Training With Virtual Visual Feedback to Alleviate Phantom Limb Pain

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Background. Performing phantom movements with visual virtual feedback, or mirror therapy, is a promising treatment avenue to alleviate phantom limb pain. However the effectiveness of this approach appears to vary from one patient to another. *Objective.* To assess the individual response to training with visual virtual feedback and to explore factors influencing the response to that approach. *Methods.* Eight male participants with phantom limb pain (PLP) resulting from either a traumatic upper limb amputation or a brachial plexus avulsion participated in this single case multiple baseline study. Training was performed 2 times per week for 8 weeks where a virtual image of a missing limb performing different movements was presented and the participant was asked to follow the movements with his phantom limb. *Results.* Patients reported an average 38% decrease in background pain on a visual analog scale (VAS), with 5 patients out of 8 reporting a reduction greater than 30%. This decrease in pain was maintained at 4 weeks postintervention in 4 of the 5 participants. No significant relationship was found between the long-term pain relief and the duration of the deafferentation or with the immediate pain relief during exposure to the feedback. *Conclusions.* These results support the use of training with virtual feedback to alleviate phantom limb pain. Our observations suggest that between-participant differences in the effectiveness of the treatment might be related more to a difference in the susceptibility to the virtual visual feedback, than to factors related to the lesion, such as the duration of the deafferentation.

Keywords: Amputation; Brachial plexus avulsion; Phantom limb pain; Mirror therapy; Virtual reality

Phantom limb pain (PLP), which is present in about 50% to 80% of amputees[1,2] and in most patients with brachial plexus avulsion,[3] is recognized as very difficult to treat and is often resistant to classical pharmacological and surgical treatment approaches including local anesthesia, sympathectomy, dorsal-root entry-zone (DREZ) lesions, cordotomy and rhizotomy, neurostimulation methods, or pharmacological interventions such as anticonvulsants, barbiturates, antidepressants, neuroleptics, and muscle relaxants (for a review see article by Flor[4]). A limitation of these approaches is that they do not take into account the mechanisms underlying the production of PLP. Following amputation or deafferentation, extensive reorganization in the sensorimotor cortex occurs.[5-16] During the last decade, several studies have shown a relationship between the extent of these cortical sensorimotor reorganizations and the occurrence of PLP.[8,11,13,16-17] This has led to the idea that maladaptive plasticity might underlie phantom pain. In line with this idea, new rehabilitative approaches have been proposed to try to reverse this maladaptive cortical reorganization.

One of these approaches is the use of behaviorally relevant sensory stimulation applied to the stump. It has been shown that a 2-week discrimination training can lead to significant improvements in PLP, accompanied by a reversal of cortical sensory reorganization.[18] A related approach has been used by Huse et al[19] who applied continuous asynchronous stimulations to the stump and lip to provoke a segregation between the cortical representations of each region. After a 2-week treatment they reported a reduction in the PLP together with an improvement in sensory perception at the stimulated sites and an expansion of the lip cortical representation.

As an alternative to the sensory approach, training with visual virtual feedback of the phantom limb has been proposed, with the aim of improving the mobility of the phantom limb, and thus reversing the maladaptative plasticity within sensorimotor cortex and reducing pain. This approach emerged from the observation of Ramachandran and Rogers-Ramachandran[20] that viewing a virtual limb moving, achieved by looking at the reflection of the intact arm in a mirror box (mirror therapy), can induce sensations of movement in the phantom limb and can sometimes alleviate pain. In their study, 6 patients out of 10 felt their phantom limb moving with the virtual feedback, and they reported a temporary or permanent (1 patient) reduction of their phantom pain. Two randomized controlled studies have shown that a similar approach used with lower limb amputees leads to significantly greater improvement in the ability to move the phantom leg[21] and to a reduction in PLP[22] as compared with repeated attempts to move the phantom limb without visual feedback or the mental visualization of movements of the limb. Giraux and Sirigu[23] used a similar approach in 3 participants with a brachial plexus

avulsion and found that a 6-week training period resulted in a decrease of PLP in 2 patients out of 3. Interestingly, in these 2 patients the amount of activity in the primary motor cortex during attempts to move the phantom hand also increased after the treatment, but this did not occur in the patient who experienced persistence of pain. On the basis of this finding Giraux and Sirigu proposed that afferent information arriving via the visual system re-establishes coherence in the limb representation within M1 and that this contributes to the restoration of voluntary access to the motor representation of the missing hand. Recent studies have also explored the use of virtual reality approaches to generate artificial visual feedback.[24,25] Results of case studies with these approaches suggest that artificial representation of a limb can elicit kinesthetic sensations in the phantom limb and might also alleviate phantom pain in some patients.

Training with visual virtual feedback, or mirror therapy, thus appears to be a promising treatment avenue to alleviate PLP, alone or in combination with motor imagery.[26] However, one aspect that emerges from both the Ramachandran and Rogers-Ramachandran[20] and Giraux and Sirigu[23] studies is that the approach appears to be effective in some patients but not in others. The difference between patients who respond to the treatment and those who do not is unclear, but this question is of great clinical importance. Giraux and Sirigu[23] proposed that the duration of the deafferentation might affect treatment effectiveness, but this remains very speculative as only 1 of their patients (4 years postamputation compared to 2-3 years for the others) did not respond to the treatment, while pain relief has been described by Ramachandran and Rogers-Ramachandran[20] in a patient 9 years after plexus avulsion.

The aim of the present study was to further examine how training with visual virtual feedback can alleviate PLP. Specifically, we used case studies to look at whether there were differences between patients who benefit from the approach and those who do not. Therefore our primary objective was not to establish the effectiveness of the approach, an aspect that has been addressed by the previous randomized controlled trials, but to provide more information on the differences in individual response to treatment that might: (1) guide clinicians in the use of mirror therapy with their patients presenting very different clinical profiles, and (2) guide further studies aimed at understanding the mechanisms underlying treatment effect.

Methods

Participants

A convenience sample was recruited through surgeons and rehabilitation physicians working in pain clinics. Of the 11 patients that met inclusion criteria, 3 declined to participate, 1 because of the geographical distance and 2 because of the constraints of their working schedule. Finally, 8 male patients decided to participate in the study. Their PLP resulted from either a complete brachial plexus avulsion (C5-T1) resulting in

a deafferentation and paralysis of the hand or a traumatic above-elbow amputation that occurred 1 to 16 years before (see Table 1 for individual patient characteristics). All participants were right-handed prior to the lesion. Patients were not admitted to the study if their medication had changed in the previous month or if they had a surgical procedure in the previous 3 months. All patients were instructed to maintain their current treatments without alteration throughout the course of the treatment protocol. All patients gave their written informed consent prior to admission to the study, and the project was approved by the local ethics committee (Centre Léon Bérard, Lyon, France).

Treatment Approach

The treatment approach consisted of presenting a virtual image of the missing limb performing different movements, while asking the participant to follow these movements as much as he could with his phantom limb. The experimental setup used for the training with visual virtual feedback was the same as the one described in Giraux and Sirigu.[23] The virtual images of the missing limb moving were obtained by filming the intact limb performing different actions. These video images were then digitally inverted and projected on a computer screen. The image on the computer screen was then reflected in a mirror placed above the position of the missing or deafferented/amputated (phantom) limb. The motor tasks used were the following: flexion/extension of the elbow, pro-supination of the forearm, flexion/extension of the wrist, opening/closing the hand, adduction/adduction of the fingers, thumb-to-fingers opposition, flexion/extension of the thumb, grasping an object (such as a glass), precision grip with small objects, and dialing a phone number. Since most patients had very little voluntary control over their phantom movements without visual feedback, the actual movements chosen were different for each patient and were chosen if he could perform the task with visual feedback. The difficulty level (ie, type of movement and movement speed) was set to be just slightly superior to the actual capacity of the phantom to promote motor improvement, and was adjusted from session to session when necessary. It is important to note that exposure to a visuomotor illusion of a movement with a difficulty level far exceeding the motor ability of the phantom limb often results in an increased feeling of cramping and pain. Also, the natural position of the phantom limb was always used as a starting point for the movements. For example, in a patient with a phantom limb usually perceived as being pronated, it was generally easier to open the phantom hand if the virtual image of the limb was also in pronation rather than in supination during hand opening. Therefore a detailed interview about phantom sensations (including phantom limb usual posture) and motor capacities was performed before the beginning of the intervention.

In each session, 10 movements were each presented 10 times for a total of 100 movements. Each movement was

Table 1
Clinical Characteristics of Participants, Percentage of Relief, and Response to Virtual Feedback[a]

Participant	Age	Duration	Side	Lesion	Previous/Current Treatment	Relief POST 1w, %	Relief POST 4w, %	Response to Visual Feedback
A	28	1	R	BPA	Medication, TENS, acupuncture, hypnosis, cannabis	–13.8%	–7.7%	Unable to actively follow the movement but kinesthetic illusion when passively looking at the movement
B	19	3	L	BPA	Medication	6.6%	-	Most movements are performed quite easily with the feedback No tactile sensation
C	33	16	R	BPA	Medication, DREZ, spinal cord stimulation, TENS, cannabis	21.2%	25.6%	Most movements are performed quite easily with the feedback No tactile sensation
D	50	13	L	BPA	Medication, DREZ, cortical stimulation	31.7%	2.5%	Movements become gradually easier with the feedback Feelings of friction between forearm and the table
E	39	11	L	BPA	Medication, DREZ, TENS, hypnosis, cannabis	42.1%	44.5%	Able to perform finger movements with the feedback, more proximal movements remain difficult Occasional tactile sensations during finger opposition Huge sensation of effort sometimes accompanied by a feeling that the hand is sweating
F	34	5	L	BPA	Medication, cortical stimulation, hypnosis	55.2%	52.0%	Most movements are much easier with the feedback, but still effortful, with sensations of muscle fatigue Tactile sensations when the hand contacts an object
G	54	4	L	Amputee	Medication, neuroma removal, TENS, acupuncture	65.2%	61.4%	Movements are easier, especially at the elbow, but still require intense effort Frequent sensations that the hand is sweating and of muscle soreness Tactile sensations when the hand contacts an object
H	40	1	R	Amputee	Medication, TENS	93.5%	88.9%	Movements are easier with the feedback but feel like they are performed against resistance Tactile sensations during finger opposition and contact with objects

Abbreviations: POST 1w, 1-week follow-up; POST 4w, 4-week follow-up; R, right; L, left; BPA, brachial plexus avulsion; TENS, transcutaneous electrical nerve stimulation; DREZ, dorsal root entry zone lesioning.

[a]A total of 5 patients out of 8 exhibited a reduction in pain of 30% or more from baseline to the first week of follow-up period (POST 1w) and this reduction was maintained in 4 of the 5 patients at the end of the 4-week follow-up (POST 4w). The 2 patients with limb amputation were those who benefited most from the intervention. During the training with visual virtual feedback, patients who benefited from the approach often reported cutaneous sensations in addition to proprioceptive sensations, while this was not the case in the other patients. In addition, they systematically reported sensations of effort (such as feeling of acting against resistance, muscle fatigue or soreness, sweating feelings in the phantom hand) while the other patients reported performing most movements quite easily (with the exception of patient A who was easily feeling the different movements when looking at it but was unable to perform the movements actively).

presented 10 times (continuously in a cyclic manner) followed by a rest period and then presentation of the next movement. During the rest period the patient was asked to report on his ability to follow the movement and sensations felt. The experimenter used only open-ended questions to avoid cueing the patient to the kinds of sensations that he might encounter. Each session lasted between 30 and 60 minutes, depending on the speed of the phantom movements. All patients underwent 2 treatment sessions per week for 8 weeks (16 treatment sessions; 1600 phantom limb movements with virtual visual feedback).

Pain Measurement

Short-term relief. At each training session, the patient was asked to rate his immediate pain level on a 100-mm visual analog scale (VAS) just before and just after training. Short-term pain relief was expressed as a percentage and was computed as: ([pretraining VAS – posttraining VAS] / pretraining VAS) × 100%.

Long-term relief. Participants completed a daily pain diary in which they made separate ratings (on a VAS) of the

intensity of the background pain (ie, pain that you feel constantly in your phantom limb, or most of the day) and of pain paroxysms during the day (ie, when your pain clearly increases above the background level), the number and the duration of pain paroxysms, the medication taken, and any special events in their day that they perceived might have affected their pain level (these often included the weather, any unusual activity, or a positive or negative emotional event).

These measurements were obtained during a baseline period (varying from 1-5 weeks prior to the intervention), the 8 weeks of intervention, and during a 4-week follow-up period (the follow-up was completed by 7 out of 8 patients, but 1 patient failed to complete the follow-up). Since there was much more between-participant variability in the report of pain paroxysms than of background pain, background pain was chosen for the measurement of long-term relief (note that in those participants who consistently reported the number of daily pain paroxysms the 2 measurements were generally closely related). The long-term relief was expressed as a percentage and was computed as: ([preintervention pain – postintervention pain] / preintervention pain) × 100%. The preintervention pain was the average VAS for the last week of the baseline period (ie, the last week before the beginning of the intervention) while the postintervention pain was the average VAS for the first week of the follow-up period (ie, the first week after the end of the intervention, except for the drop-out participant in which the last week of the intervention was used). Thus, the weeks during which the patients received direct intervention were not considered in the calculation of long-term pain relief. Patients exhibiting a long-term relief of 30% or more were classified as responders. This cut-off point was chosen since it was considered as a clinically significant difference and was superior to the maximal placebo effect (<25%) observed in a nonpharmacologic randomized double blind clinical trial conducted on PLP.[27] The same approach was used to measure pain relief at the end of the follow-up period compared to baseline.

Statistical Analysis

Group differences on pain between the baseline (average VAS during the last week of the baseline), the end of the treatment (average VAS during the first week of the follow-up), and the end of the follow-up (average VAS during the last week of the follow-up) were assessed with paired t tests. Pearson correlations were used to test the association between long-term relief and short-term relief, and between long-term relief and the duration of the lesion.

Results

Table 1 shows the clinical characteristics of each patient, the percentage of pain relief (on background pain), and the feelings experienced by the patients in response to the virtual feedback. Patients included in the study all experienced background pain (average score of 4.9 on a VAS [range = 2.2 to 6.7] with pain paroxysms of 7.9 on average [range 6.6 to 9.2]). All participants reported that phantom movements were easier to perform with the visual feedback. The most striking case was participant D who felt his phantom limb completely frozen for 13 years and experienced a strong kinesthetic illusion at the first exposure to the virtual feedback: "I know that it's a trick but it feels so real that I have to restrain myself from looking under the mirror just to make sure whether my hand is actually moving . . ." (this participant had a brachial avulsion, not an amputation, so he still had his hand). A total of 5 patients out of 8 reported a pain reduction of 30% or more relative to the baseline period. The average pain relief was of 38% at the end of the treatment (n = 8) and at the end of the 4-week follow-up period (n = 7). Paired t tests showed a significant group difference between pretreatment and posttreatment pain both at 1 week ($P = .02$) and at 4 weeks ($P = .03$). No difference was found between week 1 and week 4 of the follow-up period ($P = .44$).

Figure 1 shows the detailed time course of the changes in PLP intensity at each week of the protocol for each patient. None of the patients changed their treatment regime during the baseline or the intervention periods, with the exception of patient H who completely discontinued using transcutaneous electrical nerve stimulation (TENS) after the first week of the intervention (he was previously using TENS occasionally during the night when he was unable to sleep because of the pain, but he reported that this was no longer necessary after he commenced the intervention). Nobody changed their medication during the treatment phase, but patient D gradually decreased his medication (morphine) during the follow-up period (an 80% decrease over the 4-week follow-up). This could account for the increase in pain seen in this patient's ratings during the follow-up period. As this patient experienced disturbing side effects from his medication he reported that it was his priority to quit morphine when he felt a decrease in his PLP. Patient F experienced an increase in his PLP in the second week of the follow-up period. This coincided with a change in the parameters of his cortical stimulator (which have been kept constant during the baseline and intervention period), but the PLP returned to the postintervention level within 2 weeks of this change.

Since it has been proposed that the time since deafferentation might affect response to treatment, we examined the relationship between long-term relief and time since injury but we found no significant relationship ($P = .48$). In addition, there was no significant relationship between short-term and long-term pain relief ($P = .50$). In fact, 3 of the patients (E, F, and G) who responded to the treatment reported an increase in pain during the visual virtual feedback training sessions (on average increase in pain of 10% to 51% from the beginning to the end of a session). The other 5 participants reported an average decrease in pain from the beginning to the end of a session (ranging from 6% to 50%). The pain increase reported by participants E, F, and G was transitory and usually faded within 5

Figure 1
Mean (and Standard Deviation) Change in Pain Intensity at Each Week of the Treatment Protocol and for Each Patient Relative to the Preintervention Pain
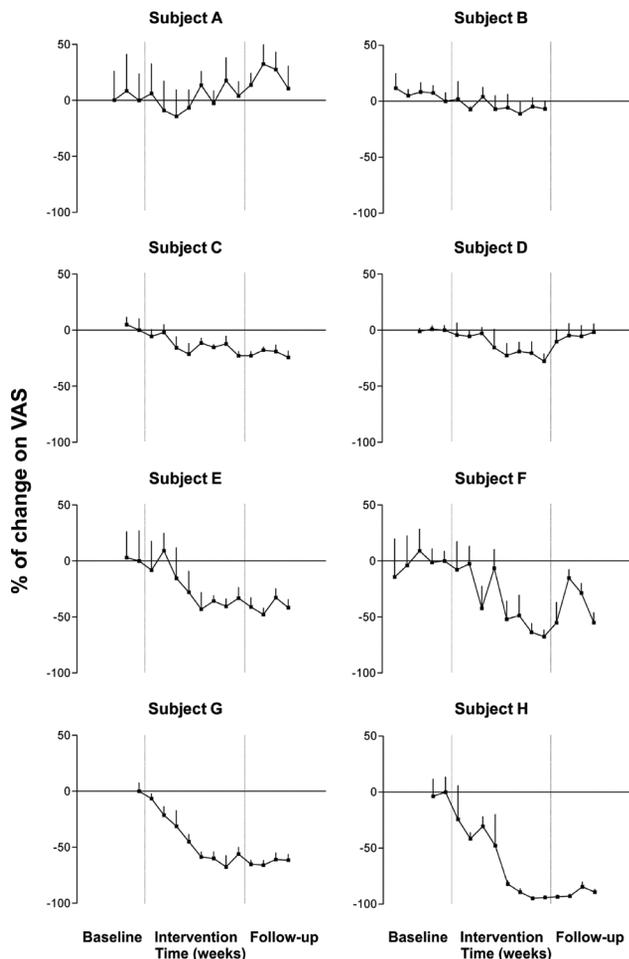
Note: The pain was assessed daily in the evening on a 100-mm visual analog scale (VAS). All pain measurements were normalized against the average pain in the last week of the baseline and were then displayed as percentage of change on the VAS. Zero value then indicates absence of change while a -100 value indicates complete pain relief. Dashed lines indicate the beginning and the termination of the intervention period. Duration of the baseline period varied from 1 to 5 weeks. All patients received 8 weeks of training with visual virtual feedback (2 sessions of approximately 1 hour per week). A 4-week follow-up was performed in 7 patients out of 8 (1 drop-out).

minutes after the end of the training. The participants reported that the increase in pain was because of the huge sensation of effort required to perform the phantom movements (movements were still very effortful although the visual feedback made the movements easier to perform as compared to without visual feedback). As reported in Table 1, this sensation of effort was verbally expressed in different ways. "I have the impression that something is preventing my [phantom] fingers from moving, like if there is a rubber band pulling on the fingers" (participant G, with similar reports from participants

F, H). "During the exercises I feel my [phantom] palm becoming wet, as if it is sweating" (patient E, with a similar report of patient G). "My pain assessment is higher at the end of the treatment session but it is not the usual phantom pain, I feel like if the muscles in my [phantom] forearm were tired and sore, a bit like after practicing an unusual sport" (participant F, with a similar report from participant G). Thus, the pain produced during the intervention was qualitatively different from the PLP usually experienced by the participant. All the participants described that their PLP included the sensation of pins and needles. Electrical sensations (all participants except B and G), burning sensations (all except C and E), and cramping and/or pressing sensations (all except B and D) were also felt by most patients. Others sensations reported included stabbing (participants A, B, and D), cutting (participant G), and a painful sensation that the hand was frozen (participant F, alternating with burning sensations). As PLP characteristics were fairly comparable across patients, no clear association was observed with the response to treatment.

In addition to the sensations of movement and effort during exposure to virtual feedback, several participants described other somatosensory sensations. "I am feeling my [phantom] forearm rubbing against the table while I move" (participant D). "When I dial a number, I feel pressure at the tip of my [phantom] index and small electrical sensations that spread in my whole hand" (participant F, with similar reports of participants E, G, and H during phone dialing, grasping tasks, and/or finger opposition). Several participants also reported the following, less specific, sensations in their phantom that were all associated with a feeling of relaxation: decrease of the pressure perceived on the hand (participants G and H); sensation of coolness (participant E) or of warmth (participants D and F) on the hand; sensation of a soft cloth caressing the limb (participant H); and small nonpainful pins and needles/electrical sensations with increased awareness of the hand (participants A, C, D, E, and G).

Discussion

Our results support the findings of previous studies showing that training with visual virtual feedback may alleviate PLP.[20-25] After 16 training sessions, patients reported an average 38% decrease in background pain, with 5 patients out of 8 reporting a reduction greater than 30%. Interestingly, this decrease in pain was maintained at 4 weeks postintervention in 4 of these 5 participants (except participant D, but he decreased his morphine dose by 80% during that period). This is, with the exception of a single case report,[20] the first evidence that phantom pain relief obtained with training with visual virtual feedback can be maintained across time. No significant relationship was found between the long-term pain relief and the duration of the deafferentation or with the pain relief during exposure to the visual feedback. Nevertheless, participants were all at least 1 year postlesion and therefore it is possible that the effectiveness would be different in the acute or

subacute stages. Moreover, all the patients included in the study experienced constant pain. While this is common in patients with brachial plexus avulsion,[3] results of a previous study on upper limb traumatic amputees reported that approximately 40% of amputees with PLP suffered from constant pain versus 60% from intermittent pain.[28] The severity of the initial pain in the participants included in this study potentially limits the generalization of the results to patients with a low level of pain or a more intermittent type of pain.

We acknowledge that placebo effects may be strong in people with chronic pain and could account for some of the observed effects of the visuomotor treatment. However, many factors argue against a purely placebo explanation. First, the patients that participated in the study already tried a large number of treatments for PLP without a satisfactory relief in pain, suggesting that they were not particularly susceptible to placebo effects. Second, the experimenter was very careful to use only open-ended questions to avoid cueing the patients on what kind of sensations they should expect to feel. Strikingly, there were many similarities in the descriptions made by different patients of the sensations induced by exposure to the visual feedback, suggesting that these sensations are truly related to physiological effects. Finally, if pain relief was because of a purely placebo effect we would have expected to see a positive correlation between short-term and long-term pain relief, since an increased susceptibility to placebo effects should have equally affected the 2 measures. However, this was not the case. For example, participant A reported a huge analgesic effect during the treatment sessions and as a consequence was very optimistic regarding the long-term outcome, but he did not receive any long-term pain relief benefits from this treatment approach. In contrast, participant E reported an increase in pain during the treatment sessions since the movements were perceived as very effortful and difficult even with the visual feedback, although the feedback enabled him to make many more phantom movements. Despite this, he experienced a 41% decrease in his pain level from the baseline to the follow-up period. This result indicates that therapists should not base their decision on the potential of training with visual virtual feedback for a given patient based on its immediate response to visual feedback exposure. It can also explain that mirror therapy was found to have no effect in a study looking at a single treatment session[29] while it was found effective when applied regularly over a 4- to 6-week period.[22-23]

Participants who responded to the treatment generally reported a sense of effort during the production of phantom movements with the visual feedback. This observation raises interesting questions regarding the mechanisms underlying this therapeutic approach. One possible explanation for the difference in the efficacy of the treatment for each patient is that movement observation might elicit an activation of the motor cortex in some patients while failing to do so in others, and that the sense of effort described by some patients might be a perceptual marker of this motor cortex activation. Giraux and Sirigu[23] reported more activity in M1 during attempts to move the phantom hand after treatment, but only in the 2 patients who received some pain relief and not in the patient who did not experience reduced pain levels. They then proposed that the arrival of visual afferent information might be sufficient to restore voluntary access to the motor representation of the hand, potentially via the mirror neuron system.[30] There is evidence that a representation of the phantom hand is preserved in the motor cortex after amputation, which might explain why the motor sensations can be retrieved almost instantaneously when facilitatory inputs are provided.[31-33]

Several studies in humans have shown that observation of a movement can affect corticospinal excitability and motor performance.[34-41] In particular, a transcranial magnetic stimulation (TMS) study of healthy participants showed that viewing a mirror reflection of a movement of the ipsilateral hand produced a M1 facilitation that was greater than that produced by ipsilateral hand movement alone.[42] All of these studies, however, focused on showing group differences between different conditions, without providing a lot of detail about across-participant variability in the motor facilitation induced by movement observation. But the existence of such variability in individual susceptibility to visual feedback is supported by 2 behavioral studies in which sensorimotor incongruence was induced in healthy participants using bilateral coordination tasks and a mirror box.[43-44] Results of these studies, as well as those of previous studies using virtual reality to elicit movement sensations in the phantom limb,[24-25] are consistent with our observation that the strength of the illusion was variable from one patient to another. Although all patients clearly indicated that it was easier to perform the movement with the visual feedback (ie, all participants had a kinesthetic illusion), some participants also reported other somatosensory illusions, especially sensations of touching surfaces, objects, or of contact between the fingers. Interestingly, these sensations were mainly seen in participants who responded to the treatment, which supports the idea that participants with increased susceptibility to these kinds of procedures might benefit more from the training with visual virtual feedback. It is therefore possible to hypothesize that difference between responders and nonresponders lays, at least in part, in their susceptibility to be influenced by visual feedback, rather than being only determined by clinical characteristics such as the duration of the deafferentation. This hypothesis might be addressed in future studies by testing whether the modulation of sensorimotor excitability in response to observation of hand action before the intervention can predict treatment outcome.

Factors other than individual susceptibility to visual feedback might interfere with or optimize the effectiveness of such training with visual virtual feedback. It was noticed during the experiments that a good alignment between the proximal limb and the virtual image was necessary to induce the illusion, an observation that is consistent with the previous observation that rubber hand illusion is dependent on the congruence between the posture of the viewed rubber hand and that of the unseen participant's hand.[45] However, the exact congruence between the virtual image of the limb and the real appearance

of the former/paralyzed limb appeared less important (some participants had a distinctive characteristic on their intact limb such as a scar or even a phalanx amputation and this did not interfere with the illusion). This observation, also supported by results of previous studies using virtual reality to generate an artificial image of the missing limb,[24-25] is clinically important since it suggests that this approach might be as effective in bilateral amputees (using videos of the moving limbs of another individual or virtual images) or in other populations with neuropathic pain and bilateral motor impairment such as individuals with spinal cord injury.

In conclusion, the results of our study support the use of training with visual virtual feedback, or mirror therapy, to alleviate PLP. Our observations suggest that between-participant differences in the effectiveness of the treatment might be related more to a difference in the susceptibility to the visual feedback, rather than to factors related to the lesion, such as the duration of PLP. To gain more insight into individual differences affecting response to treatment it would be interesting to use this treatment approach in amputees with PLP while documenting the motor facilitation induced by movement observation (using TMS, for example) and comparing this to the treatment effectiveness. Psychometric measurements of body plasticity[44] and assessments of the vividness of the sensations evoked during exposure to the visual feedback would also provide interesting information regarding the response to the treatment. Both physiological and psychological measures are likely to be helpful in identifying those patients most likely to benefit from training with visual virtual feedback for the treatment of PLP. These same measures might also be useful for choosing patients who would most likely benefit from training with visual virtual feedback, or mirror therapy, for the treatment of other motor-related problems, like stroke-induced hemiparesis.[46-50]

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