 40% decrease in pain after one month of mirror therapy. Sumitani et al. (2008) reported, after combining all of the participants’ ratings, the average NRS also decreased, indicating an overall decrease in pain. The eleven amputees reports varied with PLP decreased from <30% to >50%. Sumitani also tracked the number of descriptive words as a means to quantify pain. The total word-count decreased from 86 to 53, this implies overall pain mitigation. In addition, the study concluded that mirror therapy was more effective at reducing deep pain than superficial pain.

All the reviewed studies agree that there is some degree of PLP improvement when patients undergo mirror therapy. Yet, the results reported by the reviewed studies utilize arbitrary and inconsistent standards of measurement. Therefore, using data from current studies to make conclusive efficacy reports remains problematic.

Study Limitations

Chan et al. (2007) was limited by a large loss to follow up, uncertainty of intention to treat methodology, and the lack of a described allocation process. It was reported that 100% of the mirror therapy group had decreased pain, however four participants did not complete the study and the article did not specify whether the data was analyzed with intention to treat methodology. Nevertheless, with a sample size of 22, a loss of 4 participants is a substantial loss, which serves to cast doubt on the quality of
evidence. The supplementary reports of decreased pain in the participants who crossed over to mirror therapy are compelling, however, when adhering to intention to treat methodology we cannot include this as supporting evidence for mirror therapy efficacy.

The application of Moseley (2006) is limited by his comprehensive analysis in which all participants results were combined regardless of their etiology of pain (CRPS 1, brachial avulsion, or amputation). Therefore, when evaluating the results for PLP efficacy, it would be inaccurate to include this pooled data. The study also lacked participant demographics, to illustrate the population heterogeneity. Withholding that information may also limit the application of these results. For instance, given the entire population were of one gender, the results may not reflect the outcomes for a population that includes both genders.

Darnall (2009) provided a detailed account of one patient’s success with home-based patient-delivered mirror therapy. This is an important addition to the evidence because all other studies provided mirror therapy in a controlled setting. However, as a case report, this article is limited by its study design. As an observational study, it inherently falls into the category of low quality evidence.

Sumitani et al. (2008), an additional case report, was also limited by the article’s study design. Furthermore, the lack of provided confidence intervals in the results and the small sample size weakened the strength of evidence.

None of the reviewed articles were blinded. It was noted that it is currently not possible to incorporate blinding into a mirror therapy experiment due to the nature of visual feedback.
GRADE approach

The GRADE approach was used to rate the outcomes presented in the reviewed articles (Table 2). The outcome of pain severity was categorized by the percent of pain relief (<30%, >30% and >50% decrease in pain) and by the standard of measurement used to determine the level of pain (100 mm VAS or 11 point NRS). Using the GRADE approach to evaluate strength of recommendations helps to minimize bias in this systematic review. Each outcome was evaluated and assigned a grade of high, moderate, low or very low. The grades were determined by factors such as study quality, inconsistency, directness, sparse/imprecise data, evidence of association, dose-response gradient, and confounders. Following analysis, the outcomes of pain measured by 100 mm VAS were each given a grade of moderate. The grade of moderate indicates that further research is likely to have an important impact on the confidence of effect and may change the current estimate. The outcomes of pain measured by NRS 0-10 were each given a grade of low, indicating that further research is very likely to have an important impact on confidence of effect and is likely to change the current estimate.

Implications for Research

It is clear that more large-scale high-quality studies are needed to more accurately determine mirror therapy’s degree of efficacy. The overall evidence suggests that mirror therapy is an effective alternative for treating phantom limb pain, yet due to the low-to-moderate quality of studies reviewed the degree of efficacy is still uncertain. Further studies are needed to evaluate mechanism of action, duration of pain relief, efficacy when compared to other PLP treatments, cost-effectiveness, and patient satisfaction.

Implications for Practice
The implications of this systematic review are applicable to patients who have undergone a limb amputation and are experiencing ongoing phantom limb pain. The author recommends that providers continue to prescribe tricyclic antidepressants, gabapentin and opioids as first line treatment, and then include mirror therapy as adjuvant therapy to minimize drug dosages. Although the quality of evidence available is low-to-moderate, the recommendation is strong because the risk of implementing mirror therapy as adjuvant therapy is minimal, therefore the benefits of therapy outweigh the risks.

Conclusion

The reviewed literature shows that mirror therapy is effective in reducing the severity of pain for patients experiencing phantom limb pain. However, as determined by GRADE, the quality of current evidence is low-to-moderate and additional large scale randomized controlled trials are needed to validate these findings. For the time being, the initiation of mirror therapy seems to safely provide short term pain relief for post-amputation patients suffering phantom limb pain.
Competing interests

The author(s) declares that they have no competing interests.

Abbreviations Used in this Systematic Review

CRPS – Complex Regional Pain Syndrome
GRADE – Grading of Recommendations Assessment, Development and Evaluation
NRS – Numerical Rating Scale
PLP – phantom limb pain
RCT – Randomized Control Trial
VAS – Visual Analogue Scale
REFERENCES


Figure 1. Quorum flow chart showing the selection process of the systematic review.
<table>
<thead>
<tr>
<th>Study</th>
<th>Title</th>
<th>Journal/Year</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome(s)</th>
<th>Sample size</th>
<th>Study type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chan et al.</td>
<td>Mirror therapy for phantom limb pain</td>
<td>The New England Journal of Medicine: 2007</td>
<td>Adults lower limb amputees</td>
<td>Mirror therapy</td>
<td>1) Covered mirror therapy 2) mental visualization</td>
<td>Severity of pain after 4 weeks of therapy (measured by VAS)</td>
<td>22</td>
<td>RCT</td>
</tr>
<tr>
<td>Moseley, G.L.</td>
<td>Graded motor imagery for pathologic pain: a randomized controlled trial</td>
<td>Neurology: 2006</td>
<td>Patients with PLP or CRPS 1</td>
<td>Graded motor imagery (including mirror therapy)</td>
<td>medical &amp; physio-therapy management</td>
<td>1) pain measured by VAS 2) function measured by NRS</td>
<td>51</td>
<td>RCT</td>
</tr>
<tr>
<td>Sumitani et al</td>
<td>Mirror visual feedback alleviates deafferentation pain...</td>
<td>Rheumatology: 2008</td>
<td>Patients with PLP or pain related to spinal cord or nerve injury</td>
<td>mirror therapy (aka mirror visual feedback)</td>
<td>none</td>
<td>1) phantom limb awareness 2) motor imagery of phantom 3) pain intensity by NRS 4) subjective descriptions of pain</td>
<td>22</td>
<td>case report</td>
</tr>
</tbody>
</table>
Table 2. Summary of Findings using the GRADE approach

<table>
<thead>
<tr>
<th>Outcome(s)</th>
<th>Quantity &amp; Type of Evidence</th>
<th>Findings</th>
<th>Starting grade</th>
<th>Study Quality</th>
<th>Inconsistency</th>
<th>Directness</th>
<th>Sparse or Imprecise Data</th>
<th>Reporting Bias</th>
<th>Evidence of association</th>
<th>Dose-response gradient</th>
<th>Confounders</th>
<th>GRADE of Evidence for Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain measured by 100 mm VAS &lt; 30% decrease in pain</td>
<td>2 RCT</td>
<td>Decreased pain</td>
<td>High</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pain measured by 100 mm VAS &gt; 30% decrease in pain</td>
<td>2 RCT</td>
<td>No difference</td>
<td>High</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pain measured by 100 mm VAS &gt; 50% decrease in pain</td>
<td>2 RCT</td>
<td>No difference</td>
<td>High</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pain measured by NRS 0-10 &lt; 30% decrease in pain</td>
<td>2 Case reports</td>
<td>Decreased pain</td>
<td>Low</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Low</td>
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<tr>
<td>Pain measured by NRS 0-10 &gt; 30% decrease in pain</td>
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