,

THE EFFECT OF ONE SESSION OF MIRROR THERAPY ON PHANTOM LIMB PAIN AND RECOGNITION OF LIMB LATERALITY IN MILITARY TRAUMATIC LOWER LIMB AMPUTEES-A pilot study

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ABSTRACT

Up to 70% of military amputees suffer phantom limb pain (PLP), which is difficult to treat. PLP has been attributed to cortical reorganisation and associated with impaired laterality. Repeated sessions of mirror therapy (MT) can benefit PLP, however anecdotal evidence suggests one MT session could be effective. In a one-group pre-test-post-test design, 16 UK military unilateral lower limb amputees (median age 31.0 (25.0-36.8) years) undertook one 10-minute MT session. Visual analogue scale (VAS) pain and laterality (accuracy and reaction time) measurements were taken Pre-Post MT. Median VAS PLP did not differ significantly between pre-MT 15 (2-53)mm and post-MT 12 (1-31)mm (p=.875) scores. For the amputated limb, there were no significant differences between pre and post-MT scores for laterality accuracy, 95.3 (90.5-97.6)% and 96.7 (90.0-99.4)% respectively (p=.778); or reaction time, 1.42 (1.11-2.11) seconds and 1.42 (1.08-2.02) seconds respectively (p=.629). Laterality was also not different between limbs for accuracy p=.484 or reaction time, p=0.716; and did not correlate with PLP severity. No confounding variables predicted individual responses to MT. Therefore, one 10-minute MT session does not affect laterality and is not effective as standard treatment for PLP in military lower limb amputees. However, substantial PLP improvement for one individual and resolution of a stuck phantom limb for another infers that MT may benefit specific patients. No correlation found between PLP and laterality implies associated cortical reorganisation may not be the main driver for PLP. Further research, including neuroimaging, is needed to help clinicians effectively target PLP.

INTRODUCTION

Recent military conflicts have produced a substantial number of traumatic amputees, with phantom limb pain (PLP) occurring in 70% of these patients,[1]. Rehabilitation for UK service personnel with such injuries begins at Queen Elizabeth Hospital Birmingham (QEHB), and continues at the Defence Medical Rehabilitation Centre (DMRC) Headley Court, UK. PLP remains poorly understood and is notoriously difficult to treat with less than 50% of patients describing a lasting benefit from conventional medical management,[2].

Cortical reorganisation is a widely-cited cause for PLP and neuroimaging studies have demonstrated cortical re-mapping with PLP,[3]. Cortical reorganisation is directly correlated with the degree of PLP in upper limb amputees and increasingly treatments are aimed at reversing cortical changes,[4]. Mirror therapy (MT) is a popular treatment and appears to restore cortical organisation, with significant reductions in PLP with multiple MT treatments,[5]. A study of 22 US military single lower limb amputees reported a decrease in PLP in 100% of 6 participants undergoing MT. At 4-weeks, 9 subjects from the covered mirror and mental visualisation groups crossed-over to MT. 89% of these subsequently reported reductions in pain,[6]. However, 4 participants were unaccounted for and biases not fully addressed. Other literature have suggested there is little evidence for MT for PLP with recommendations that dosage and type of therapy be investigated,[7].

Anecdotal evidence suggests one MT session could be effective. Statistically significant reductions in de-afferentation pain, including in 11 amputees, have been reported, following one MT session,[8]. However, participants had undergone daily MT prior to the study. Significantly greater motor control of the phantom lower limb and slight improvements in PLP have been reported with one MT session, however this was similar to the control group using a covered mirror and only 15 of the 80 participants were experiencing PLP pre-intervention,[9]. Additionally, there is some evidence of the ability to move a previously 'fixed' phantom limb, after a single MT session,[9]. Other research has noted that baseline PLP scores is linked to the number of sessions required to be effective,[10].

Separate research demonstrates that PLP following upper limb amputation is associated with reduced accuracy and delayed response time in recognising differences between left and right, known as laterality,[11]. Laterality is thought to be based on an intact cortical body representation,[11]. However, for lower limb amputees no statistical difference between the amputation and control group in laterality accuracy or response times are reported,[12].

Research is limited supporting the efficacy of one MT session. This novel research is the first to investigate the effects of one session of MT on PLP and laterality. Laterality scores could potentially highlight those amputees with cortical reorganisation and, therefore that respond to MT. This study aims to investigate whether one 10-minute MT session affects pain and laterality scores in UK military traumatic lower limb amputees. A secondary aim will test laterality differences between the amputated and intact limb, and explore associations between pain and laterality scores.

METHODS

Study design and participants

A one-group pre-test-post-test experimental study design aimed to determine whether one session of MT affects pain or laterality scores. A convenience sample of 16 UK military personnel participated; all in-patients at either QEHB or DMRC Headley Court. Unilateral traumatic lower limb amputees (excluding digits), reporting PLP and any level of prosthetic use were included. Patients currently undertaking MT and those with head injuries, visual impairment or visible injury to the intact limb were excluded. Additionally, psychological instability (assessed by the mental health team), dyslexia,[13]and any neurological or motor disorder,[13]were excluded.

PROCEDURE

The intervention consisted of one 10-minute session of MT with a mirror box (Reflex Pain Management Ltd, Cheshire, UK, Patent Pending), used to create an intact and complete image of the missing limb by reflecting the unaffected limb(Fig 1). The mirror was positioned perpendicular to the patient's midline and sock/shoes were removed. Participants were asked to move the unaffected limb while imagining and attempting to execute the movement with the amputated limb to match those seen in the mirror. The participant was asked to undertake movements for 10-minutes (e.g. flexion-extension cycles, rotation of the relevant body part and wiggling of toes) at their discretion,[9]and was in addition to conventional treatments. No attempt was made to control medication or record psychological therapy input.

Fig. 1, shows the setup of the mirror box that was used to create the illusion of an intact and complete image of the missing limb. This is achieved by reflecting the unaffected limb.

OUTCOMES

PLP scores were measured by participants' marking the 100mm (with the anchors as 'No pain' and 'worst pain imaginable') Visual Analogue Scale, pre and post MT intervention and defined as pain in the missing limb,[14].

Laterality accuracy and response times were measured using Neuro-Orthopaedic Institute (NOI) Recognise™ software (Noigroup Publications, Adelaide, Australia) presented on a tablet computer. Participants sat comfortably in a well-lit room and faced a tablet screen, approximately 30cm from their frontal plane. After 2 attempts for habituation participants completed 3 tests pre and post the MT intervention using Recognise™. The software recorded the patients' 'touch-keyed' entry as they attempted to identify 30 pictures of feet as left or right (Fig 2), automatically logging the accuracy and response time,[15]. Recognise™ laterality accuracy scores greater than 80%, with reaction times less than 2 seconds and similar results between sides (as per NOI referenced values), were considered 'normal values' for the study,[16]. Both pain and laterality measurements were undertaken without encouragement or feedback, by a single researcher(AW).

Fig.2, shows an example of the pictured foot using the Neuro-Orthopaedic Institute Recognise™ software. This could be either left or right and subjects entered their decision on a key touch pad.

The research protocol was approved by the Cardiff University School of Healthcare Studies Research Ethics Committee and the Ministry of Defence Research Ethics Committee, Whitehall, London, Protocol no. 422/MODREC/13. The research was conducted in accordance with the Declaration of the World Medical Association and written informed consent was obtained from all participants.

DATA ANALYSIS

All data was analysed using Statistical Package for the Social Sciences® (SPSS®) software (IBM Corps, USA). Descriptive data, not normally distributed, was summarised as median and weighted average percentiles. Wilcoxon Signed-Rank test compared PLP and laterality scores; the non-normally distributed data for the laterality accuracy and reaction time data was logarithmically transformed to improve distribution of the residuals. Repeated-measures ANOVA tested the interactions between laterality (accuracy and reaction time) for the intact and amputated limb, pre and post MT. Spearman's Correlation Coefficient determined correlations between pain and laterality scores. Additional exploratory analysis was undertaken of the supplementary demographic baseline data to allow comparison of confounding factors with related studies. For all analyses, an alpha-level <.05 was considered as significant.

RESULTS

Demographic data

16 participants with a median age 31.0 (25.0-36.8) years, range 22-45, all experiencing PLP were included. There were no withdrawals and all data sets were complete. 9 participants self-reported their amputated lower limb as dominant (all right side). Table 1 presents the characteristics of the participants. Two participants stated their prosthetic limb helped PLP.

Table 1, Descriptive characteristics of Participants and Phantom limb characteristics

	Totals (ratio)
Gender (male:female)	15:1
Mechanism of injury	
- Gunshot Wound	3
- Blast	6
- Other	7
Level of amputation (total (right:left))	
- Above-knee	4(3:1)
- Through-knee	2(1:1)
- Below-knee	10(7:3)
Dominant limb (right:left)	14:2
Functional prosthetic use (yes:no)	13:3
Phantom limb sensation (present:absent)	6:10
Phantom movement (present:absent):	13:3
(willed/imagined/involuntary/cramping/stuck/nill)	(7/4/2/1/1/1)

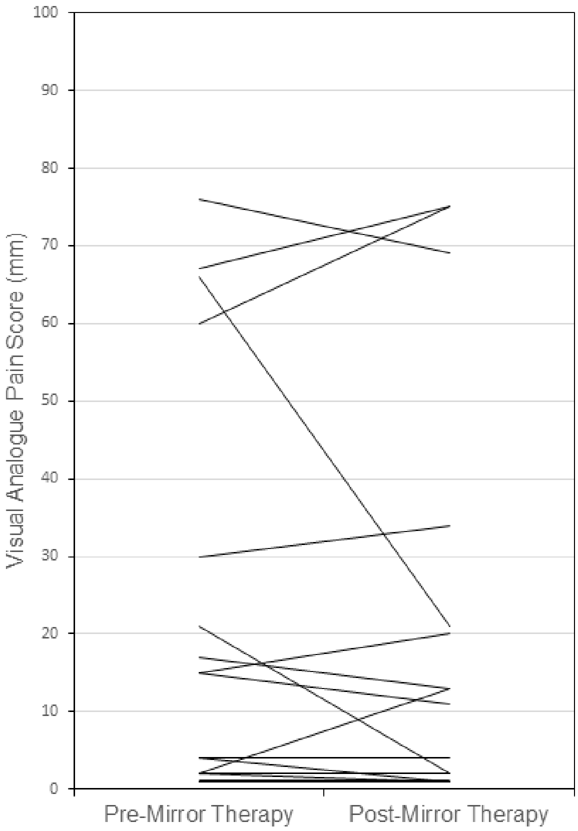
The median time since amputation was 0.95 (0.38-1.42) years, range 5 days-11.78 years, with the three non-prosthetic limb users all less than 1-week since amputation.

Phantom Limb Pain

VAS PLP ratings did not differ significantly (p=.875), with a median pre-MT score of 15 (2-53) mm, compared with 12.0 (1-31) mm post-MT. Figure 3 demonstrates considerable variation in PLP responses to MT. One participant had a substantial (45mm VAS) reduction in pain. One participant reported being able to move a stuck foot 8 minutes into the MT, yet marked an identical VAS pain rating following MT. Five participants stated that they had previously used MT and found it improved PLP. No harm or grief reaction was reported. In

5 participants' pain rating worsened, including all 3 non-prosthetic wearers. No unique difference in confounding variables was identified to differentiate response to MT.

Fig. 3, shows the visual analogue pain scores pre and post the one session of mirror therapy for the 16 participants.



Laterality accuracy and reaction times

In the amputated limb, median laterality accuracy scores showed no significant difference between pre-MT 95.3 (90.5-97.6)% compared with post-MT 96.7 (90.0-99.4)% (p =.778). Median laterality accuracy for the intact limb was 93.5 (90.9-97.6)% pre-MT, compared with 96.5 (91.8-99.6)% post-MT.

For the amputated limb pre-MT, a median laterality reaction time score of 1.42 (1.11-2.11) seconds did not differ compared with 1.42 (1.08-2.02) seconds post-MT (p =.629). The median laterality reaction time for the intact limb was 1.42 (1.18-1.97) seconds pre-MT, compared with 1.43 (1.14-1.93) seconds post-MT and again not significant (p =.955).

Comparisons between the intact and amputated limb

Participants did not perform any differently in recognising the intact or amputated limb, with no significant main effect seen for the Log 10 transformed data for either laterality accuracy $F(1,15)= 0.516$, $p=.484$ or laterality reaction times $F(1,15)= 0.138$, $p=.716$. Moreover, there was no significant interaction between pre or post MT for the amputated or intact limbs for either laterality accuracy or reaction times (Table 2).

Table 2. Repeated-measures ANOVA p values for Log10 transformed laterality data

	Laterality Accuracy		Laterality Reaction Time	
	F	p value	F	p value
Pre-MT -Post-MT	F(1,15)= 0.569	0.462	F(1,15)= 0.091	0.767
Pre-MT-Post-MT – Amp.-Intact limb	F(1,15)= 0.697	0.417	F(1,15)= 1.758	0.205

Key: MT Mirror Therapy, Amp. Amputated

CORRELATION BETWEEN PLP AND LATERALITY

There was no significant correlation between PLP and laterality (accuracy or reaction time) for either the amputated or intact limb for the pre-MT data or the post-MT measures(Table 3

Table 3. Spearman's Rank Correlation rho and p value significance (2-tailed) pre and post-mirror therapy

Pre-Mirror Therapy	Laterality Accuracy		Laterality Reaction Time	
	Amputated	Intact	Amputated	Intact
Phantom limb pain	rho=-0.043, p=0.874	rho=-0.295, p=0.268	rho=0.004, p=0.987	rho=0.037, p=0.892
Post-Mirror Therapy				
Phantom limb pain	rho=-0.464, p=0.070	rho=-0.085, p=0.755	rho=0.141, p=0.601	rho=0.201, p=0.456

Exploratory data analysis showed participants did not produce more accurate responses (p=.629) or quicker reaction times (p=.875) pre-MT when recognising their dominant limb. There was no correlation found between age and PLP or laterality.

DISCUSSION

This study aimed to establish the effect of one session of MT on PLP and laterality. Although non-significant findings were noted in all variables certain factors need to be considered. The 16 participants were generally younger than related studies and with different causes of amputation compared to some studies, with gunshot or blast injury being the leading causes of amputation in armed conflict. Furthermore, 2 participants' have through-knee amputations which are rare in historic or civilian populations. The mechanism of injury may explain results conflicting with previous studies. Despite the wide range in time since amputation, 13 of the 16 participants were within 2 years which may, in part, explain symptom variation for similar presentations and circumstances of limb loss, plus highlighting that MT may not address all aspects of pain. Finally, influences from the participants' unique military in-patient environment, including rating their pain 4 times a day and regular access to drugs rounds, may have affected the acceptance, perception or reporting of pain.

These non-significant results appear to concur with literature which could not recommend MT for PLP mainly due to low levels of evidence and various methods of application of MT,[17]. The greatest PLP reduction appears to be during the first week of MT,[6]with PLP severity affecting the number of treatment sessions required,[10]. Previous MT or Graded Motor Imagery(GMI) training was not excluded, which raises the possibility that some cortical training or central adaptations may have already occurred. Our results also concur with previous work which found no effect of a single session of MT,[9]in a population with universal use of prosthetics. The high use of prosthetics in our sample may explain the reduced PLP and MT effect.

Group results can potentially miss clinically important individual responses. Military traumatic amputees have reported a painful limb fixed in the position immediately post injury,[18]. The significant reduction in pain for one individual and the ability to move a 'stuck' limb for another corresponds with anecdotal reports of the resolution of phantom limb symptoms or restoration of movement following a single session of MT,[9]. Visual feedback corresponding with proprioceptive memory,[19]rather than cortical reorganisation, may explain why this individual marked identical VAS pain ratings following MT.

As 11 of the participants had relatively low PLP ratings, they may have had minimal cortical reorganisation for MT to 'normalise'. However, of 5 baseline pain ratings that could be classified as moderate or severe, only 1 showed substantial improvement with a single session of MT. A flaw of the cortical reorganisation theory is that it's not clear why shifting representations would cause pain, rather than just altered perception. As the vast majority of the evidence demonstrating cortical shift and improvement in PLP with MT is for upper limb amputees,[20]one explanation may be that lower limb amputees respond differently; possibly due to smaller sensory homunculus representation. Other potential explanations include that there is a peripheral driver for some PLP, a distraction effect of MT, or that movement combined with MT influences reported success in treating PLP. Similarly, imagining rather than 'willing' movements may relieve PLP,[21]or be more important than the mirror itself. However, previous work did not find any effect on PLP with mental imagery,[12]and PLP has been shown to correlate only with executed, but not imagined movements,[22].

In this study laterality was unaffected by a single session of MT and did not replicate reported slower and less accurate upper limb amputee data,[11]. This study concurs with previous work with an older non-traumatic population, who found no significant differences between laterality accuracy or response times for lower limb amputees,[12]. The fact that impaired laterality was not demonstrated indicates that participants either maintained or regained laterality recognition ability. Despite no control group, participants demonstrated better laterality scores than published normative values. The relatively young and otherwise fit military participants could explain these high baseline scores. Normal laterality scores could also be due to different laterality measurement tools used or functional prosthetic use, as early prosthetic use appears to be crucial for cortical re-mapping,[23]. Equally, previous GMI or the intensive in-patient rehabilitation could mean that training adaptions have already occurred. The relatively low PLP ratings for 11 of the participants could imply intact cortical representations and, therefore, explain why the values remained normal post-MT.

Participants were requested to execute phantom limb movements, however there is no way of measuring whether they executed, imagined or merely observed the mirrored movement. Previous studies found that, although executed phantom limb movement speed was reduced, imagined movement speed remained unchanged,[24]. Participants may have therefore employed compensation strategies to demonstrate normal laterality scores. Previous exercises for the phantom limb and prosthetic use may have generated motor adaptations to normalise laterality and/or cortical organisation. Slower laterality reaction times for 2 of the 3 non-prosthetic wearers in this study all within 1-week of amputation supports this observation.

When directly comparing PLP and laterality, no correlation either pre-MT or post-MT was found, concurring with previous research who found no correlation between CPRS pain intensities and GMI laterality scores,[15].

In this study PLP increased with MT for all 3 non-prosthetic wearers who were 1-week post amputation and would not yet have developed many peripheral adaptations, such as neuromas or heterotrophic ossification. Early use of prosthetics may improve cortical reorganisation and explain why MT did not improve PLP or laterality. Interestingly, if the functional element of the prosthetic, which has a much higher lower limb uptake, is beneficial [24], this could explain why positive results to MT are more abundant in upper limb studies. It would not explain, however, the significant improvement in PLP symptoms seen for one individual who used a functional prosthesis. Early prosthetic use may play a role in alleviating PLP, however, caution should be exercised due to the small sample size and other confounding factors not measured

3 patients in this study reported not being able to move their phantom limb. Perception of phantom movement may rely on preservation of a cortical representation of the missing limb. A lack of intact representations could be a reason why 2 of these 3 participants experienced pain worsening with MT.

The results infer that PLP is not a unitary condition and that no single treatment is likely to be a panacea due to the disorder originating from multiple mechanisms,[24]. A targeted approach to treatment seems appropriate,[25]. Further research is needed including MT being undertaken with concurrent neuroimaging to help elucidate the relationship between risk factors and the different proposed mechanisms underlying PLP. Investigations into the use of technologies such as supported tele-rehabilitation,[26]and virtual reality would allow development of alternatives to MT for amputees.

LIMITATIONS AND STRENGTHS

This is a pilot study with a low number of subjects. The study is not controlled in any way so the results need to be viewed with caution. A strength of the study is that this is one of the first studies that has reported laterality combined with PLP.

CONCLUSION

The results demonstrate that one 10-minute session of MT is not effective as a treatment for PLP in military traumatic lower limb amputees. It also indicates that, for this population, laterality measurements do not improve with MT or help to predict which patients may respond to MT. However, the substantial improvement in pain scores for one individual and the resolution of a stuck phantom limb for another infer that MT may benefit specific patients. MT should therefore continue to be offered as part of a wider multimodal rehabilitation approach, with early functional prosthetic provision considered as part of a strategy to alleviate PLP.

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