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Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a 'virtual' limb upon phantom limb pain, sensation and movement

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Abstract

The extent to which viewing a 'virtual' limb, the mirror image of an intact limb, modifies the experience of a phantom limb, was investigated in 80 lower limb amputees before, during and after repeated attempts to simultaneously move both intact and phantom legs. Subjects were randomly assigned to one of two conditions, a control condition in which they only viewed the movements of their intact limb and a mirror condition in which they additionally viewed the movements of a 'virtual' limb. Although the mirror condition elicited a significantly greater number of phantom limb movements than the control condition, it did not attenuate phantom limb pain and sensations any more than the control condition. The potential of a 'virtual' limb as a treatment for phantom limb pain was discussed in terms of its ability to halt and/or reverse the cortical re-organisation of motor and somatosensory cortex following acquired limb loss.

Keywords: Virtual limbs; Acquired limb loss; Phantom limbs; Movement; Phantom limb pain; Phantom limb sensations

1. Introduction

A phantom limb is experienced by most individuals who acquire a limb loss and is in itself seldom distressing (Whyte, 1999). Additionally, many amputees experience sensations in their phantom limb (PLS) which can range from pleasant warmth to an unpleasant intense itch (Whyte, 1999). However, chronic phantom limb pain (PLP) following limb loss is experienced in up to 85% of amputees and is a major cause of distress, physical limitation and disability (Ehde et al., 2003; Jensen et al., 1985; Whyte, 1999).

PLP has received considerable attention in the literature, with more than 68 different treatment strategies having been reported as being effective, including a variety of medical, surgical, psychological and alternative options (Sherman, 1994). However, the success of these treatments is poor, with response rates rarely exceeding that of placebo treatments of surgical pain. Additionally, the majority of treatment studies in this area suffer from significant methodological weaknesses as the published literature has mainly consisted of single-group designs, clinical commentaries and case studies, with very few randomized controlled clinical trials (for

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reviews see Flor, 2002b; Nikolajsen and Jensen, 2001; Sherman, 1980, 1997).

A phantom limb is thought to be experienced because the same brain processes that generate the experience of an existing limb remain present following amputation (Melzack, 1990), a view confirmed by numerous brain imaging studies (Campos de Paz et al., 2000; Roux et al., 2002). However, PLP is a complex phenomena that results in part from pathological changes to numerous brain regions including somatosensory and motor areas (Flor, 2002a,b; Karl et al., 2004). It is surprising therefore that given the importance of vision in controlling both upper (Goodale et al., 1994) and lower (Patla, 1997) limb activity, little research has been carried out into the interaction between visual feedback and the experience of phantom arms and legs.

It has been reported that when the reflection of an intact arm in a mirror is superimposed upon the felt position of a phantom arm, viewing its movement can modify the experience of the phantom limb (Ramachandran and Hirstein, 1998; Ramachandran and Rogers-Ramachandran, 1996). It was found that viewing a 'virtual' arm, whilst sending commands to move both arms, induced a number of effects in the phantom arm including movement and the alleviation of pain. However, these studies did not adequately control for attempted movement alone. In a randomised controlled study of lower limb amputees it was confirmed that viewing a 'virtual leg' does induce significantly more phantom leg movements than attempted movement alone though it was not possible to confirm the analgesic effect as none of the subjects were in pain at the time of the intervention (Brodie et al., 2003).

The purpose of this study was to establish empirically, in a randomised controlled trial, the effect that viewing a moving virtual leg and/or the repeated attempt to move the phantom leg whilst simultaneously moving the intact leg, has upon phantom limb pain, sensation and movement.

2. Methodology

2.1. Ethics

Prior to the commencement of the study ethical approval was granted by the South Glasgow University Hospitals NHS Trust Ethics Committee (Ref. EC/02/S/70) and by The South Sefton Research Ethics Committee, Aintree Hospitals NHS Trust (Ref. EC.125.02).

2.2. Subjects

Lower limb amputees who had reported the presence of a phantom leg and who were attending the Artificial limb and Appliance Centre, Southern General Hospital, Glasgow and The Donald Tod Rehabilitation Centre, Fazakerley Hospital, Liverpool, were invited to participate in this study.

3. Statistical analysis

The data are presented as mean (±SD) for pain and sensation measures and mean (±SE) for movement measures. Categorical variables are presented as *n*. Statistical analysis was performed with SPSS for Windows Version 10.0 (SPSS Inc., Chicago, IL). Parametric data were analysed using one and independent sample *t* tests, and for multiple comparisons, analysis of variance (ANOVA) was used with Bonferroni correction. MPQ, NWC and PRI scores and VAS intensity scores were tested with a mixed-design analysis of variance with repeated measures. Categorical data (gender, frequency of side of amputation, position of amputation etc) were analysed with the χ^2 test. The level of significance was set at $P < 0.05$.

3.1. Apparatus

Two virtual limb boxes (640 mm depth × 630 mm width × 900 mm height) was constructed of wood, open at the front and top and with a central mirror (640 mm × 900 mm) positioned vertically half way between the box sides. This allowed the mirror to be aligned in the saggital plane of each subject, the intact limb placed to one side and the subject able to look down into the mirror to view a 'virtual' limb, the mirror reversed image of the intact limb. The side of the box in which the phantom limb was placed was obscured and

Fig. 1. Example of an intact and a virtual leg, the mirror reflection of the intact leg, in the virtual limb box.

the mirror could be reversed to accommodate left and right sided amputations. See Fig. 1 for an example of an intact leg and a 'virtual' leg, its mirror image, in a mirror box.

3.2. Procedure

A pseudo random series was computer generated in order to allocate subjects to one of two conditions; a mirror condition, in which the subject was asked to place their intact limb into the mirror box, direct their gaze onto the mirror image of their intact limb and align their phantom with this image; and a control condition in which the subjects aligned their intact leg and phantom leg to either side of the mirror whilst it was obscured. This allowed the subject to view the intact limb but not its mirror image.

In both conditions the subjects were instructed to attempt to carry out 10 movements, each repeated 10 times, with both phantom and intact limb by the experimenter who ensured that the movements were carried out. The movements were identical to those fully detailed in Brodie et al. (2003). Subjects who did not report the presence of a phantom limb at the start of the intervention aligned their stump and their intact leg to either side of the mirror as it is known that exposure to the mirror may induce the presence of a phantom limb (Hunter et al., 2003).

Suggestive demands were kept to a minimum with no direction of effect indicated to subjects for any one aspect of their phantom limb experience. Subjects were asked to remove their prosthesis and carry out a series of gentle movements using their intact limb and their phantom limb. They were informed that each type of movement would be followed by a rest period, that the researcher would administer a questionnaire about phantom sensation and stump pain, and would ask about levels of painful or non-painful feelings before, during and after the procedure. Additionally they were told that the procedure was not expected to produce any additional pain or side effects, but if at any point they wished to stop, the procedure would be discontinued.

3.3. Assessment of phantom limb awareness, phantom limb sensation and phantom limb pain

The presence of a phantom limb (PLA), defined as the conscious awareness of the missing leg, phantom sensations (PLS), defined as the perception of non-painful sensations such as heat, cold or itch in the phantom leg, and phantom pain (PLP), defined as the perception of painful sensations in the phantom leg, were each recorded immediately before and after the intervention to tease apart the complex subjective experience of a phantom limb (Fraser et al., 2001; Hunter et al., 2003; Whyte, 1999). Subjects who reported the presence of a phantom limb were asked whether they could voluntarily move the phantom. Visual analogue scales were used to record the intensity of phantom limb sensation (PLS) and phantom limb pain (PLP). These were administered pre- and post-intervention, along with the McGill pain questionnaire (MPQ) (Melzack, 1975). The MPQ is a theoretically grounded, multi-dimensional assessment tool, made up of adjectives which can be selected to describe a large range of sensory, affective, and evaluative components of a pain experience. In this study it was used to generate a description of the subject's experience of PLP and of the non-painful sensations involved in PLS. The number of descriptors selected was used as a measure of both PLP and PLS, thereby maintaining consistency in the assessment of these different aspects of the phantom experience. The total number of descriptors was broken down into sensory descriptors and others, which included affective, evaluative and miscellaneous categories (Melzack, 1975). In addition, MPQ data was conventionally analysed, to produce Total Pain Ranking Index (PRI) scores and subcomponent scores for sensory and non sensory dimensions of the phantom experience (Melzack, 1975).

3.4. Phantom limb movement

The ability to move a phantom limb (PLM) was defined as the ability to intentionally move part or all of the phantom leg, foot or toe. Subjects were asked to report upon the presence or absence of this ability prior to the intervention. It was made clear that unintentional movements of the phantom were not to be considered as these are known to also be experienced by amputees (Ramachandran and Hirstein, 1998). Whilst carrying out the movements the subjects were instructed to describe verbally any changes in position they experienced in their phantom limb. The qualitative verbal description of changes in the phantom made by subjects was recorded onto an audio cassette during the procedure. There was a pause between each type of movement and if at any point the subject felt unable to continue and wished to stop, the procedure was discontinued. This did not happen for any of the subjects. A successful movement response was scored for each of the 10 types of movement if any one of the 10 repetitions was reported to elicit a movement in the phantom.

4. Results

Eighty amputees participated in the study, 40 from the Westmarc Prosthetic Fitting Centre at the Southern General Hospital, Glasgow and 40 from The Donald Tod Rehabilitation Centre, Fazakerley Hospital, Liverpool. Full informed consent was obtained from all participants.

4.1. Subject characteristics

The characteristics of the 80 subjects are shown in Table 1. There were no significant differences between the subjects randomly allocated to the mirror and control conditions in terms of gender, age, age at amputation, years since amputation or self reported ability to move the phantom leg. One subject failed to report whether or not he was able to move his phantom.

4.2. Modification of the phantom limb

4.2.1. Awareness, sensations and pain

Of the 80 subjects, 41 were randomly allocated to the mirror group and 39 to the control group. All subjects reported that they had experienced PLA but the presence and strength of the phantom leg fluctuated as is normal in this population (Whyte et al., 1996).

Table 2 shows the number of subjects reporting the presence or absence of phantom limb awareness (PLA), phantom limb pain (PLP) and phantom limb sensations (PLS) pre- and post-intervention as a function of condition, mirror and control.

Table 1
Characteristics of subjects

	Total ($n = 80$)	Mirror ($n = 41$)	Control ($n = 39$)
Gender (m:f)	63:17	35:6	28:11
Mean age in years (range)	55 (20–83)	54 (20–83)	57 (25–80)
Mean age at amputation in years (range)	47 (7–82)	45 (7–82)	49 (14–75)
Mean years since amputation (range)	9 (1–50)	10 (1–50)	8 (3–47)
Side of amputation			
R	39	20	19
L	41	21	20
Position of amputation			
TF, trans femoral	35	16	19
TT, trans tibial	45	25	20
Reason for amputation			
Congenital	1	1	0
Cancer	4	2	2
Accident	26	17	9
Medical	49	21	28
Ability to move phantom			
Present	49	25	24
Absent	30	15	15
Regular use of prosthetic			
Yes	74	39	35
No	4	2	2
Phantom limb pain (PLP)	68	35	33
Onset of PLP			
<2 weeks	44	21	23
<1 year	20	11	9
>1 year	4	3	1

4.3. Pre- and post-intervention PLA

Table 2 shows the numbers of subjects reporting PLA pre- and post-intervention, due to the appearance, abolition or change in size of the existing PLA. Of the 12 subjects allocated to the mirror condition reporting no PLA pre-intervention, 4 subjects reported the appearance of PLA, 2 to incomplete and 2 to full. Of the 9 subjects allocated to the control condition reporting no PLA pre-intervention, none reported the appearance of PLA.

4.4. Pre- and post-intervention PLS

Table 2 shows the numbers of subjects reporting PLS pre- and post-intervention, due to the appearance, abolition, or a change in intensity of PLS.

The means and standard deviations for the number of verbal descriptors chosen (NWC) and the intensity measures of PLS are presented in Table 3. Between and within subject ANOVAs were performed on these variables as a function of condition (mirror/control) and time (pre/post). A significant main effect for time was found for the number of descriptors [$F(1,41) = 6.831$; $p = < .05$] with an observed power of 72%. Although a significant decrease in the number of descriptors reported by subjects was found in both conditions, power failed to reach 80%, due to the large observed variability for this measure. Significant main effects for time was found for intensity measures Total [$F(1,41) = 5.254$; $p < .05$], Sensory [$F(1,41) = 4.404$; $p < .05$], and VAS Intensity [$F(1,41) = 5.484$; $p < .05$] with observed power of 61%, 54% and 63%, respectively. Although significant decreases in intensity of the sensations being experienced were reported by subjects in both conditions, the low power resulted from the large observed variability for these measures. No other significant main effects or interactions were found. Thus the visual feedback of a virtual leg was not found to modify the quality or quantity of the PLS experienced any more than movement alone, both mirror and control conditions resulted in a significant attenuation of PLS.

Thirty-four subjects reported the presence of PLS with no associated PLP prior to the intervention. Sixteen of these subjects were randomly allocated to the mirror condition and 18 to the control condition. ANOVAs were performed on the number of descriptors and the intensity measures as a function of condition (mirror/control) and time (pre/post). A significant main effect for time was found for number of descriptors [$F(1,32) = 5.826$; $p < .05$] due to a decrease in the number of verbal descriptors reported by subjects in both conditions. No other significant main effects or interactions were found.

4.5. Pre- and post-intervention PLP

Table 2 shows the number of subjects randomly allocated to the mirror condition and the control condition,

Table 2
Numbers of subjects reporting the presence of a phantom (PLA), of phantom limb pain (PLP) and of phantom limb sensations (PLS) pre- and post-intervention as a function of mirror and control conditions

Phantom Limb Awareness		Absent	Incomplete	Full
Mirror	Pre-	12	16	13
	Post	11	15	15
Control	Pre-	9	16	14
	Post	11	18	10

Phantom Limb Awareness		Incomplete		Full	
Phantom Limb Pain		Present	Absent	Present	Absent
Mirror	Pre-	4	12	3	10
	Post	2	13	3	12
Control	Pre-	3	13	5	9
	Post	4	14	3	7

Phantom Limb Awareness		Incomplete				Full			
Phantom Limb Pain		Present		Absent		Present		Absent	
Phantom Limb Sensations		Present	Absent	Present	Absent	Present	Absent	Present	Absent
Mirror	Pre-	3	1	9	3	2	1	7	3
	Post	2	0	8	5	1	2	8	4
Control	Pre-	2	1	10	3	2	3	8	1
	Post	3	1	11	3	2	1	5	2

Table 3
Mean (±SD) phantom limb sensation (PLS) measures pre- and post-intervention

	Variable	Pre-intervention		Post-intervention	
		Mirror ($n = 21$)	Control ($n = 22$)	Mirror ($n = 21$)	Control ($n = 22$)
Verbal descriptors	NWC	5.33 (±5.05)	6.91 (±4.84)	4.05 (±4.41)	5.32 (±4.57)
	Total	9.71 (±10.5)	11.59 (±8.8)	7.76 (±9.3)	8.82 (±7.2)
	Sensory	6.81 (±7.1)	7.50 (±6.1)	5.38 (±6.1)	5.77 (±4.9)
	Other	2.91 (±3.9)	4.09 (±3.2)	2.38 (±3.5)	3.05 (±2.98)
Visual analogue scale	Intensity score	48.85 (±30.18)	49.22 (±27.74)	37.60 (±36.05)	44.08 (±31.81)

who were experiencing phantom pain immediately before and after the intervention. 3 subjects in both conditions reported the abolition of PLP following the intervention.

The means and standard deviations of the number of words chosen (NWC) and the MPQ intensity scores (Melzack, 1975) and the VAS intensity score are presented in Table 4. Between and within subject ANOVAs were performed on these variables as a function of condition (mirror/control) and time (pre/post). A significant main effect for time was found for the number of words chosen [$F(1,13) = 6.864$ $p < 0.05$] with an observed power of 68%. Although a significant decrease in the number of descriptors reported by subjects was found in both conditions, power failed to reach 80%, due to the large observed variability for this measure. Significant main effects for time were found for MPQ Pain Rating Index (PRI) total score [$F(1,13) = 7.195$ $p < 0.05$] and MPQ PRI Sensory score [$F(1,13) = 8.374$ $p < 0.05$] with observed power of 70% and 76%. Although a significant decrease in the pain intensity reported by subjects was found in both conditions, power failed to reach 80%, due to the large observed variability for this measure. No other significant main effects or interactions were found. Thus the visual feedback of a virtual leg does not modify PLP any more than attempted movement alone. Although numbers are small, at a group level both mirror and control conditions resulted in a significant decrease in PLP.

4.6. Post-intervention PLS and PLP

Of the 31 subjects who reported neither PLP nor PLS pre-intervention, 10 reported the presence of a phantom leg of which 6 were randomly allocated to the mirror condition and 4 to the control condition. No subjects in either the mirror condition or the control condition reported the appearance of PLP post-intervention.

Table 4
Mean (±SD) phantom limb pain (PLP) measures pre- and post-intervention

	Variable	Pre-intervention		Post-intervention	
		Mirror ($n = 7$)	Control ($n = 8$)	Mirror ($n = 7$)	Control ($n = 8$)
MPQ	NWC	9.57 (±4.43)	7.38 (±3.78)	5.43 (±6.83)	3.38 (±3.42)
	Total PRI	19.14 (±11.5)	20.13 (±13.3)	12.86 (±18.0)	6.00 (±7.2)
	Sensory PRI	14.57 (±8.9)	11.38 (±7.5)	9.29 (±12.6)	3.88 (±4.7)
	Other PRI	4.57 (±3.2)	7.62 (±9.1)	4.86 (±9.1)	2.13 (±2.9)
Visual analogue scale	Intensity score	57 (±24.2)	33 (±21.0)	40 (±41.0)	29 (±31.9)

However, 3 subjects in the mirror condition and 1 subject in the control condition reported the appearance of PLS post-intervention.

4.7. Phantom limb movement (PLM)

Of the 41 subjects randomly allocated to the mirror condition 33 reported the presence of a phantom leg at the time of the intervention and of the 39 allocated to the control condition 30 reported the presence of a phantom leg. An ANOVA was performed upon the mean number of movement responses elicited in the phantom leg during the intervention as a function of condition (mirror/control) and self reported prior ability to move their phantom leg (present, absent). A significant main effect for condition was found [$F(1,59) = 21.654$ $p < 0.001$] due to the mirror condition resulting in significantly more movement responses (6.39 ± 0.52) than the control condition (2.97 ± 0.52). A significant main effect for movement ability was found [$F(1,59) = 4.408$ $p < 0.05$] with subjects reporting no prior ability to move their phantom leg producing significantly fewer movements (3.91 ± 0.58) than subjects reporting a prior ability to move their phantom leg (5.45 ± 0.44).

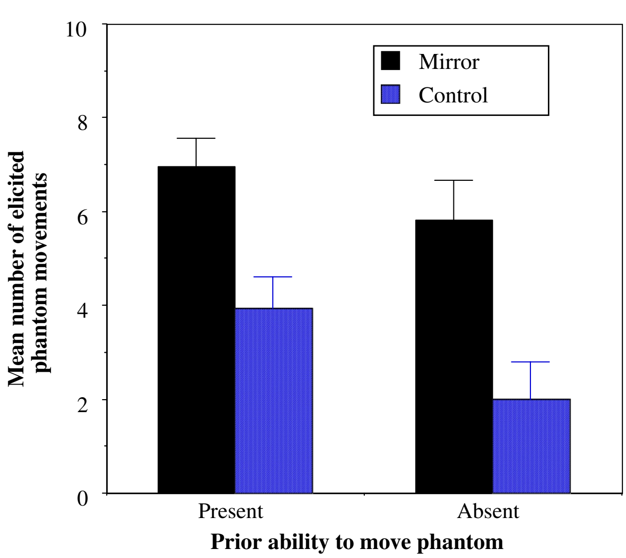

Fig. 2. Mean (±SE) number of phantom movement responses in the mirror and control conditions as a function of prior ability to move the phantom.

One sample t-tests revealed that the number of movement responses for the no prior ability subjects significantly differed from zero in both conditions ($p < 0.05$). Thus not only did the mirror condition increase significantly the ability to move a phantom limb over the control condition but the control condition also resulted in the ability to intentionally move a phantom leg when no such ability was previously present (see Fig. 2).

5. Discussion

This study, utilising a randomised controlled design, has established that one session of viewing a ‘virtual’ leg whilst attempting to move the phantom leg at the same time as moving the intact leg (the mirror condition), does not modify phantom limb sensations and phantom limb pain, any more than simply attempting to move the phantom at the same time as moving the intact leg (the control condition). Both conditions resulted in significant attenuation of sensations and pain. However, the mirror condition was found to elicit significantly more PLM than the control condition and to introduce PLA, whilst the control condition although found to increase significantly PLM in those subjects who reported being unable to move their phantom, did not to introduce PLA.

Thus the complexity and the unpredictability of the phantom limb experience and the importance of differentiating between PLA, PLP, PLS and PLM is confirmed by this study (Hunter et al., 2003; Jensen et al., 1984; Whyte, 1999). At the time of the intervention, PLA was not present in all subjects despite experiencing a phantom limb being one of the inclusion criteria. Of the subjects experiencing PLA few were experiencing PLP despite 68 out of the 80 reporting having suffered from PLP following amputation. However, this pattern is not surprising as the presence of PLA, PLP and PLS is known to fluctuate as a function of physiological and psychological factors (Flor, 2002b; Jensen et al., 1984; Ramachandran and Hirstein, 1998; Whyte et al., 1996).

Both the mirror and the control conditions were effective in reducing the intensity of phantom limb sensations (PLS) and modifying the nature of the sensations, but the mirror condition conferred no additional benefit over the control condition. The experience of PLS is extremely variable, but can be highly unpleasant with some amputees having described PLS as far more distressing than PLP (Whyte, 1999). For example, when an intense itch is experienced, it cannot be relieved, as a 'phantom' itch cannot be scratched. Thus an intervention which reduces these sensations may be of considerable clinical value. The findings of this study suggest that repeated attempts to move the phantom leg and the intact limb may form the basis for such an intervention.

A number of studies have explored the effects of viewing a virtual arm on PLP (e.g. Ramachandran and Hirstein, 1998; Ramachandran and Rogers-Ramachandran, 1996). However, these were not randomised controlled trials and they utilised subjects drawn from the relatively small population of upper limb amputees whose PLP results from 'clenching spasms' in their phantom arms. Because the subjects in this study were lower limb amputees, none of whom reported 'clenching spasms', it remains to be empirically tested whether lower limb amputees exhibiting a similar cause of their phantom limb pain would benefit more from the provision of the visual feedback of a moving virtual leg than from the repeated attempted movement of the phantom leg. This study would suggest that viewing a virtual limb may be beneficial.

The findings of this study that both the mirror condition and the control condition reduced PLP is in keeping with the literature that reports phantom limb movement therapy has been beneficial for a proportion of amputees (Sherman, 1980) as may prosthesis induced use of the stump and phantom (Lotze et al., 1999; Weiss et al., 1999). However, as the movement of the limb contralateral to a noxiously stimulated limb has been found to reduce experimental pain (Brodie and Kane, 2005), repeated movement of the limb contralateral to the phantom limb may also reduce PLP due to attenuation of cortical activity in the somatosensory cortex and the anterior cingulate cortex (Nakata et al., 2004; Vrána et al., 2005). Movement of the intact limb without any involvement of the phantom may in itself result in a reduction in PLP. Thus, the relative contribution of moving the phantom limb and of moving the intact limb in the attenuation of PLP requires further investigation.

Directing visual attention towards a moving virtual limb or a moving intact limb confounds the effects of limb movement with that of visual distraction. Visually attending to external stimuli is known to attenuate pain significantly due to cross modality sensory modulation (Villemure and Bushnell, 2002). Therefore further studies, that eliminate the influence of visual attention, by the use of imagined phantom limb movements, are required.

An additional finding of this study which is of clinical relevance, is that a single session produced significant reductions in PLS and PLP. Previous studies involving a range of interventions based on a variety of sensory feedback mechanisms have all utilised a larger number of intervention sessions. For example, the virtual limb studies all involved repeated administration over periods of weeks (Ramachandran and Hirstein, 1998), the treatment programme of tactile sensory stimulation lasted for 2 weeks (Huse et al., 2001) as did sensory discrimination training (Flor et al., 2001) and a training program of virtual limb movement matching lasted for 8 weeks (Girauz and Sirigu, 2003). The results of this study imply that significant improvements can be made in a single intervention session. However, how long these improvements may last and whether multiple sessions are more beneficial, requires further investigation.

This study examined the effects of both mirror and control conditions on the amputees' ability to move their phantom leg. Evidence for the 'learned non-use' of a phantom limb was found in this study with a number of subjects reporting that they had stopped trying to move their phantom leg and that they were unable to move it (Taub et al., 1998). Repeated attempts to move the phantom leg in the control condition resulted in a small but significant increase in reported movement amongst those amputees who reported no voluntary control of their phantom at the start of the study. This finding is in keeping with previous research that has demonstrated that phantom limb exercise can modify the experience of phantom limbs (Sherman, 1980) as can the use of a functional prosthesis (Lotze et al., 1999; Weiss et al., 1999). However, the mirror condition was found to be twice as effective as the control condition at eliciting PLM.

The mirror condition increased significantly the ability of all amputees to move their phantom leg, over and above that of the control condition. This vindicates the conclusions of previous studies that did not include a control condition (e.g. Girauz and Sirigu, 2003; Hunter et al., 2003; Ramachandran and Hirstein, 1996; Ramachandran and Rogers-Ramachandran, 1996) that the visual feedback of a moving virtual limb does modify the experience of a phantom limb. Although it need not abolish PLP in all amputees, it has the potential for reversing both the acute or chronic cortical re-organisation thought to subserve PLP (Flor, 2002b; Wall et al., 2002). The mirror box in addition to reinstating and/or improving PLA also promotes the use of the phantom, a factor known to prevent telescoping and other indices of cortical re-organisation (Whyte, 1999).

In the mirror condition, a number of the amputees reported surprise when they viewed the virtual leg and joked about not having seen their limb recently. This may be because the visual and non-visual cues necessary to ascribe ownership of the virtual image of a limb were present (Bos and Jeannerod, 2002; Ehrsson et al., 2005). In this study both spatial and movement cues were present; amputees aligned their phantom limb spatially to the mirror image and their intact and virtual limbs moved appropriately in response to the motor commands issued. However, the significant effect upon the position and movement of the phantom leg experienced by amputees in the mirror condition may not depend upon their beliefs about the ownership of the virtual leg. It may reflect the operation of the 'mirror neuron' system which directly maps visually observed limb movements onto those cortical areas responsible for that movement (Buccino et al., 2004). The fact that not all amputees were subject to the effect may be due to a complex interaction between visual areas and the reorganised motor and somatosensory areas that result from an acquired limb loss (Wall et al., 2002).

The finding that the visual feedback of a 'virtual' arm can both introduce and enhance the experience of phantom arms (Hunter et al., 2003) was extended by this study to phantom legs. Unlike Hunter et al. (2003) this study did not measure the spontaneous conscious awareness of a static virtual leg. Nevertheless, 33% of the amputees allocated to the mirror condition who reported no PLA pre-intervention, reported PLA post-intervention; whereas 0% of the amputees in the control group who reported no PLA pre-intervention, reported PLA post-intervention. However, in this study PLA was also abolished or reduced for 17% of subjects in the control condition and for 14% in the mirror condition. This variability may result from considerably less motor and sensorimotor cortex being devoted to the lower limbs compared with the upper limbs and fewer neural pathways linking these areas of cortex with visual centres (Goodale et al., 1994; Patla, 1997).

6. Conclusion

Viewing a virtual limb whilst moving both a phantom and an intact limb, does not reduce PLP or PLS any more than moving both limbs. However, viewing a virtual limb does significantly increase the ability of amputees to be aware of and to move a phantom limb. This may have important implications for the treatment of PLP as a prolonged virtual limb treatment may well reverse the chronic cortical re-organisation thought to be responsible for PLP. Furthermore it may help prevent acute cortical reorganisation following acquired limb loss by preserving and maintaining the ability to move a fully intact phantom limb.

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References

Bos E, Jeannerod M. Sense of body and sense of action both contribute to self recognition. Cognition 2002;85:177–87.

Brodie EE, Whyte A, Waller B. Increased motor control of a phantom leg in humans results from the visual feedback of a virtual leg. Neurosci Lett 2003;341(2):167–9.

Brodie EE, Kane F. Modulating experimental pain by attending to real and virtual limbs. In: 11th World Congress on Pain. Sydney: IASP Press; 2005. p. 128–9.

Buccino G, Binkofski F, Riggio L. The mirror neuron system and action recognition. Brain Language 2004;89:270–376.

Campos de Paz Braga LW, Downs HJ. A preliminary functional brain study on amputees. Appl Neuropsychol 2000;7:121–5.

Ehde DM, Jensen MP, Engel J, Turner JA, Hoffman AJ, Cardenas DD. Chronic pain secondary to disability: a review. Clin J Pain 2003;19:3–17.

Ehrsson HH, Holmes NP, Passingham RE. Touching a rubber hand: feeling of body ownership is associated with activity in multisensory brain areas. J Neurosci 2005;25(45):10564–73.

Flor H. The modification of cortical reorganisation and chronic pain by sensory feedback. Appl Psychophysiol Biofeedback 2002a;27(3): 215–27.

Flor H. Phantom-pain characteristics, causes and treatment. Lancet Neurol 2002b;1(3):182–9.

Flor H, Schaefer M, Grusser S. Effect of sensory discrimination training on cortical reorganisation and phantom limb pain. The Lancet 2001;357:1763–4.

Fraser CM, Halligan PW, Robertson IH, Kirker SGB. Characterising phantom limb phenomena in upper limb amputees. Prosthet Orthotics Int 2001;25(3):235–42.

Girauz P, Sirigu A. Illusory movements of the paralyzed limb restore motor cortex activity. Neuroimage 2003;20:107–11.

Goodale MA, Meenan JP, Buthoff HH, Nicolle DA, Murphy KH, Racicot CI. Separate neural pathways for the visual analysis of object shape in perception and prehension. Curr Biol 1994;4:604–10.

Hunter JP, Katz J, Davis KD. The effect of tactile and visual sensory inputs on phantom limb awareness. Brain 2003;126:579–89.

Huse E, Preissl H, Larbig W, Birbaumer N. Phantom limb pain. Lancet 2001;358:1015.

Jensen TS, Krebs B, Nielsen J, Rasmussen P. Non-painful phantom limb phenomena in amputees: incidence, clinical characteristics and temporal course. Acta Neurol Scand 1984;70:407–14.

Jensen TS, Krebs B, Nielsen J, Rasmussen P. Immediate and long-term phantom limb pain in amputees: incidence, clinical characteristics and relationship to pre-amputation limb pain. Pain 1985;21(3):267–78.

Karl A, Diers M, Flor H. Neuroelectric source imaging of steady-state movement-related cortical potentials in human upper extremity amputees with and without phantom limb pain. Pain 2004;110:90–102.

Lotze M, Grodd W, Birbaumer N, Erb M, Huse E, Flor H. Does use of a myoelectric prosthesis prevent cortical reorganization and phantom limb pain? Nature Neurosc 1999;2(6):501–2.

Melzack R. The McGill pain questionnaire: major properties and scoring method. Pain 1975;1:277–99.

Melzack R. Phantom limbs and the concept of a neuromatrix. Trends Neurosci 1990;13(3):88–92.

Nakata H, Inui K, Wasaka T, et al. Movements modulate cortical activities evoked by noxious stimulation. Pain 2004;107:91–8.

Nikolajsen L, Jensen TS. Phantom limb pain. Brit J Anaesth 2001;87:107–16.

Patla AE. Understanding the role of vision in he control of human locomotion. Gait Posture 1997;5:54–69.
Ramachandran VS, Hirstein W. The perception of phantom limbs. Brain 1998;121:1603–30.
Ramachandran VS, Rogers-Ramachandran D. Synaesthesia inphantom limbs induced with mirrors. Proc R Soc London 1996;263:377–86.
Roux FE, Ibarrola D, Lazorthes Y, Berry I. Virtual movements activate primary sensory areas in amputees: report of three cases. Neurosurgery 2002;49:736–41.
Sherman RA. Published treatments of phantom limb pain. Am J Phys Med 1980;59:232–44.
Sherman RA. Phantom limb pain Mechanism based management. Pain Manage 1994;11(1):85–106.
Sherman RA. Phantom pain. New York: Plenum Press; 1997.
Taub E, Crago JE, Uswatte G. Constraint-induced movement therapy; A new approach to treatment in physical rehabilitation. Rehabilit Psychol 1998;43:152–70.
Villemure C, Bushnell MC. Cognitive modulation of pain: how do attention and emotion influence pain processing? Pain 2002;95:195–9.
Vrána J, Poláček H, Stančák A. Somatosensory-evoked potentials are influenced differently by isometric muscle contraction of stimulated and non-stimulated hand in humans. Neurosci Lett 2005;386:170–5.
Wall JT, Xu J, Wang X. Human brain plasticity: an emerging view of the multiple substrates and mechanisms that cause cortical changes and related sensory dysfunctions after injuries of sensory inputs from the body. Brain Res Rev 2002;39:181–215.
Weiss T, Miltner WHR, Adlet T, Bruckner L, Taub E. Decrease in phantom limb pain associated with prosthesis-induced increased use of an amputation stump in humans. Neurosci Lett 1999;272:131–4.
Whyte (Hill) A. Phantom limb pain: a review of the literature on attributes and potential mechanisms. J Pain Sympt Manage 1999;17:125–43.
Whyte (Hill) A, Niven CA, Knussen C. Pain memories in phantom limbs: a case study. Pain 1996;66(2–3):381–4.