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REVIEW

Evaluating Mirror Therapy Protocols in Phantom Limb Pain Clinical Trials: A Scoping Review

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Abstract: Mirror therapy is among the most widely used treatments for phantom limb pain. However, discrepancies exist in the way it is conducted, and its effectiveness varies widely. The aim of this scoping review was to evaluate the application of mirror therapy across the literature and to identify treatment features unique to studies with clinically significant pain reduction outcomes. Articles published until July 2024 were identified through a systematic search of the following electronic databases: Medline (via EBSCOhost), PubMed, Cochrane Central Register of Controlled Trials, Physiotherapy Evidence Database, PsycINFO (via EBSCOhost), Cumulative Index to Nursing and Allied Health Literature (via EBSCOhost), Africa-Wide Information (via EBSCOhost), and Scopus. Two reviewers independently conducted the screening of titles and abstracts, review of full-text articles, and data extraction. The results were analyzed descriptively. We included 32 studies in this review, 21 of which were deemed effective for achieving clinically significant pain reduction of 50% or 2 points on a 0–10 scale. There were inconsistencies in various treatment components including treatment setting, type of pre-treatment education, treatment technique, method of exercise delivery, treatment duration, and frequency of treatment sessions. Despite identifying common treatment features across studies with clinically significant pain reduction outcomes, we found no evidence of unanimous consensus in the literature towards any specific protocol for mirror therapy. Establishing a standardized treatment protocol could enhance the reliability and reproducibility of treatment outcomes in future studies and ensure a meaningful comparison between mirror therapy and other treatments in clinical trials and meta-analyses.

Keywords: amputation, phantom limb pain, mirror therapy, rehabilitation

Introduction

Phantom limb pain (PLP) is a common post-amputation condition characterized by painful sensations in the missing limb. Approximately 80% of people report PLP within the first year following their amputation procedure, and up to 87% will experience PLP at some point in their lifetime.[1] PLP is difficult to treat and contributes to the burden of physical disability, emotional well-being, and psychological disorders in people with amputations.[2]

Most pharmacological treatments for PLP are based on limited evidence and do not offer benefits over placebo.[3–5] On the other hand, a few non-pharmacological treatments are showing some benefit, with mirror therapy being one of the most widely employed treatments. For example, recent meta-analyses revealed that mirror therapy was more effective than control interventions,[6,7] however, contradictory findings have also been reported, highlighting the need for further analysis.[8,9] Additionally, in a study that generated treatment recommendations for PLP, mirror therapy had the highest level of expert consensus for its efficacy in reducing PLP.[10] Despite mirror therapy appearing to be the gold standard for PLP management amongst healthcare professionals, a standardized treatment protocol is yet to be established to facilitate rigorous testing of the effectiveness of mirror therapy between groups.

There are several discrepancies in how mirror therapy is conducted in clinical practice. Most notably, inconsistencies exist in its application (for instance, moving vs resting the phantom limb), the method of delivery (ie, self-guided vs clinician-led), and the number, duration, and frequency of treatment sessions.[11] We hypothesized that variations in mirror

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therapy protocols are the source of conflicting results, and perhaps developing a standardized treatment protocol could address this aspect of clinical heterogeneity.

A standardized treatment protocol may enhance the reliability and reproducibility of treatment outcomes in future studies and ensure a meaningful comparison between mirror therapy and other treatments in clinical trials and meta-analyses. In consideration of this, we conducted this study to evaluate how mirror therapy is performed and reported in the literature on PLP. In addition, we aimed to identify treatment features unique to studies with clinically significant pain outcomes. These features will inform the development of a standardized mirror therapy protocol in an ongoing expert consensus Delphi study.

Materials and Methods

This scoping review was conducted in accordance with the Joanna Briggs Institute (JBI) manual for evidence synthesis[12] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews guidelines (PRISMA-ScR).[13] The protocol for this review has been registered on Open Science Framework.[14]

Identification of Studies

We used a customized search strategy (Supplementary file 1) to search for relevant studies across the following databases: Medline (via EBSCOhost), PubMed, Cochrane Central Register of Controlled Trials, Physiotherapy Evidence Database, PsycINFO (via EBSCOhost), Cumulative Index to Nursing and Allied Health Literature (via EBSCOhost), Africa-Wide Information (via EBSCOhost), and Scopus. In addition, we searched clinicaltrials.gov, Pactr.gov, and the European Union clinical trials register for ongoing research. Electronic databases and clinical registries were searched from their inception until July 2024.

Eligibility Criteria

We considered clinical studies which investigated the efficacy of mirror therapy for reducing PLP in adults (≥18 years) with an amputation of the upper or lower limb. We only considered studies published in English due to a lack of translation resources. Systematic reviews and retrospective analyses of previously published data were excluded to avoid duplication.

Screening and Study Selection

Two reviewers (K.L. and E.M) independently screened titles and abstracts of studies identified from the literature search in duplicate. Eligible full-text articles were retrieved and screened independently by the reviewers to confirm inclusion. Where additional information was required to confirm eligibility, K.L. contacted authors up to two times within two weeks for clarification. Disagreements between reviewers were resolved by discussion. We calculated Cohen's kappa to determine inter-rater agreement as minimal (0–0.39), weak (0.40–0.59), substantial (0.60–0.79), or strong (0.80–0.90).[15]

Data Extraction

Two reviewers (K.L. and E.M) independently extracted data from included studies using a piloted, customized form. Extracted data included study characteristics (ie, design and setting), treatment characteristics (details of pre-mirror therapy participant education, treatment technique, types of limb exercises, duration and frequency of treatment sessions, and overall treatment period), and treatment efficacy. Treatment efficacy was judged as either "effective" or "not effective", depending on whether the study achieved a clinically meaningful reduction in pain, defined as at least a 50% reduction or a 2-point decrease on a 0–10 numerical rating scale.[16,17] We reviewed extracted data and identified common treatment features across studies with clinically significant pain outcomes. Disagreements between reviewers were resolved by discussion.

Results

The screening process is illustrated in Figure 1. The literature search yielded 702 studies, from which, 233 were retained after de-duplication. Following the screening of titles and abstracts, 39 studies were deemed eligible for full-text review.

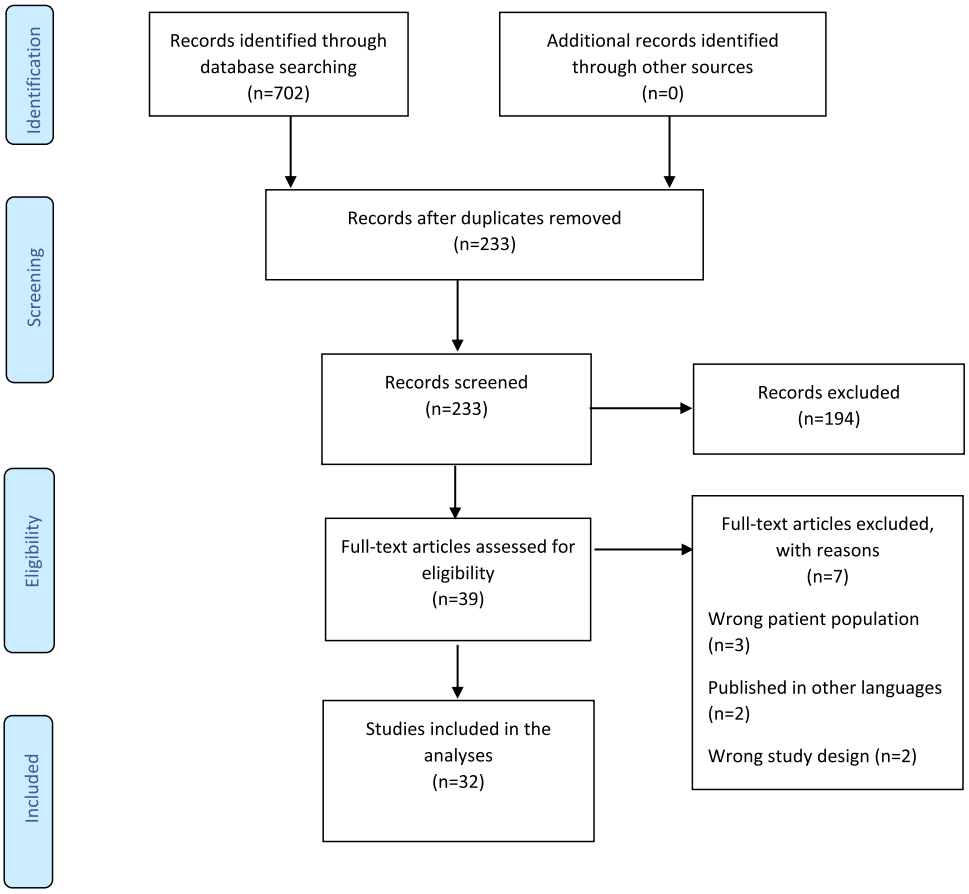

Figure 1 The PRISMA flow chart.

Of these studies, 32 met our eligibility criteria and were included in this review. Fourteen studies are Randomized Controlled Trials (RCTs),[18–31] 11 are case studies,[32–42] four are single-arm trials,[43–46] two are prospective studies,[47,48] and one is a non-randomized controlled trial.[49] Additional characteristics of the included studies are summarized in Table 1. The screening of titles and abstracts and full-text articles reflected a substantial (0.64) and strong (0.84) inter-rater agreement, respectively. Mirror therapy was deemed "effective" in 21 studies for achieving a clinically meaningful reduction in pain. However, it was considered "ineffective" in 11 studies due to a lack of observed effect.

Study Setting

Among the studies showing clinically meaningful pain reduction, 15 were conducted in a clinical setting,[24–26,29,31,33–35,38–42,46,50] four were conducted both in a clinical environment and at home,[18,47,49,51] and two were purely home-based.[20,37] In contrast, among the studies showing no effect, seven were conducted both in a clinical setting and at home,[21–23,27,32,36,43] three were conducted in a clinical setting,[19,30,44] and one was home-based.[48]

Pre-Treatment Education

Among the studies showing clinically meaningful pain reduction, two provided both pain science education and instructions on the practical aspects of mirror therapy.[20,37] In fifteen studies, only the instructions on the practical aspects of mirror therapy were provided,[18,24,26,28,31,33–35,38–40,46,47,49,51] and four studies did not report any pre-treatment education.[25,29,41,42] The clinicians did not demonstrate the exercises in 12 out of 21 studies.

Similarly, among studies showing no effect, one provided both pain science education and instructions on the practical aspects of mirror therapy.[32] In nine studies, only the instructions on the practical aspects of mirror therapy

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Table 1 Components of Mirror Therapy for PLP Management

Authors	Study Design	Setting	Education	Technique	Types of Exercises	Exercise Demonstration	Treatment Duration [min]	Treatment Frequency	Treatment Period	Treatment Efficacy [>50% or 2 points reduction]
Anaforoglu et al, 2019[18]	RCT	Clinic + home-based[i]	Practical aspects of mirror therapy	Phantom motor execution	CMD[ii]	Self-guided	15	Daily	4 weeks	Y
Brodie et al, 2007[19]	RCT	Clinic	Practical aspects of mirror therapy	Phantom motor execution	NR	Self-guided	NR	Once-off	Once-off	N
Brunelli et al, 2023[28]	RCT	Clinic	Practical aspects of mirror therapy	Phantom motor execution	SMA only	Self-guided	26–30	4 sessions / week	3 weeks	Y
Chan et al, 2007[24]	RCT	Clinic	Practical aspects of mirror therapy	Phantom motor execution	NR	NR	15	Daily	4 weeks	Y
Clerici et al, 2012[36]	Case study	Clinic + home-based	NR	No phantom movement	SMA	Self-guided	30	Daily	24 weeks	N
Darnall, 2009[37]	Case study	Home-based	Practical aspects of mirror therapy + pain science education	No phantom movement	SMA + CMD	Self-guided	20–30	3 sessions / week	4 weeks	Y
Darnall. and vLi, 2012[48]	Prospective study	Home-based	Practical aspects of mirror therapy	No phantom movement	NR	Clinician-lead	25	Daily	4 weeks	N
Datta and Dhar, 2015[39]	Case study	Clinic	Practical aspects of mirror therapy	Phantom motor execution	NR	NR	NR	Daily	1 week	Y
Deng and Li, 2023[38]	Case study	Clinic	Practical aspects of mirror therapy	Imagined phantom movements	NR	Self-guided	20	Every weekday	4 weeks	Y
Finn et al, 2017[30]	RCT	Clinic	Practical aspects of mirror therapy	Phantom motor execution	SMA	Self-guided	15	Every weekday	4 weeks	N

Foell et al, 2014[43]	Single-arm trial	Clinic + home-based	Practical aspects of mirror therapy	Phantom motor execution	SMD + CMD	Clinician-lead	15	Daily	4 weeks	N
Folch et al, 2021[41]	Case study	Clinic	NR	No phantom movement	SMD	Self-guided	NR	NR	2 years	Y
Gover-Chamlou. and Chan, 2016[35]	Case study	Clinic	Practical aspects of mirror therapy	Phantom motor execution	SMA + CMD	Clinician-lead	15	Every weekday	4 weeks	Y
Gunduz et al, 2021[22]	RCT	Clinic + home-based	Practical aspects of mirror therapy	Phantom motor execution	SMA + CMD	Clinician-lead	15	10 sessions	4 weeks	N
Houston and Dickerson, 2016[45]	Single-arm trial	Clinic + home-based	Practical aspects of mirror therapy	Phantom motor execution	NR	NR	15	Daily	4 weeks	Y
Kim. and Kim, 2012[34]	Case study	Clinic	Practical aspects of mirror therapy	Phantom motor execution	NR	NR	15	Daily	4 days	Y
Mallik et al, 2020[27]	RCT	Clinic + home-based	Practical aspects of mirror therapy	No phantom movement	NR	NR	30	Daily	Unclear	N
Noureen et al, 2022[31]	RCT	Clinic	Practical aspects of mirror therapy	Phantom motor execution	SMA	Self-guided	15	Every weekday	4 weeks	Y
Ol et al, 2018[20]	RCT	Home-based	Practical aspects of mirror therapy + pain science education	No phantom movement	SMD	NR	5	Daily	4 weeks	Y
Ramachandran et al, 2018[42]	Case study	Clinic	NR	No phantom movement	SMD	Self-guided	NR	Once-off	Once-off	Y
Ramadugu et al, 2017[26]	RCT	Clinic	Practical aspects of mirror therapy	Phantom motor execution	SMA + CMD	Self-guided	15	Daily	4 weeks	Y

(*Continued*)

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Table 1 (Continued).

Authors	Study Design	Setting	Education	Technique	Types of Exercises	Exercise Demonstration	Treatment Duration [min]	Treatment Frequency	Treatment Period	Treatment Efficacy [>50% or 2 points reduction]
Rothgangel et al, 2018[21]	RCT	Clinic + home-based	Practical aspects of mirror therapy	Phantom motor execution	NR	Self-guided	30	≥ 10 sessions	4 weeks	N
Segal et al, 2021[29]	RCT	Clinic	NR	Unclear	SMA	Self-guided	20	Every weekday	2 weeks	Y
Seidel et al, 2011[47]	Prospective study	Clinic + home-based	Practical aspects of mirror therapy	Phantom motor execution	SMA	Self-guided	26–30	4 sessions / week	3 weeks	Y
Sumitani et al, 2008[46]	Single-arm trial	Clinic	Practical aspects of mirror therapy	Imagined phantom movements	SMD + CMD	Self-guided	10	Daily	Variable	Y
Thomas, 2015[40]	Case study	Clinic	Practical aspects of mirror therapy	No phantom movement	SMD	NR	15	2 sessions / week	8 weeks	Y
Tilak et al, 2015[25]	RCT	Clinic	NR	No phantom movement	NR	NR	20	Daily	4 days	Y
Wareham et al, 2018[44]	Single-arm trial	Clinic	Practical aspects of mirror therapy	Imagined phantom movements	SMD + CMD	Self-guided	10	Once-off	Once-off	N
Wilcher et al, 2011[33]	Case study	Clinic	Practical aspects of mirror therapy	Phantom motor execution	SMA + CMD	NR	15	daily	2 weeks	Y
Yildirim et al, 2016[49]	Non-RCT	Clinic + home-based	Practical aspects of mirror therapy	Phantom motor execution	CMD	Self-guided	20–30	Daily	4 weeks	Y
Yildirim et al, 2020[32]	Cast study	Clinic + home-based	Practical aspects of mirror therapy + pain science education	Phantom motor execution	CMD	Self-guided	30	Daily	4 weeks	N
Zaheer et al, 2021[23]	RCT	Clinic + home-based	Practical aspects of mirror therapy	Phantom motor execution	NR	Self-guided	15	Daily	4 weeks	N

Notes: [i] This involves a once-off in person treatment session with the clinician and the continuation of treatment at home. [ii] This involves a combination of multiple joint movements in different anatomical planes (eg, toe flexion + plantar flexion + ankle inversion).

Abbreviations: SMA, simple movements of all the affected joints; SMD, simple movements of distal joints; CMD, complex movements of distal joints.

were provided,[19,21–23,27,30,43,44,48] and one study did not report pre-treatment education.[36] The clinician did not demonstrate the exercises in seven out of 10 studies.

Treatment Technique

Among the studies showing clinically meaningful pain reduction, twelve involved synchronous movements of the phantom and intact limbs while viewing the reflection of the intact limb in the mirror.[18,24,26,28,29,33–35,39,45,47,49] In two studies, the participants imagined moving the phantom limb,[38,46] and in six studies, the participants did not move the phantom limb.[20,25,37,40–42] One study did not report the technique used.[29]

Among studies showing no effect, seven involved synchronous movements of the phantom and intact limbs while viewing the reflection of the intact limb in the mirror.[19,21–23,30,32,43] In one study, the participants imagined moving the phantom limb,[44] and in three studies, the participants did not move the phantom limb.[27,36,48]

Exercises

Among the studies showing clinically meaningful pain reduction, fourteen involved clinician-guided mirror therapy exercises,[20,26,28,29,31,33,35–37,40,41,45,47,49] and two involved self-guided exercises.[42,46] Five studies did not report the method of exercise delivery.[24,25,34,38,39] The majority of these studies focused on exercises involving both the simple movements of the affected joints and complex movements of distal joints.

Among studies showing no effect, eight involved clinician-guided mirror therapy exercises,[19,21,22,30,32,36,43,44] and two studies involved self-guided exercises.[23,48] One other study did not report the method of exercise delivery.[27] Most of these studies focused on exercises involving simple movements of the affected joints.

Treatment Duration

Among the studies showing clinically significant pain reduction, nine had 15-minute treatment sessions.[18,24,26,31,33–35,40,45] In seven studies, treatment sessions ranged between 20 and 30 minutes,[25,28,29,37,38,47,49] and lasted for 10[46] and 5 minutes[20] in two individual studies. Three studies did not report the duration of treatment sessions.[39,41,42]

Among studies showing no effect, five had treatment sessions ranging between 20 and 30 minutes.[21,27,32,36,48] In four studies, treatment sessions lasted 15 minutes,[22,23,30,43] and for 10 minutes in one study.[44] One study did not report the duration of treatment sessions.[19]

Treatment Frequency

Among the studies showing clinically significant pain reduction, eleven involved daily treatment sessions,[18,20,24–26,33,34,39,45,46,49] and four involved one treatment session every weekday.[29,31,35,38] One[40] and two[28,47] studies involved two and four treatment sessions per week, respectively. One study involved three treatment sessions per week.[37] One study had a once-off session,[42] and another did not report the frequency of treatment sessions.[41]

Among the studies showing no effect, seven studies involved daily treatment sessions,[23,27,32,36,43,44,48] one study involved one treatment session every weekday,[30] and another study involved a once-off treatment session.[19] The frequency of treatment sessions was unclear in two studies.[21,22]

Treatment Period

Among the studies showing clinically significant pain reduction, ten had a treatment period of four weeks,[18,20,24,26,31,35,37,38,49,51] and two had a treatment period of four days,[25,34] two weeks,[29,33] and three weeks,[28,47] respectively. The five individual studies had a treatment period ranging from one day[42] to two years.[41]

Among the studies showing no effect, seven had a treatment period of four weeks,[21–23,30,32,43,48] two had a treatment period of one day,[19,44] and one had a treatment period of 24 weeks.[36] One other study did not report the treatment period.[27]

Discussion

This scoping review aimed to evaluate the application of mirror therapy across the literature and to identify treatment features unique to studies with clinically significant pain outcomes. Our findings revealed a wide variation in the

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application of mirror therapy across PLP studies. In addition, most of the treatment features were common in studies both with and without a clinically significant pain reduction. However, some differences were seen in features including the treatment setting, types of exercise, and treatment session duration.

Of the 32 studies included in this review, only 14 were RCTs, and were consistently judged in previous systematic reviews as having high risk of bias, stemming from inadequate participant blinding, and using a small sample size.[6,7,11] These missing key features of high-quality trials could have had an impact on the imprecision of the effect estimates commonly seen in mirror therapy trials. Consequently, in a recent meta-analysis,[11] the certainty of the evidence indicating the effectiveness of mirror therapy for reducing PLP was downgraded to "very low". Nevertheless, the evidence on mirror therapy is promising, and it remains one of the most preferred options for clinicians to manage PLP.[10] Therefore, it is imperative to refine its application and conduct high-quality, blinded RCTs with larger sample sizes to increase our confidence in mirror therapy as an effective treatment for PLP.

Most studies conducted in a clinical setting showed significant improvements in pain compared to home-based studies. Early studies were conducted in person, whereas more recent ones were conducted virtually, with substantial responsibility placed on the participant to manage and adhere to the treatment protocol.[52] The sub-optimal treatment outcomes in home-based studies could be attributed to poor treatment adherence.[53] A study by Nicholas et al[54] revealed a negative association between adherence to self-management strategies and pain severity, in that the participants who adhered to the treatment protocol showed significantly greater improvement in pain compared to those who deviated from it. Monitoring adherence to treatment remains a significant challenge, particularly in home-based studies investigating non-pharmacological treatments such as mirror therapy. Virtual mirror therapy, utilizing digital technologies to deliver visual feedback, addresses some of the limitations of traditional mirror therapy, including the ability to monitor treatment adherence. The software employed in virtual mirror therapy has built-in capabilities for monitoring treatment duration and frequency, as well as the types of exercises performed during a treatment session.[55] Therefore, utilizing digital technologies in clinical practice can improve treatment adherence, and thus treatment efficacy.

We noted important variations in the technique implemented across mirror therapy studies. While in some studies the participants moved the phantom limb, in other studies, they imagined moving or did not move the phantom limb while viewing the reflection of the intact limb in the mirror. Actively attempting to move the phantom limb has been hypothesized as a key feature for treatment success.[56] A lack of a statistically significant difference in PLP severity in a meta-analysis comparing mirror therapy and sham (covered mirror) suggests that phantom motor execution, instead of visual feedback, is a key therapeutic component.[11,57] Considering these findings, we found it surprising that clinically significant pain reductions were not unique to studies that prioritized phantom motor executions. This could be an artefact of methodological challenges unique to the application of mirror therapy in individuals with amputations. Unlike in individuals with limbs, it is difficult to confirm if movement of the phantom limb has been executed.[58] Therefore, it is likely that some participants might have not executed phantom movements, hence the varying pain outcomes. Surface electromyography (sEMG) on the distal part of the residual limb has previously been used as a proxy measure for phantom movements, in that the contraction of the residual limb muscles suggests phantom movements.[59] Along with other technological aids, such as machine learning on sEMG,[60] virtual reality, and augmented reality have also been used to promote phantom motor execution.[61]

Complex phantom limb exercises during mirror therapy appear to play a significant role in pain alleviation. In this review, studies focusing on complex phantom exercises demonstrated greater efficacy compared to those focusing solely on simple joint movements. This is potentially because complex phantom limb movements, involving multiple joints and a range of motions, engage a wider network of neurons related to the control of the affected limb.[56] For example, a mechanistic study comparing the effects of simple versus complex movements on corticospinal excitability found that complex movements led to higher corticospinal excitability.[62] In addition, a recent study demonstrated that complex exercises resulted in better motor learning compared to simple exercises.[63] However, given that complex mirror therapy exercises can trigger or aggravate pain in some patients, we recommend initiating treatment with simple exercises within a comfortable range of motion and gradually progressing to performing complex limb movements efficiently and fluidly.

We noted a high variability in treatment dosage across the included studies. However, a protocol comprising 15-minute daily sessions conducted over 4 weeks, was commonly seen across studies with positive pain outcomes. Although

a consensus on the optimal dosage for MT is yet to be reached,[64] it is known that individuals with chronic PLP tend to benefit from a longer treatment period, with those experiencing acute PLP of an early onset post-amputation, requiring only a few sessions to achieve significant pain reductions.[18] It could be argued that a 15-minute treatment session is not sufficient to achieve a therapeutic effect. However, considering that excessive mirror training can aggravate pain or result in fatigue, stiffness, or spasms of the phantom limb, longer treatment sessions should be practiced with caution.[65] Moreover, the evidence suggests that treatment frequency is more important than the duration of a treatment session.[7] Nevertheless, the etiology of PLP varies significantly across individuals with limb amputations. Therefore, it is imperative to tailor treatment according to the clinical presentation of each individual.

It can be argued that there is an overrepresentation of studies with favorable outcomes, despite indications that mirror therapy outcomes in clinical practice sometimes fall short of the exceptional results often reported in the literature. This is likely due to several reasons, one of which is poor adherence in clinical practice versus prospective clinical studies. The lack of representation of studies with less favorable outcomes may be an artefact of publication bias, where studies with negative or neutral results are less likely to be published. This bias could distort our understanding of the factors that affect the efficacy of mirror therapy in reducing PLP. On the contrary, addressing this bias would help identify the factors that contribute to its success or limitations in reducing PLP, ultimately guiding more effective treatment strategies for individuals with limb amputations.

Conclusion

This review highlights common trends and inconsistencies in the practice of mirror therapy in people with limb amputations. Despite identifying common treatment features across studies with clinically significant pain outcomes, there remains a lack of a standardized mirror therapy protocol. Mirror therapy remains one of the most promising and preferred non-pharmacological treatments for PLP due to its ease of accessibility, adaptability to patient-specific complaints, and low cost. Establishing a standardized treatment protocol could enhance the reliability and reproducibility of treatment outcomes in future studies and ensure a meaningful comparison between mirror therapy and other treatments in future clinical trials and meta-analyses.

Disclosure

The authors report no conflicts of interest in this work.

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