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Is Mirror Therapy an Effective Treatment for Reducing Pain Associated with Phantom Limb Syndrome in Unilateral Amputees?

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Is mirror therapy an effective treatment for reducing pain associated with phantom limb syndrome in unilateral amputees?

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A SELECTIVE EVIDENCE-BASED MEDICAL REVIEW

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Abstract

OBJECTIVE: The objective of this selective EBM review is to determine if “Mirror therapy is an effective treatment for reducing pain associated with phantom limb syndrome in unilateral amputees.”

STUDY DESIGN: Review of three randomized controlled trials published between 2017 and 2018, with selection based on patient-oriented outcomes and contributing to development of an answer to the clinical question.

DATA SOURCES: All three randomized controlled trials were found using searches within PubMed, published in English in peer-reviewed journals.

OUTCOMES MEASURED: Each randomized controlled trial assessed changes in severity of pain using a survey known as the visual analog scale, where patients reported their pain being between zero, which means no pain at all, up to 10, the most intense pain they have ever felt.

RESULTS: Both Finn et al. (*Front Neurol.* 2017;8:267. doi:10.3389/fneur.2017.00267) and Ramadugu et al. (*Indian J Psychiatry.* 2017;59(4):457-464. doi:10.4103/psychiatry.IndianJPsychiatry_259_16) demonstrated that mirror therapy for 15 minutes daily for four weeks reduced both severity of pain and daily pain time in phantom limb syndrome patients versus controls. Ol et al. (*Scand J Pain.* 2018;18(4):603-610. doi:10.1515/sjpain-2018-0042) concluded that mirror therapy for 10 minutes daily, especially when utilized in addition to other methods like tactile therapy, produced more than a 50% decrease in visual analog scale scores measuring severity of pain associated with phantom limb syndrome.

CONCLUSIONS: Mirror therapy has been shown across multiple randomized controlled trials to be effective in reducing both pain severity and duration of pain episodes associated with unilateral amputees who report having phantom limb syndrome.

KEYWORDS: mirror therapy, phantom limb syndrome

INTRODUCTION

Phantom Limb Syndrome is a condition that occurs in 80% of patients who have limbs amputated and is characterized as sensations of feeling or pain that feel like they are coming from the area where the limb used to be. Roughly 1.5 million Americans live with limb amputations, and around 40,000 have limbs amputated annually. The average lifetime cost of care associated with a limb amputation sits at around $500,000, which includes the preparation and surgery itself, post-op management of complications, medications, and office visits.[2,3]

The feelings of pain associated with phantom limb syndrome vary in both duration and quality between patients. Pain can arrive in short bursts or be a constant sensation, it can manifest as a cramping, burning, shooting, or aching pain, and there is also broad variance as to how long after amputation the first pain episode appears.

The exact mechanism behind the cause of phantom limb syndrome is not totally understood, but it is known that the damage to nerves and tissues associated with the actual amputation (via trauma or surgery) can cause several problems that may contribute to the condition. When nerves are cut during an amputation, they can shorten and form neuromas (nerve "tumors") around the amputation site. The formation of these neuromas is associated with an increase in sodium channels, which ultimately can lead to these nerves being in a state of hyperexcitability, where they can fire without warning or direction.[2] However, some patients have reported phantom limb pain before onset of these neuromas, meaning that this cannot be the sole contributor to the ailment.[4] In addition, limb amputation has been shown in studies to trigger changes in both the primary motor and primary somatosensory cortices of the brain in the areas that controlled that limb.[5] It has been shown that these now seemingly defunct areas may then be "invaded" by areas of the cortices that control other parts of the body, such as the mouth or legs

and that this reorganization may be an attempt by the brain to compensate for the limb loss and cause the patient to experience pain.[1] However, not all patients with phantom limb pain have shown similar cortex changes so this again cannot be the single cause of this syndrome.[4]

Current treatment for phantom limb pain is extremely variable, and efficacy is almost impossible to predict. Pharmacologic options most commonly include NSAIDs and acetaminophen, along with tricyclic antidepressants like amitriptyline, NMDA antagonists like ketamine and memantine, botulinum toxin injections, and local anesthetics at the site of amputation such as lidocaine or bupivacaine. Opioids may be used as a last resort pharmacologic option for severe pain or pain resistant to other treatments. All medications come with potentially serious side effects and contraindications, making them not open for all to use, in addition to the fact that many patients find little to no relief using them.[2,4] Non-pharmacologic treatments include transcutaneous electrical nerve stimulation (TENS), where a device attached to the skin delivers an electric current that sends impulses along a nerve in an attempt to reduce pain.[2] Another option is dorsal column stimulation, where a device is implanted onto the spinal cord in a surgical procedure to send impulses along targeted nerves to try and alleviate pain. While some studies have shown these methods to be effective, patients seem to have the ability to build a tolerance to repeated stimulation, causing the devices to only work for a short time.[6] In addition, these devices and procedures carry potential complications, including skin reactions and infections where the device implants, and more serious problems like migration of device leads along the spinal cord, or epidural hematomas and subsequent brain and nerve damage.[7]

Currently, there is no permanent cure or reliable treatment that has been shown to reduce pain associated with phantom limb syndrome for extended periods of time or without causing other possibly serious complications.[4] Finding a new treatment that does not carry the risk of a

surgical procedure, open up a patient to medications with potentially risky side effects, or cause patients to turn to dangerous substances like opioids for their phantom limb pain would be a breakthrough that can keep patients safe and increase their quality of life. A new emerging treatment for phantom limb pain is known as mirror therapy, where a large mirror is set up vertically between a patient's remaining limb and amputation site, and as the patient reaches out and completes a series of movements with their remaining limb while attempting to also do it with their missing limb, it gives the visual illusion that the amputated limb is still present.[8] This treatment is being studied due to its potential to reverse the physiological pathology that occurs when a limb is amputated that triggers pain. To date, the mechanism behind how exactly mirror therapy might be effective is unclear, but researchers predict that the illusion of seeing their former limb move in the mirror helps reverse the motor and somatosensory "invasion" that occurs in the brain when the limb is removed. This allows patients who have in the past lived with both limbs to re-experience the feeling of seeing both limbs intact again, helping to resolve the sensory and motor mismatches the brain experiences when trying to control a limb that is not present.[8] There are no invasive procedures or medications that must be used alongside this treatment, and it can be done anywhere a patient can fit a mirror. In addition, it has the potential to drastically cut costs related to managing the condition if it proves to have the ability to erase the need for further evaluations and prescriptions. If this therapy is shown to be effective, it will be the most practical and accessible treatment for phantom limb syndrome to date.

OBJECTIVE

The objective of this selective EMB review is to determine whether or not "Mirror therapy is an effective treatment for reducing pain associated with phantom limb syndrome in unilateral amputees."

METHODS

Each of the studies was published in peer-reviewed journals in English between 2017 and 2018 and were found via Pubmed, with the key words “mirror therapy” and “phantom limb syndrome” being used to find them. Each study was selected based on its ability to give an answer either for or against the objective, with a concluding outcome that was a patient-oriented one (POEM). The inclusion criteria included randomized controlled trials that investigated the effect of mirror therapy on unilateral amputees with phantom limb pain, and studies were excluded if they contained non-patient-oriented outcomes, such as cost reduction. Statistics used in these studies included p-values and confidence interval.

Three separate studies that outlined randomized controlled trials involving the use of mirror therapy in patients of any age with unilateral limb amputations that reported phantom limb syndrome were picked to help answer the EBM question. Treatment groups received mirror therapy for between 5 or 15 minutes, once or twice daily, for 4 weeks. Several comparison groups were also included among the studies, one being covered mirror therapy, where mirrors given to patients were covered by an opaque board that prevented the patient from being able to see their present limb. Patients perform the same movements that they would if the mirror was uncovered, but they are unable to see their limb moving in the mirror, and thus do not get the visual illusion that their amputated limb is still present.[9,10] Another comparison was mental visualization therapy, where patients were instructed to imagine moving their intact limb without the use of a mirror.[9] Finally, the last comparison group completed tactile therapy, where a family member would expose the amputation site and press objects of different texture around the site; a rock, wooden stick, feather, cloth and brush for 10 minutes daily.[11] The measured outcomes over

the course of the studies was changes in severity of phantom limb pain after undergoing mirror therapy, along with daily duration of phantom limb pain compared to the control groups.

Table 1 – Demographics & Characteristics of included studies

Study	**Type**	**Pts**	**Pt age**	**Inclusion Criteria**	**Exclusion Criteria**	**W/D**	**Interventions**
Ol[11] (2018)	RCT	45	55.7 mean, >16 years	Patients over 16 with a history of unilateral amputation after landmine trauma, at least 1 year removed from amputation, with phantom limb pain	Patients with amputation stump anomalies like chronic infection, soft tissue deformities, drug or alcohol abuse, mental health problems that prevent reliable scoring	1	Mirror therapy for 5 minutes twice daily for 4 weeks
Finn[9] (2017)	RCT	15	18-70 years	Unilateral amputees above the age of 18 at Walter-Reed Medical Center who have used medications without relief	Amputee patients under 18 or those who have not tried medications for their pain	0	Mirror therapy for 15 minutes daily, 5 days weekly for 4 weeks
Ramadugu[10] (2017)	RCT	64	15-75 years	Amputees between 15-75 with phantom limb pain that could communicate in English or Hindi	Amputees below 15 or above 75, or those with traumatic brain injury or major psych illness	4	Mirror therapy for 15 minutes daily for 16 weeks

OUTCOMES MEASURED

In each study, patients evaluated their phantom limb pain before, during, and after each therapy using the visual analog scale (VAS), a scoring system from 0.0 to 10.0 with 0.0 being no

pain being felt at all, to 10.0 being the worst pain this patient has ever felt before.[9-11] Finn et al. completed a total of 20 therapy sessions over 4 weeks and a VAS score from the patient was given after each session.[9] Ramadugu et al. had patients give a baseline VAS score, followed by scores every four weeks over the 20-week period. The higher the score, the more severe the patient's phantom limb pain was at that time in the respective study.[10] Also, Finn et al. had each patient record the number of phantom limb pain episodes they experienced daily, and for how long each pain episode lasted. The frequency and duration of the episodes were then multiplied together to calculate the daily phantom limb pain time experienced by each patient in the study.[9]

RESULTS

All three randomized controlled trials were assessed to see if mirror therapy would emerge as a viable option in reducing phantom limb pain in unilateral amputees. Each study compared mirror therapy to either tactile therapy, a covered mirror using the same procedure, or simply mental visualization without the use of a mirror. Across each study, no patient reported complications stemming from the use of mirror therapy, with dropouts being due to a patient with an unrelated stump infection, one transferring to another facility for unrelated illness, and three undergoing unrelated surgical procedures that prevented them from completing therapy.[9,11]

Ol et al. is a randomized controlled clinical trial that selected 45 Cambodian patients, all but one being male, with each over the age of 16 who were all victims of landmine trauma that resulted in a unilateral amputation of their leg below the knee, who reported experiencing phantom limb pain.[11] The study was conducted in rural Cambodia. Patients with chronic stump infections, drug or alcohol abuse, or mental health problems that prevented reliable scoring were excluded from the study. Three groups of 15 patients were randomly selected, with the experimental group receiving mirror therapy for five minutes twice daily, another group

receiving tactile therapy, and the final group receiving both mirror and tactile therapy, each for four weeks.[11] Those who had a 33% reduction in their VAS score were labeled responders to their therapy, and instructed to continue that therapy at their own leisure until three months had passed since day one of the study. Those who did not achieve 33% VAS reduction were dubbed non-responders and were told to change to the other form of therapy (from tactile to mirror therapy or vice-versa) and if the other therapy worked, to continue that until 3 months had elapsed. If a patient did not "respond" to either therapy, they were not followed after their four-week therapy sessions. One patient from the combined therapy group withdrew from the study due to development of an infection at the site of amputation. At baseline, the mirror therapy group reported a mean phantom limb pain VAS score of 6.7±2.7, the tactile therapy group at 7.8±1.9, and the combined group at 7.34±1.4. After 4 weeks, mirror therapy patients reported a mean VAS decrease of 5.0 (95% CI 3.6-6.4), a reduction of 65.1%. The tactile therapy group also reported a significant VAS reduction, with a mean reduction of 4.3 (95% CI, 2.9 to 5.7), an average decrease of 56.6%. The combined mirror and tactile therapy group reported the largest improvements in pain, with a mean VAS decrease of 6.2 (95% CI, 4.8 to 7.6), an average reduction of 84.7% (Table 2).[11] After the four-week session, the "non-responders" from either the tactile or mirror groups were reclassified into the opposite group. At the end of an additional four weeks, those who had participated in both the mirror and tactile therapy groups were then placed into the combined mirror and tactile therapy group until the end of the three-month study, which had 100% compliance with the exception of the one early dropout. Throughout the three months, patients being treated with mirror therapy continued to report drops in their VAS, and even more-so when combined with another practical treatment, being tactile therapy (Table 3).[11]

Table 2 – VAS changes after four weeks of therapy, Ol et al.[11]

	Mirror Therapy		Tactile Therapy		Combined Therapy	
Phantom Pain	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Baseline VAS	6.7±2.7	--	7.8±1.9	--	7.34±1.4	--
Decrease in VAS	5.0	3.6-6.4	4.3	2.9-5.7	6.2	4.8-7.6
% Reduction	65.1	50.4-79.8	56.6	41.8-71.2	84.7	69.5-99.9

Table 3 – VAS Changes after three months of therapy and group reclassification, Ol et al.[11]

	Mirror Therapy		Tactile Therapy		Combined Therapy	
Phantom Pain	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Decrease in VAS	5.2	4.0-6.4	5.9	4.5-7.3	6.5	5.5-7.5
% Reduction	67.5	57.6-77.5	77.3	65.5-89.1	91.8	83.5-100.2

Finn et al. is a randomized controlled trial that followed 15 male unilateral upper extremity amputee patients at Walter Reed and Brooke Army Medical Centers who were older than 18, and had used medication for their phantom limb pain without relief.[9] Nine participants underwent mirror therapy, with the control group having three patients undergoing covered mirror therapy and three performing mental visualization without mirrors. Groups completed exercises for 15 minutes daily, five days weekly for four weeks, completing a VAS before each session and at baseline, along with reporting the number of pain episodes and duration of each episode that day.[9] The mirror therapy group's baseline VAS mean score was 4.14±1.76, and ended at 2.75±1.72 after four weeks, with a p-value of 0.001, which is statistically significant as it lies <0.05 (Table 4). The mirror therapy group also had a decrease in time spent experiencing having pain, dropping from a baseline mean of 1,022±673 minutes daily to 448±565 minutes daily, a mean reduction of 56%, p=0.003. The control group began with a mean baseline VAS score of 3.52±2.55, and after four weeks their score had increased to 4.85±2.90, with a p-value of 0.601, meaning there was no significant reduction in pain severity. The control group also did not experience a statistically significant change in total daily time spent experiencing phantom limb pain, starting with a mean of 743±806 minutes and ending with 725±825 minutes (p=0.49).[9]

Table 4 – Changes in VAS score and daily pain time after treatment, Finn et al.[9]

	Mirror Therapy	Control
Baseline VAS Score	4.14±1.76	3.52±2.55
VAS Score After Treatment	2.75±1.72 (p=0.0001)	4.85±2.90 (p=0.601)
Daily PLP Time Before Treatment	1,022±673	743±806
Daily PLP Time After Treatment	448±565 (p=0.003)	725±825 (p=0.490)

Ramadugu et al. is a randomized controlled trial organized as a single crossover study, where 64 amputees living in India between ages 15 and 75 reporting phantom limb pain were split into a mirror therapy group and covered mirror group.[10] Each group completed therapy 15 minutes daily for four weeks, with the covered mirror group then crossing over to mirror therapy for another four weeks. Once groups completed therapy, they were followed until the end of 16 weeks, and reported VAS scores for pain at 0, four, eight, 12, and 16 weeks. The control group was followed for an additional four weeks since they were subject to the covered mirror for the first four weeks.[10] The mirror therapy group reported statistically significant VAS reductions in their pain, with a mean reduction of 1.755±0.183 from baseline after four weeks, 2.795±0.275 after eight weeks, 3.299±0.286 after 12 weeks, and 3.491±0.302 after 16 weeks, with $p<0.0001$ for all values. Contrarily, the control group using covered mirrors for four weeks did not experience a significant reduction in pain, reporting a mean VAS difference of 0.140±0.083 (p=1.000) from baseline. However, once this group crossed over and underwent mirror therapy, they reported significant VAS reductions, with an average decrease of 1.054±0.139 from baseline after a total of eight weeks into the study, 1.593±0.179 after 12 weeks, 2.036±0.196 after 16 and 2.283±0.199 after 20 weeks. Once the control group crossed over to mirror therapy for four weeks, their VAS reductions became statistically significant (all p-values <0.0001), with each group continuing to report decreases in pain up to 12 weeks after ceasing treatment.[10]

Table 5 – VAS Score Reductions from Baseline in four-week intervals, Ramadugu et al.[10]

	Mirror Therapy			Control		
Time (weeks)	Mean VAS decrease from baseline	95% CI	P-value	Mean VAS decrease from baseline	95% CI	P-value
4	1.76±0.18	1.20-2.31	<0.001	0.14±0.08	0.13-0.41	1.00
8	2.80±0.28	1.97-3.63	<0.001	1.05±0.14	0.61-1.50	<0.001
12	3.30±0.29	2.43-4.17	<0.001	1.60±0.18	1.08-2.17	<0.001
16	3.49±0.30	2.58-4.40	<0.001	2.04±0.20	1.41-2.67	<0.001
20	--	--	--	2.28±0.20	1.64-2.92	<0.001

Note: Control group crossed over to mirror therapy after four weeks of treatment.

DISCUSSION

All reviewed trials showed mirror therapy providing statistically significant reduction in phantom limb pain severity and daily duration, supported with p-values and confidence intervals, with Finn et al. specifically demonstrating that mirror therapy can work in patients that have previously failed trails of pain medication.[9] These results are a promising sign for the future of safe treatment of this still relatively unknown condition.

These studies did not come without limitations. Ol et al. mentioned that the word "pain" in Khmer (the official Cambodian language) has a different connotation to English, and that while they did their best to explain that they were asking about physical pain, it is possible that subjects reported their scores based on the overall emotion and feeling that their amputations caused them. This may have impacted patient recruitment, as some who may not have had physical pain from their amputation but rather emotional pain could have been recruited.[11] In addition, patients in the experiment performed by Ol et al. who were deemed non-responders for not having at least a 33% VAS reduction during the combined mirror and tactile therapy treatment were excluded from further therapy and did not contribute further data to the study. Ramadugu et al. also had 4 patients who dropped out during the study without their scores being followed to the end. These are potential examples of attrition bias, as these patient's VAS scores

were not factored in after they left, and could have caused final conclusions based on data provided to not be as statistically significant, especially since these patients did not have a dramatic change in their phantom limb pain as compared to those who stayed. Across all three studies, there was one female, meaning that findings can only be generalized across male amputees. Some studies show that males and females differ in pain thresholds and perceptions, so it cannot be guaranteed that similar studies with female patients would generate the same results.[12] In addition, the highest sample among the studies was 64, with Finn et al. and Ol et al. admitting that due to the small groups, they could not separate based on time elapsed since amputation, and suggested that time since surgery could affect response to mirror therapy.[9,11]

CONCLUSION

The objective of this selective EBM review was to determine whether mirror therapy was effective in reducing phantom limb pain in amputee patients, and all three studies suggested that for pain severity, with one concluding this for duration of pain episodes. Studies observed unilateral amputees over a variance of age, race, and time from amputation that reported phantom limb pain and showed that mirror therapy outperformed comparison groups over the length of treatment time, preventing pain relapses for weeks after treatment stopped. While these three studies come to a similar conclusion, further research can be done to better establish the efficacy of mirror therapy in females, as there was one female across all studies, to see if efficacy changes across sexes. Ol et al. demonstrated that when mirror therapy combined with another practical treatment, tactile therapy, pain severity decreased more than when the two were separate.[11] Investigating mirror therapy in tandem with other practical options could further boost efficacy and patient outcomes. Other research ideas include a cohort study longer in length to investigate efficacy of mirror therapy over a longer period of time to see if efficacy changes.

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