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Review

The effects of mirror therapy on pain and motor control of phantom limb in amputees: A systematic review

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ABSTRACT

Background and objective: Phantom limb pain (PLP) is a major problem after limb amputation. Mirror therapy (MT) is a non-pharmacological treatment using representations of movement, the efficacy of which in reducing PLP remains to be clarified. Here, we present the first systematic review on MT efficacy in PLP and phantom limb movement (PLM) in amputees (lower or upper limb).
Methods: A search on Medline, Cochrane Database and Embase, crossing the keywords "Phantom Limb" and "Mirror Therapy" found studies which were read and analyzed according the PRISMA statement.
Results: Twenty studies were selected, 12 on the subject of MT and PLP, 3 on MT and PLM, 5 on MT and both (PLP and PLM). Among these 20 studies, 5 were randomized controlled trials (163 patients), 6 prospective studies (55 patients), 9 case studies (40 patients) and methodologies were heterogeneous. Seventeen of the 18 studies reported the efficacy of MT on PLP, but with low levels of evidence. One randomized controlled trial did not show any significant effect of MT. As to the effect of MT on PLM, the 8 studies concerned reported effectiveness of MT: 4 with a low level of evidence and 4 with a high level of evidence. An alternative to visual illusion seems to be tactile or auditory stimulation.
Conclusion: We cannot recommend MT as a first intention treatment in PLP. The level of evidence is insufficient. Further research is needed to assess the effect of MT on pain, prosthesis use, and body representation, and to standardize protocols.

1. Introduction

Limb amputation gives rise to pain of different types, among which should be distinguished pains localised on the stump, and projected pains described by the patient as being perceived in the area of the lost limb, known as phantom limb pain (PLP) [1]. These should be differentiated from the mere perception of an amputated limb, which is not painful or disagreeable (known as phantom limb sensation [PLS]). The phantom limb can also be perceived in movement (phantom limb movement [PLM]) [2]. These different types of pain can coexist in a single patient, and the relative place of each type can be difficult to identify, in particular because of the subjective nature of pain and the emotional setting, often seriously affected by the amputation. PLP is thought to affect 50% of patients, appearing in the 6 months following amputation and sometime lasting several years [3,4]. When PLP becomes chronic, it affects quality-of-life and increases the restrictions in activity caused by the amputation, possibly compromising social and/or professional reintegration [5].

There are various therapeutic options for PLP. Some are pharmaco-therapeutic: gabapentine, amitriptyline, tricyclic anti-depressants, morphine-based reparations, ketamine [3,6]. Others are based on non-pharmacological treatment–transcutaneous electric nerve stimulation (TENS), transcranial magnetic stimulation, spinal cord stimulation, the use of prostheses, hypnosis, acupuncture etc.

In this second category, mirror therapy (MT) is one of the techniques consisting in representing movement, like motor imagery and movement observation. Using the reflection of voluntary movements in a mirror performed by the intact limb, it consists in creating the visual illusion of non-painful movement in the phantom limb.

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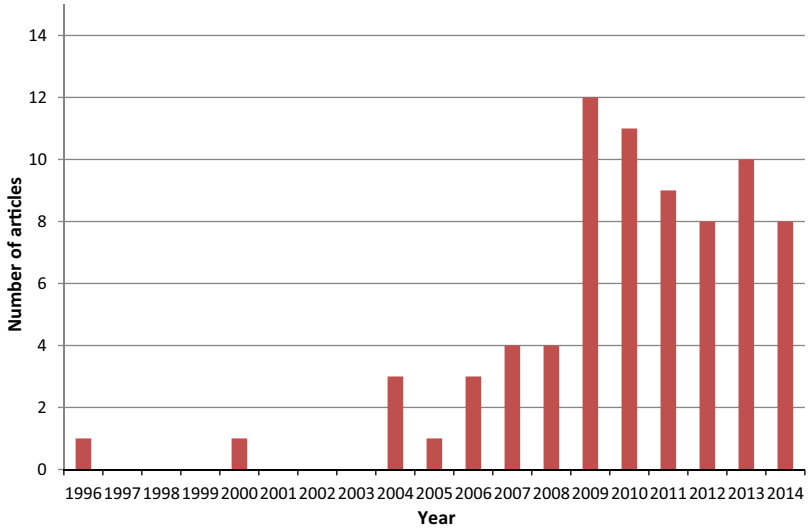

Fig. 1. Evolution of the number of articles published on MT among amputees by year.

The aim, by way of this representation of the missing limb in imaginary movement, is to obtain the restoration of its projection in the corresponding cortical motor and sensory areas, and thus to reduce the pain linked to the breaking-off of sensory information [7–13]. Indeed, after an amputation, the primary somato-sensory and motor cortical areas connected to the amputated limb are no longer solicited. Functional neuro-imagery has shown that they are progressively replaced by adjacent cortical areas [7–10]. The extent to which this post-amputation cortical reorganisation occurs could be correlated with pain scores [8]. MT is thought to establish enhanced coherence between motor command and sensory feedback by way of the reflected image [14,15], and in the medium term to reduce this deleterious cortical reorganisation [16–18]. It has also been suggested that the activation of the contra-lesional mirror neurones derived from MT could have a pain-killing function [11,18].

MT was initially proposed by Ramachandran et al. for the treatment of PLP [14], and it was subsequently applied to other chronic pains, such a complex regional pain syndrome and neuropathic limb pain.

We propose here a review of the literature concerning the application of MT to PLP following upper or lower limb amputation, aiming to assess contra-indications, beneficial effects, conditions of application and any deleterious effects.

2. Method

2.1. Study eligibility criteria

A systematic review of the literature was performed with two independent perusals in accordance with the Prisma guidelines (www.prisma-statement.org/). Only articles in English were retained. The eligibility criteria were any articles on the subject of MT applied to patients following amputation of upper or lower limbs. Articles concerning the application of MT to other pathologies such as stroke sequellae, complex regional pain syndrome, brachial plexus lesions, or sequellae of limb fractures were excluded, as were articles on virtual immersion. Literature reviews were not analysed.

2.2. Sources

The Medline, Cochrane and Embase databases for the period 1996 to 2015 were consulted. The words sought in the titles, abstracts and keywords were: phantom limb, mirror therapy.

2.3. Studies selected and data collection procedure

Up to the 26th November 2015, 85 articles were retrieved on the Medline, Cochrane and Embase databases with using the keywords phantom limb and mirror therapy. It was noted that from 2009, the number of articles increased markedly (Fig. 1), showing increased interest in MT following amputation. The flow diagram in Fig. 2 shows the article selection procedure. Among the 85 articles, 5 were literature review [19–23]. Only one was a review of the literature on MT among amputees [19]. This article is a narrative review of the literature run in parallel with a survey among practitioners and patients. No table synthesising the articles analysed is presented. To our knowledge, our study is the first systematic review to specifically concern MT among amputees.

Finally, 20 studies on the subject of MT and PLP and/or PLM in amputees were included and analysed. Twelve were on the subject of MT and PLP, 3 on MT and PLM, and 5 on MT and both PLP and PLM. Among these 20 studies, 5 were randomized controlled trials (163 patients) [24–28], 6 prospective studies (55 patients) [29–34], 9 case studies (40 patients) [14,35–42] and methodologies were heterogeneous.

3. Results

In the 20 articles selected, the following were explored: MT contra-indications, efficacy, terms of application, and side effects in the setting of PLP.

3.1. Contra-indications for the use of MT in PLP

The most frequently mentioned contra-indications were the existence of neurological or psychological comorbidities, pain in the remaining limb, or sight disturbances making visual feedback impossible [30,33,41].

3.2. The efficacy of TM on PLP

This was the main assessment criterion in the 20 studies retained (Tables 1 and 2). Therapeutic efficacy was assessed by applying the criteria recommended by the French *Haute Autorité de la santé* for the evaluation of the level of scientific proof: 4 levels of proof ranging from 1–the most favourable level–(well-powered, randomised, comparative trials) to 4–the lowest level of proof

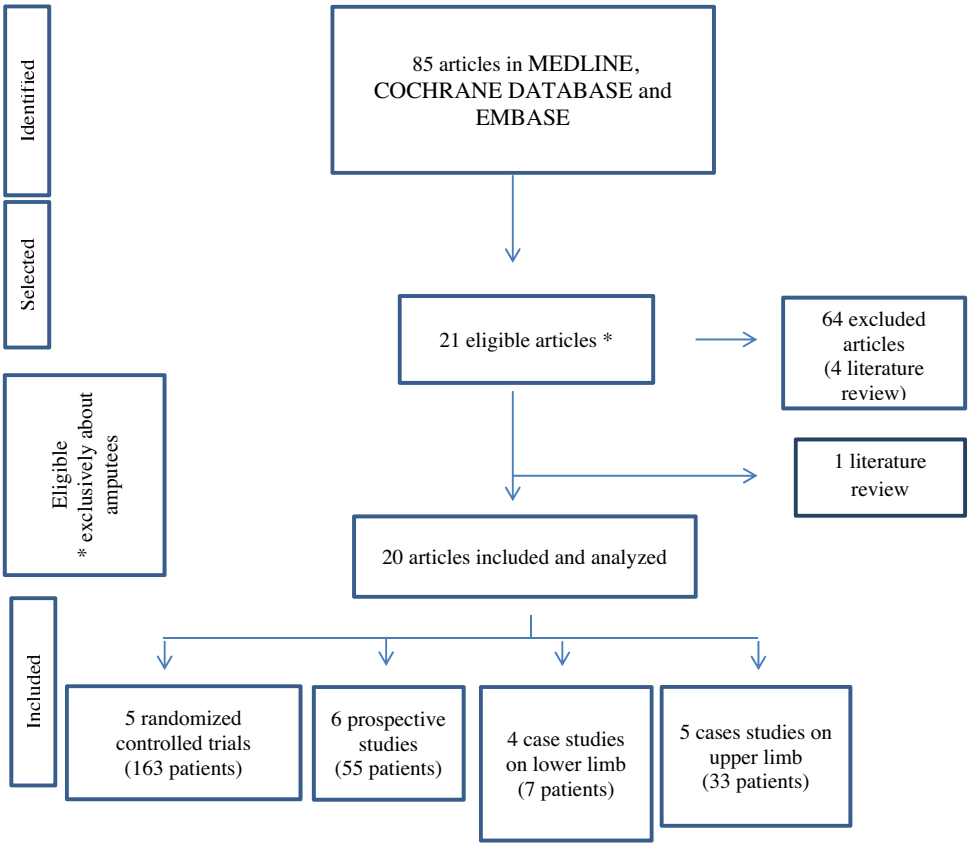

Fig. 2. Flow diagram for the selection of studies for this systematic review.

(comparative studies with marked biases, retrospective studies, case series) [43].

For 17 studies of the 18 assessing the impact of MT on PLP, efficacy was evidenced, but with poor levels of proof of 3 or 4, while one randomised controlled study did not evidence any significant effect of MT in comparison with the control group (who were shown only movements in the intact limb) [26]. It also appeared that the deep pain component of PLP could be more sensitive to MT than the superficial pain component [32].

Regarding the specific effect on the control of perceived movements in the phantom limb (PLM), the 8 studies that envisaged this aspect concluded to an impact, but with a poor level of proof for four of them (levels 3–4), and a rather better level of proof (2) for the other four (Tables 1 and 2). It can be noted that when MT does not show any efficacy, the generation of illusions of tactile stimuli in the phantom limb could provide an alternative, according to a preliminary study on 6 upper-limb amputees [29], but this is the subject of debate [14]. Likewise, associating auditory stimuli could potentialise the effects of MT according to other authors [39].

3.3. Terms of application of MT

The conditions in which MT was implemented in the different studies are reported in Table 2 for the treatment of PLP and in Table 3 for the treatment of PLM.

Table 4 shows the terms of application in the randomized controlled trials. In particular, Moseley [27] proposed 3 sequences lasting 2 weeks each–a phase for recognition of the laterality of the limb, a phase for imagining movements, and finally a MT phase.

Concerning the terms of application in non-controlled trials, it is suggested by certain authors that the existence of a depressive syndrome requires treatment prior to MT, so as to improve its results [30]. It was also reported that the conditions of preparation (information) and positioning of the patient are important, so as to favour both compliance with MT and concentration during sessions: in particular being comfortably settled in a quiet area [30,36,38,39,41]. Some authors advocate that the intact limb should be completely reflected and the residual limb completely masked in the mirror [14]. According to other authors again, any appearance of muscular pain in the intact limb should lead to asking

Table 1
Summary data on MT efficacy on phantom limb.

Phantom limb studies	PLA			PLS			PLM			PLP		
MT efficacy	+	–	NT	+	–	NT	+	–	NT	+	–	NT
Randomized controlled trials (5 studies)	1	0	4	0	1	4	2	0	3	3	1	1
Prospective studies (6 studies)	1	0	5	0	0	6	2	0	4	5	0	1
Case studies												
LL (4 studies)	0	0	4	0	0	4	2	0	2	4	0	0
UL (5 studies)	0	0	5	1	0	4	2	0	3	5	0	0
Number of studies	2		18	1	1	18	8		12	17	1	2

a: MT efficacy evidenced; –: MT efficacy not evidence; NT: Not Tested; PLA: phantom limb awareness; PLS: phantom limb sensation; PLM: phantom limb movement; PLP: phantom limb pain; LL: lower limb; UL: upper limb.

Table 2
Mirror therapy application (studies on efficacy for phantom limb pain).

Studies	Application					
	Article	Period	Number of sessions	Session duration	Instructions	Addition sensory stimulus
Randomized controlled trial	Chan et al., 2007 [24]	4W	1/d	15 min	BSM	
	Moseley, 2006 [27]	6W	NI	NI	3 phases[a]	
	Tilak et al., 2015 [28]	4d	1/d	20 min	BSM	
Prospective studies	Darnall et al., 2012 [30]	4W	Every day	25 min	BSM	
	Seidel et al., 2011 [33]	3W	12 sessions (2/d, 2X/W)	25–30 min	BSM	
	Schmalzl et al., 2013 [29]	8 sessions	NI	1 min	BSM	Tactile
	Sumitami et al., 2008 [32]	20.4W	1/d	10 min	BSM	
	Mercier et al., 2009 [34]	8W	2 sessions/W	10 × 10 mvts–30 min–1 h	BSM	
Case studies						
LL	Hanling et al., 2010 [35]	2W	1/j, 14 sessions	NI	NI	
	Darnall 2009 [36]	3M	3X/W	20–30 min	Vacant	Respi
	MacLachlan et al., 2004 [38]	3W	3X/d, 7/7 d	10X10 mvts	BSM	
	Clerici et al., 2012	24W	1/d	30 min	BSM	Tactile
UL	Ramachandran et al., 1996 [14]	NI	NI	NI	BSM	Tactile
	Kim et al., 2012 [40]	3M	4X/W	15 min	BSM	
	Wilcher et al., 2011 [39]	NI	2X/d	15 min	BSM	Auditory
	Ramachandran et al., 2009 [42]	NI	NI	NI	BSM	
	Grunert-Pluss et al., 2008 [41]	NI	5–6X/d	5–10 min	BSM	Tactile

Min: minutes; Mvts: movements; NI: not indicated; MBS: bilateral symmetric movements; d: day; W: week; f: frequency; X: times/sec: second; M: month; Respi: respiratory exercises; h: hour; NT: not tested; LL: lower limb; UL: upper limb.
[a] Three phases: 1: laterality recognition phase, 2: imagined movements phase, 3: mirror phase.

Table 3
Mirror therapy application (studies on efficacy for phantom limb movements).

Studies	Application					
	Articles	Period	Number of sessions	Session duration	Instructions	Addition sensory stimulus
Randomized controlled trial	Brodie et al., 2007 [26]	NI	NI	10X10 mvts	BSM	
	Brodie et al., 2003 [25]	NI	NI	10X10 mvts	BSM	
Prospective studies	Kawashima et al., 2013 [31]	NI	NI	30 s	BSM	
	Sumitani et al., 2008 [32]	20.4W	1/d	10 min	BSM	
Case studies						
LL	Darnall et al., 2009 [36]	3M	3X/W	20–30 min	Vacant	Respi
	MacLachlan et al., 2004 [38]	3W	3X/d, 7/7 d	10X10 mvts	BSM	
UL	Ramachandran et al., 1996 [14]	NI	NI	NI	BSM	Tactile
	Kim et al., 2012 [40]	3M	4X/W	15 min	BSM	

Min: minutes; Mvts: movements; NI: not indicated; BSM: bilateral symmetric movements; d: day; W: week; f: frequency; X: times; sec: second; M: month; Respi: respiratory exercise; h: hour; NT: not tested; LL: lower limb; UL: upper limb.

the patient to make slower movements suited to his physical capacities [30,32,34]. It is sometimes suggested that the MT procedure should be implemented very gradually, with an initial phase of several observation sessions with the intact limb immobile, before active mobilisation [41] and that in situations where the amputation is planned, prior practice session of MT over 2 weeks could potentialise the efficacy on post-amputation PLP [35]. MT is recommended by some authors in the home for sessions of 20 to 30 mins at least 3 times a week, provided the patient is previously trained and autonomised [9,37,38]. When a particular position of the phantom limb is perceived as being more painful, the recommendation is to use MT to find a more comfortable position [40].

3.4. Undesirable side effects of MT

Side effects are not systematically reported. Sometimes, a reverse effect to that expected is reported, with an aggravation of the PLS and/or PLP [24,30,34], or even a phenomenon of telescopic distortion, whereby the distal part of the phantom limb is felt as moving towards the residual limb [10]. The perception of the reflected image of the lost limb can also aggravate a depressive syndrome [30]. When deleterious side effects are systematically sought, they are sometimes frequent, in particular with episodes of confusion and dizziness [44].

4. Discussion

MT is among the treatments for chronic post-amputation pain that are fairly widely used, although no really robust proof of its efficacy has yet been provided. There are only 5 randomised controlled trials including fairly small numbers of patients, using heterogeneous methods, particularly for the terms of application (often some time from the amputation), and without comparisons across protocols. This means that currently no meta-analysis is possible. The side effects for their part are only rarely sought. In addition, the evaluation of the impact of an intervention programme, whatever the type, concerning pain following amputation is a difficult task, because the situation is often complex (interwoven aetiologies of pain), and because mood

Table 4
Summary of randomised controlled trials.

ECR	Lower limb amputees		
Chan et al., 2007 [24]	*N* = 18 3 groups: Mirror/covered mirror (CM)/mental visualization (MV) After 4S, CM and MV groups switch with mirror group	N of sessions: 1/day Length of sessions: 15 min Instruction: perform movements with both limbs Duration: 4 W No sensory addition	Significant decrease (100%) on VAS in mirror group compared to other groups (p= 0.04) for CM/ *P* = 0.002 for VM) After switch, decrease of PLP in the 2 groups (*P* = 0.008)
Brodie et al., 2007 [26]	*N* = 80 Study group (41): patient looks his intact limb's reflection, moving in the mirror Control group [39]: patient looks his intact limb, moving in the covered mirror on the same side his amputated limb	N of sessions: not specified Length of sessions: 10 × 10 mvts, with rest between each mvt Instruction: intensive mvts with the therapist = knee, foot, toe Duration: NI/No sensory addition	PLP/PLS: no significant decrease on VAS in either groups PLM: study group significantly more effective than control group to PLM ($P < 0.05$)
Brodie et al., 2003 [25]	*N* = 21 Study group: mirror (11) Control group: covered mirror [10] In center		Significant improvement of PLM in study group compared to control group using visual feedback (6.91 vs 2.3 performed movements respectively, ($P < 0.01$)
Moseley, 2006 [27]	*N* = 9 Study group: MIP [5] Control group: standard medical tt and rehabilitation care. [4]. At home	*N* of sessions: not specified Length of sessions: not specified Instruction: First 2 W: hand laterality recognition phase; next 2 W MIP; next 2 W: mirror phase. Increasing difficulty Duration: 6 W/No sensory addition	Significant decrease on VAS in study group (*P* = 0.002)
Tilak et al., 2015 [28]	*N* = 25 Study group: mirror [12] Control group: Tens [13]	N of sessions: 1/day Length of sessions: 20 min Instruction: perform movements with both limbs Duration: 4 d No sensory addition	VAS decreased significantly in the 2 groups: MT (*P* = 0.003), Tens (*P* = 0.001) No differences between the 2 groups (*P* = 0.223)

D: days; Gpe: group; Min: minute; MIP: mental imagination program; MT: mirror therapy; mvts: movements; N: number; N: number; PL: phantom limb; PLA: phantom limb awareness; PLM: phantom limb movement; PLP: phantom limb pain; PLS: phantom limb sensation; RCT: randomized controlled trial; Tens: transcutaneous electrical nerve stimulation; tt: treatment; VAS: visual analogue scale; W: week.

disorders are frequent, in particular as a result of the altered body image–depression is present in at least 30% of patients [45].

It thus appears following this review that the level of proof of the efficacy of MT is currently inadequate to recommend it as a first-intention treatment. Moreover, a review of the literature concerning MT across all its potential applications concluded to poor evidence of efficacy for PLP [22]. This was confirmed recently by a systematic review of the techniques for representing movement [46]. Consequently, there are no recommendations concerning the indication of MT in PLP, and its place among the other treatments available cannot be specified. In order to compensate for this lack of data, a survey using the Delphi method was conducted among experts [47]. This study evidenced considerable heterogeneity concerning practices in MT, and an absence of consensus on optimum duration and frequency of the MT sessions, as well as on the total duration of treatment [47].

One treatment that is close to MT with regard to the basic physio-pathological approach is mental imagery, which consists in imagining movements in the phantom limb to compensate for the sensory deafferentation. A non-controlled study evidenced a reduction in PLP intensity among 13 upper-limb amputees that was correlated with the reversibility of cortical reorganisation evidenced by functional MRI [8].

There is also the question of whether, when an illusion that the missing limb is intact, MT might not be an obstacle to the psychological acceptation of the amputation, and to the construction of a new body image enabling the prosthetic limb and its use to be integrated. The positioning of a prosthetic limb, by means of the fixation system used, creates new sensory stimuli, and this is in itself a treatment for PLP that could be more oriented towards restoring function [48]. Beyond the impact on functional rehabilitation, the early fitting of a prosthesis by rigid socket contact has long been known to favour the healing of the stump, to prevent venous thrombosis, and to play a part in pain control via a better realisation of the amputation [49]. It can be noted that after trans-femoral amputation, percutaneous osteointegrated prostheses, while improving functional capacities, do not alter PLP any more than conventional fitting (socket-suspended prostheses) [50]. There may also be a degree of antagonism between MT and the early fitting of a prosthesis, since MT might delay the construction of a new motor pattern, and a new body image... Responding to this question by controlled studies, however, appears problematic for ethical reasons, since it would involve comparing patients receiving a prosthetic limb post-amputation with another matched group undergoing MT and not receiving a prosthetic limb. Other therapeutic innovations are worth exploring in the treatment of PLP: there is, in particular, somatosensory restoration by stimulation of the peripheral nerves, which via a neural interface can be coupled with the fixing of a prosthetic limb. On the basis of a preliminary application, this appears to yield interesting results [51].

5. Conclusion

The proof of efficacy of MT on PLP is so far inadequate to recommend it as a first-line treatment. Randomised controlled trials are still needed to assess the effects of MT more thoroughly,

on both pain and the integration and use of the prosthetic limb, and also to determine the optimal terms for its application.

Disclosure of interest

The authors declare that they have no competing interest.

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