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Psychophysical investigations into Ramachandran's mirror visual feedback for phantom limb pain: video-based variants for unilateral and bilateral amputees, and temporal dynamics of paresthesias

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Abstract

It is widely reported by Ramachandran, Altschuler and others that simple mirror visual feedback can cause phantom sensations in normal observers, and reduce phantom limb pain in amputees. First, a recent experiment designed to replicate classic findings (59 amputees) is reviewed, along with a mirror-based variant developed for bilateral amputees. Then, two variants are described which were intended to intensify effects without eliciting fatigue, and to sometimes reduce phantom pain when the simple mirror is ineffective. The first (simple video feedback) uses a laptop video movie of another (intact) person's limb movement (with metronome-paced periodic movement). The second ("phantom pulse") uses a real-time video image of the observer that flickers between a normal image and a mirror-reversed image at rates varying form 0.5 to 2 cycles/sec (with an 0.2-sec delay). For both conditions, preliminary data from amputees support the finding that movement of one limb causes phantom sensations in the opposite limb, followed by seemingly permanent pain reduction in some amputees. Moreover when normal observers view their movements in these ways, they often report paresthesias, with optimal stimulation occurring in most individuals at 1-2 Hz. Thus psychophysical results may indicate that neural mechanisms underlying mirror visual feedback are temporarily tuned.

1. Introduction

It is widely reported by Ramachandran, Altschuler and others that simple mirror reflections can cause phantom sensations in normal observers and reduce phantom limb pain in amputees.[11] Additionally, this **mirror visual feedback (MVF)** may enhance recovery from unilateral hemiparesis following stroke and a wide range of neurological disorders [1].

However, MVF sometimes seems ineffective for some single-limb amputees, and the basic method does not treat pain following bilateral amputations or paralyses. I review a collection of preliminary studies intended to expand the range of MVF, and to elucidate visual processes underlying successful MVF.

Phantom Limb Pain

When one loses a limb to disease, surgery or trauma, the conscious perception of the missing body part persists in up to 85% of amputees[2]-[6]. The individual may feel some combination of numbness, tingling, heaviness, temperature change, pressure, constriction, reduced or changing limb length. Some may experience a sense of voluntary movement in the phantom limb. For some, the overall experience is intriguing and pleasurable, but for up to 80% of amputees, phantom limb sensations are painful and debilitating. The pain is characterized as 'cramping,' 'shooting,' 'squeezing', 'stabbing,' 'throbbing,' or 'burning'. In addition, painful phantom limbs are often perceived as 'frozen stiff,' or paralyzed in an unnatural position or shape. (**Figure 1**) The individual differences in phantom limb pain are striking [1],[7]-[10].

Figure 1. Phantom-limb experience and pain. The amputated limb is felt as both present and painful. Current research supports neurological explanations, with the psychological, experiential projection (Ψ) of the limb linked to Penfield-like cortical body representations [1]. Image modified from DesCartes, 1664.

Until recently, amputees were rarely asked or told about phantom limb pain by medical personnel. The amputee who admitted to phantom limb pain risked having his or her integrity and mental health questioned [11]-[12]. Now it is known that although salient thoughts, feelings and events can trigger these painful phantom sensations [12], research supports neurological rather psychosomatic explanations [8], [10], [13]-[19]. Current evidence links phantom limb pain to cortical re-mapping or re-organization [1], [17], [20], [21].

Although at least 50 interventions exist to treat phantom limb pain, it is rarely treated successfully. For many sufferers, the ensuing chronic pain results in a decreased quality of life, and an increased dependence upon costly medicines and medical

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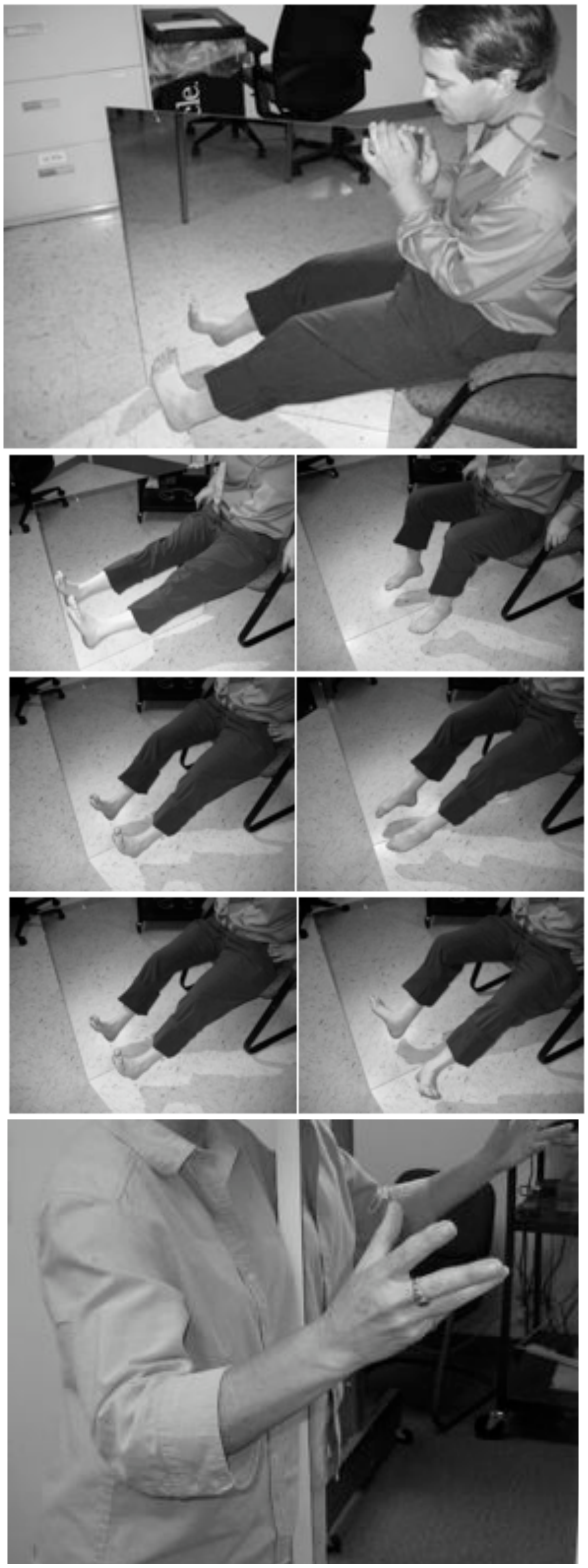

Figure 2. Mirror visual feedback with a single-panel mirror. Shown for use with unilateral lower and upper limb amputations. (Note the use of BoPET [Mylar] mirrors; front-reflecting, frameless, unbreakable, lightweight)

resources [12]. Sufferers attempt to utilize a wide variety of coping strategies [22]-[23].

Mirror-Based Therapies

Advances in understanding the role of visual feedback in neural plasticity provide promise for development of better treatments for phantom limb pain.

Beginning with Ramachandran's classic studies, a simple mirror reflection has been shown to reduce or eliminate phantom pain, and the perception of phantom limb paralysis, in some amputees [24]-[30]. A mirror is placed perpendicular to the amputee's chest (e.g. in a 'mirror box'), with the reflective pane facing in the direction of the amputee's intact arm or leg, as shown in **Figure 2**. When the mirror is viewed off-center, the reflection of one's intact limb creates the illusion of having two intact limbs. Upon observing the movement of the transposed limb, some individuals experience sensations within the phantom, including the perception of movement. A subset of these individuals experience dramatic and permanent cessation of phantom pain. A recent randomized control study of combat veterans, for instance, found significantly more pain reduction with mirror treatment than in a control condition (treatment-as-usual) [30]. Neuroimaging research indicates that the mirror causes the reversal of cortical re-mapping and re-organization, and this reversal is correlated with reductions in phantom pain [17], [21]. The implication of this line of research is that neural connections in the human brain are much more malleable than previously assumed, in a way that offers hope to phantom pain sufferers.

Despite the published treatment successes with mirrors, some amputees experience no such relief using a basic mirror. At this time, the rates of response are not known, and the individual differences influencing mirror therapy are not well understood. In my experience, I find that some individuals fail to experience any effects. Others feel tingling, stimulation, and a sense of movement without pain reduction. Yet others lose motivation to complete mirror therapies due to fatigue. Some of these 'near misses' appear to be tantalizingly close to 'moving' the phantom out of its painful state, thereby reducing the pain. If treatment failures are not caused by inherent limitations of MVF, what modifications or alternatives are possible?

Alternative MVF Therapies

The promising, but sometimes limited, results of mirror therapy caused some to hypothesize about techniques that may improve the effectiveness and ease of mirror treatments.

One general strategy for improving upon the basic mirror technique has been to borrow principles used to design computer-based virtual reality environments, which may help to optimize the patient's sense of 'immersion' and 'presence'—the sense of being highly engaged in a virtual environment[31]. Within this context, a promising yet relatively expensive modification involves using computer-based augmented or virtual reality systems[32-41]. The virtual reality methods have reduced pain successfully in a number of cases, and in some instances did so when the standard single-pane mirror was previously found to be ineffective.

But such methods are sometimes viewed as "cumbersome, sluggish and expensive" relative to a simple mirror[1], and may not be inherently more effective than simple mirror therapies.

The aim in the series of studies reviewed here was to explore possible ways to modify, optimize and individualize MVF therapies, perhaps leading to additional treatment successes. Improved mirror treatments may better control the optical, neural,

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Figure 3. Mirror visual feedback for bilateral amputees with a single-panel mirror[47]. Shown for use with unilateral upper and lower limb amputations. Models are wearing contrasting colors to demonstrate method, but in practice, colors of clothing were matched, approximately.

and sensory components that underlie successful mirror therapy. Moreover, such modifications may further elucidate the neuroscientific understanding of these components. The present report describes various modifications of Ramachandran's basic mirror, and preliminary results of their application.

2. Replication of classic findings

First, a randomized, controlled experiment designed to replicate classic findings is reviewed [42]-[43]. In an 8-week, randomized clinical trial we (McQuaid *et al.)* compared the combination of MVF and cognitive behavioral therapy (CBT) with an active control condition (Supportive Psychotherapy Care, SC), for the management of phantom limb pain. (n=59 unilateral amputees). Mirrors like those in **Figure 2** were used. We hypothesized that MVF+CBT would lead to significant reductions in pain. Although significant reductions in pain were evident in MVF+CBT group means, including follow-up, a near majority of individuals in the MVF+CBT condition did not show considerable pain reduction compared to SC. Our results may not reflect an inherent limitation of MVF, especially in older, weaker pain patients who may find MVF tiring. (See also [44]). Others, studying younger patients with daily supervision of MVF, report higher success rates [30].

3. Simple Mirror for Bilateral loss (lower limb)

In 2006, there were no known attempts to use MVF with simple mirrors to treat phantom limb pain in bilateral amputees. There are now studies by others showing at least preliminary efficacy for some treatment variants with lower limb amputees [45]-[46]. In my own preliminary work [47], Ramachandran's mirror technique was used on two individuals with amputations below both knees.

The mirror was positioned to reflect the left side of each amputee's body as he sat in a folding chair viewing the mirror, as shown in **Figure 3**. I (the experimenter) positioned my left leg underneath the chair, facing the mirror. As I moved my left ankle and toes slowly and predictably, the amputee watched the reflection and imagined that he was seeing and moving his missing right ankle and toes. While viewing the mirror for 10 minutes, both individuals reported a sense of (a) movement in the right phantom ankle and toes, (b) a growing or "telescoping" of the shrunken, retracted phantom to normal size, and (c) an at least temporary reduction of stress and pain in the phantom right ankle, foot and toes.

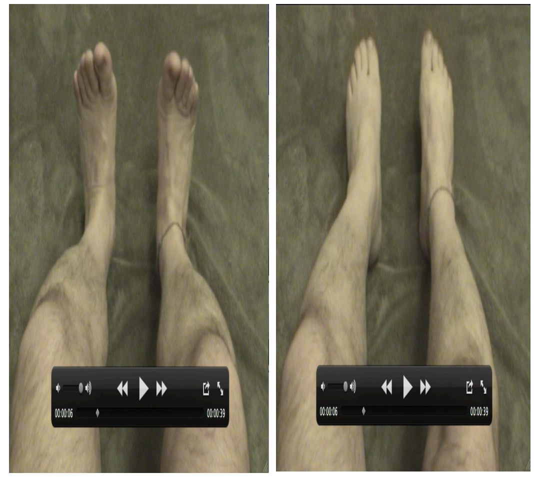

Figure 4 Mirror visual feedback for bilateral amputees with a laptop video (for unilateral and bilateral lower limb amputees.

4. Video-based interventions.

It was hypothesized that video-based interventions may achieve effects similar to mirror-based MVF without causing fatigue, and that these approaches could extend to bilateral amputees. Two visual conditions are described which seemed to intensify effects (paresthesias, sense of movement) in some people, and sometimes reduced phantom pain when the simple mirror was ineffective.

A. Simple video feedback with metronome-paced periodic limb movement (lower limb).

This method uses a laptop video movie of another (intact) person's limb movement, as shown in **Figure 4** [48], [49]. Preliminary data indicate that a simple video may achieve pain-reduction effects similar to the mirror in lower limb amputees, without causing fatigue, and can extend to bilaterals. First, a video was created of an intact individual's legs and feet, with the individual flexing his ankles, feet, and toes up and down. This flexing was periodic with each cycle occurring every 2 seconds. The flexing was filmed from a subjective point of view, looking down from eye level upon the legs and feet. Patients observed the repeating video loop on a 13-inch laptop computer for ten minutes. Each observer placed the computer on his or her lap and imagined that the flexing limbs were his or her own, and that he or she was causing the flexing. When individuals experienced the illusion of internal (egocentric) locus of control, they experienced strong phantom sensations (paresthesias) and a sense of movement in the missing or paralyzed legs.

Pain was measured using: Trinity Amputation and Prosthetic Experience Scale, Short Form McGill Pain Questionnaire [64], and the Descriptor Differential Scale.

The intervention preceded significant measurable, apparently long-term pain reduction in two bilateral amputees, as shown in **Figure 5**, and two unilateral amputees who had not benefitted from using the simple mirror. (Also, a stroke patient reported sensing movement in his paralyzed legs when exposing himself to the

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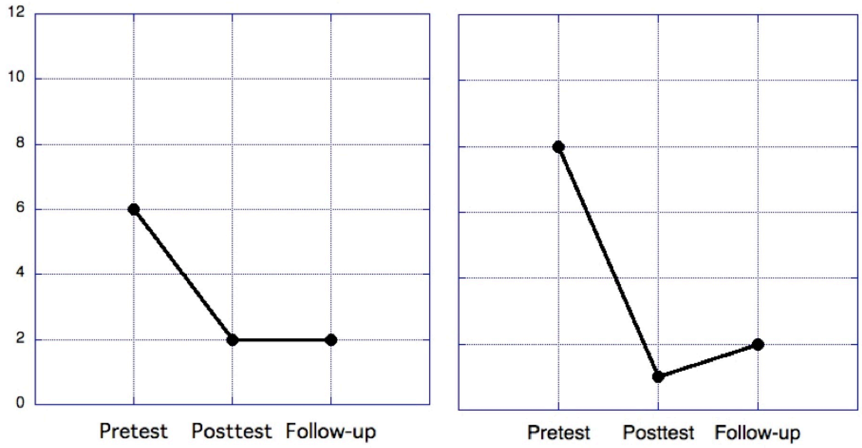

Figure 5. Pain ratings (Visual Analogue Scale) before, after and at follow-up for two bilateral amputees exposed to MVF using simple video feedback [47].

mirror.) While periodic limb movement (with 2-second cycles) resulted in improved pain outcomes, further studies need to examine the comparative efficacy of other temporal cycles, using larger samples of participants.

(Some non-amputee normals experience some of the following in their legs while observing the video: tingling, numbness, tickling, pressure, heat, cold, or involuntary movement.)

B. Rapid left-right mirror reversals, stroboscopic self-motion, and the "phantom pulse" (upper limb)

Stroboscopic self-motion and mirror reversals were found to amplify mirror effects in some upper-limb amputees and normal individuals [47], [49]-[53]. This "phantom pulse" was generated in two ways. The first, shown in **Figure 6**, involves using a real-time video image of the observer that flickers between a normal image and a mirror-reversed image at rates varying from 0.5 to 2 cycles/sec (with an 0.2-sec delay). The second involves using simple MVF with a strobe light, in a dark room. For both methods, movement of one limb causes powerful phantom sensations and a sense of movement in the opposite limb. The mirror-reversal intervention preceded significant measurable, apparently permanent pain reduction in four unilateral, upper-limb amputees. Pain data for two participants are shown in **Figure 7**.

5. Psychophysics and temporal dynamics of MVF in non-amputee normal, using rapid left-right mirror reversals.

Exploratorium artist Bob Miller was perhaps the first report "strange sensation" (paresthesias) in response to MVF, in a description of the exhibit he designed, "Mirrorly A Window" [54]. (See **Figure 8**, and many other of his mirror based exhibits, which elicit a variety of unusual body and out-of-body sensations: "Anti-

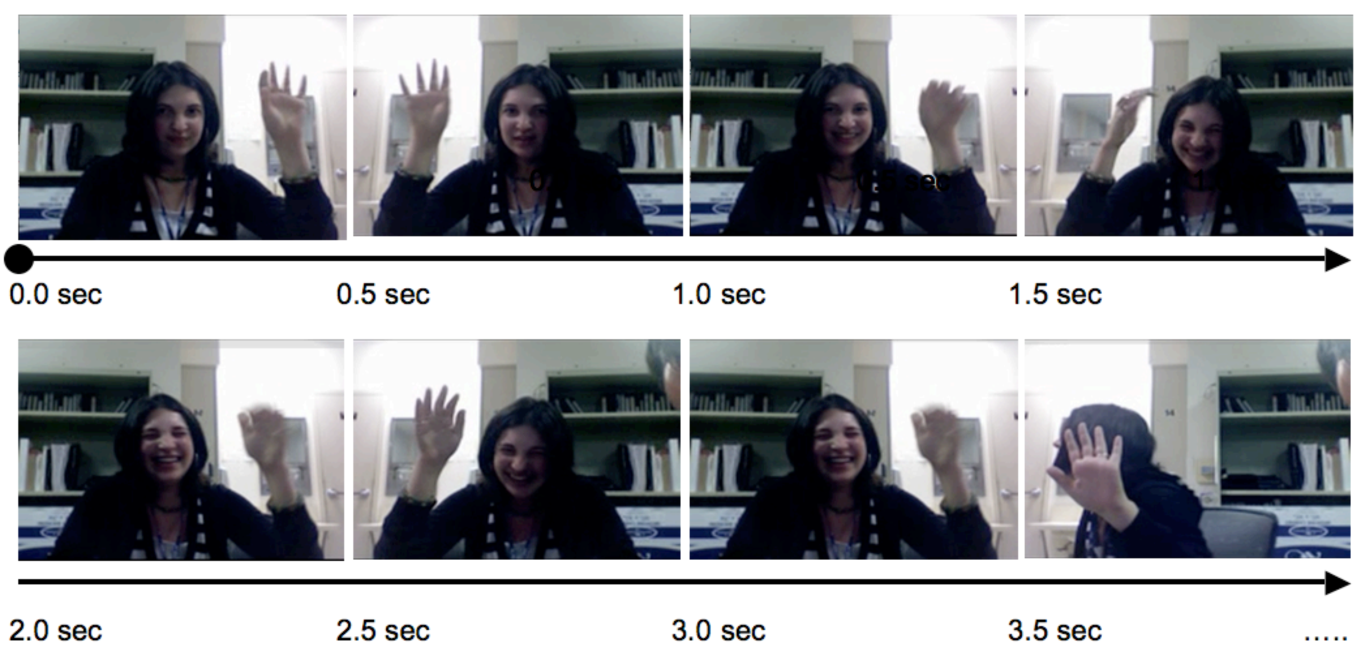

Figure 6. The "Phantom Pulse" method. Real-time stroboscopic self-motion and mirror reversals integrate MVF and temporal flicker [47], [49]-[53].

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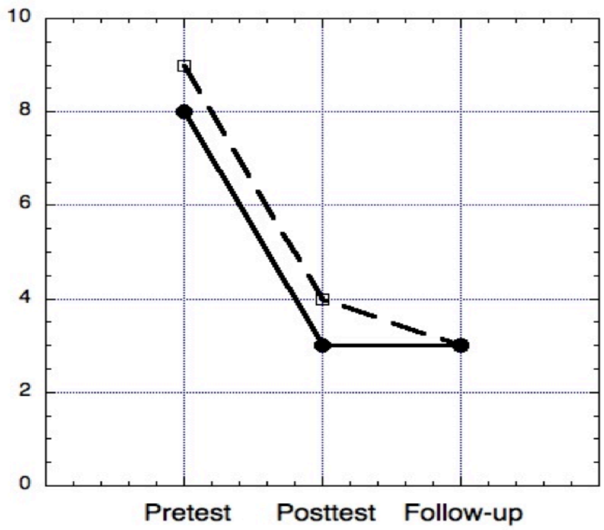

Figure 7. Pain ratings (VAS) before, after and at follow-up for two bilateral amputees exposed to MVF using the "phantom pulse" method [47], [49]-[53].

Gravity Mirror," "Everyone is You and Me," "Cheshire Cat," "Christmas Tree Balls," "Image Mosaic," "Tail Yourself," "Duck-Into-Kaleidoscope," and "Look Into Infinity").

My colleagues and I have observed that the various mirror interventions described here elicit paresthesias and phantom sensations in some healthy non-amputees (e.g., tingling, pressure, 'pins and needles' sensations, and a sense of movement). These sensations are consistent with results from other reports (primarily by McCabe, and Altschuler) of healthy non-amputees using a single pane mirror [54]-[58]. In the instances that I have observed, the right-left mirror reversals (stroboscopic self-motion) often elicit a more intense response than those experienced with the single mirror. Moreover, some individuals report aftereffects in which the paresthesias persist for several minutes after exposure. These lingering effects seem not to occur when using a single mirror pane.

Figure 8. Miller's Exploratorium museum exhibit, which elicited "strange sensation" in many normal observers [54].

Use of a temporally modulated stimulus may enable researchers to (1) conduct psychophysical investigations of mirror-phantom phenomena, (2) examine physiological correlates these effects using EEG and FMRI, and (3) create more effective MVF interventions.

In normal observers [49][53][59][60], we found that approximately 50% experience at least mild to moderate phantom-like phenomena using the method described in 4-B (n=300). The reversal or flicker rate that optimizes effects occurs at approximately 1 to 2 cycles/sec for most individuals, as shown in **Figure 9**. Normal individuals typically experience some combination of the following in their fingers and hands: tingling, numbness, tickling, pressure, heat, cold, or involuntary movement. In some, these sensations move gradually from the wrist to the shoulder. In perhaps 1 or 2% of individuals, the face tingles. In these most powerful instances, the individual is unable to close just one eye when instructed to "wink." Another 1-2% find the paresthesias in hand and arm too intense to participate for more than approximately one minute.

It seems likely that neurons or neural systems with similar transient temporal properties contribute to these profound effects. And the psychophysical results imply that some neural mechanisms underlying mirror therapy for phantom limb pain may be temporarily tuned.

These findings are in some ways consistent with the hypothesis that pain is, in some instances, attributable to discordance between motor intent and motor movement [57]-[58], [61] (but see [62]). In the case of non-amputees using the single-pane mirror, the 'discordance' or 'incongruence' occurs because one's hidden limb appears to move, despite any volitional instruction to move the limb. Within this framework, an amputee's relief from phantom limb pain occurs using mirrors when there is congruence between the motor intent to move one's phantom limb, and the perception of motor movement based on the mirror illusion.

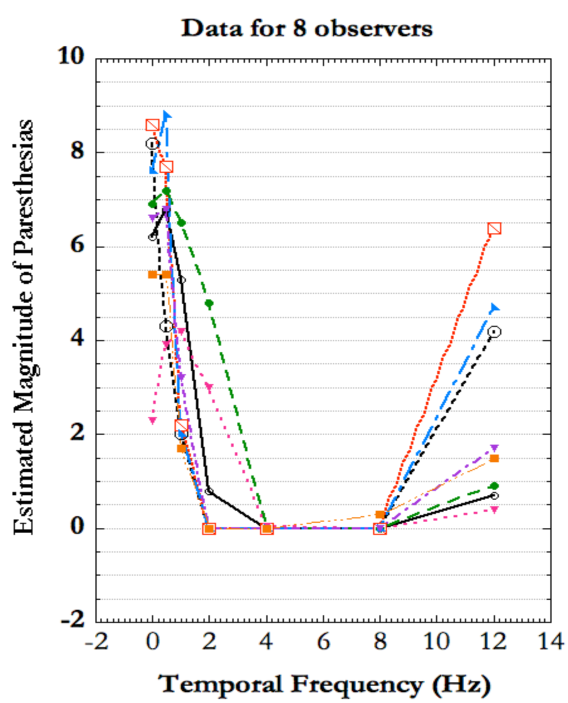

Figure 9. Magnitude estimation of paresthesias as a function of mirror-reversal temporal frequency, in non-amputee normals ("phantom pulse" method). Data for 8 observers.

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However, these findings with non-amputees are not entirely explainable based on discordance between motor intent and motor movement. This hypothesis seems unable to explain why the mirror-reversing method evokes stronger sensations than the single mirror.

6. Conclusions

The results provide preliminary support to suggest that video-based modifications to mirror visual feedback may help achieve relief for phantom limb pain in some patients, including those who do not experience benefits using the single panel mirror.

More research on amputees and non-amputees using randomized controls is needed to evaluate the comparative effects of these modifications. Data were obtained from a small number of individuals. A more definitive study will need to include a series of proper controls to fully rule out placebo effects, and to demonstrate that the these video variants are effective in instances in which the single pane mirror does not succeed in reducing pain.

Possible mechanisms

These preliminary results add weight to the suggestion that there may be therapeutic value in modifying Ramachandran's single mirror approach to treating phantom limb pain. As with virtual reality approaches, video approaches may strengthen the perception of the limb being intact, and amplify sensations of immersion and presence in some amputees. As such, both approaches may provide the clinician with new mirror-based methods to treat phantom pain. These video approaches, like the original single mirror approach, have the added advantages of being inexpensive and easily implemented relative to elaborate virtual reality approaches.

The putative neural mechanisms underlying phantom limb pain and mirror therapy are not fully understood, but have been discussed extensively elsewhere [1], [3]. MVF seems to produce its effects at least partly by influencing the long-term cortical reorganization of brain maps. But additional factors must be involved because immediate or rapid reduction of pain is difficult to explain based on relatively slow-changing processes [1].

At present, we do not fully understand why the mirror-reversal method's experiential and possibly therapeutic effects differ from those for the single reflected image, at least in our small samples. One possibility is that seeing an unusual image of self, from a reversed view, is especially powerful. Such images have been studied in great detail recently [56], [63]-[64], and seem to evoke two alarming perceptions simultaneously: one is a perception that the image is one's self, and the other is that the image is not quite one's self. If the brain processes information about self and others using separate neural processes (e.g. based on 'efferent copy' or 'mirror' neuron systems), then an unusual image like the 'out of body' image may activate two neural systems rather than just one.

A second explanation may have to do with the complex nature of viewing reflections of one's self and one's limbs in a mirror. A neurologically intact person who views reflected images in a single pane mirror has comparatively little difficulty making inferences about reflected vs. actual objects; this is in contrast to some stroke patients with unilateral neglect who suffer 'mirror agnosia' [66]. The difficulty in distinguishing left from right limbs in a mirror-reversing frame may force the perceptual system to simply make guesses, thus amplifying the sense that the phantom limb is present and moving.

Finally, seeing one's missing limb as intact is a novel experience for most amputees, and the sensitizing effects of novelty may be curative in their own right. For instance, in the case of virtual reality exposure therapies [67]-[68], patients are re-immersed into a virtual environment that mimics a previously traumatic situation (e.g. a combat scenario) which led to various posttraumatic syndromes. Such exposures often evoke heightened attentional, emotional and physiological states of arousal, and operate through classical conditioning, by either extinguishing or counter-conditioning away anxiety. Similar principles may help explain pain reduction from mirror therapy. The resulting arousal (limbic stimulation) from seeing the 'virtual limb' may itself be curative, or it may combine with the perception of one's limb as intact to cause therapeutic change. Based on such possibilities, we are currently investigating the possible value of a mirror-based exposure therapy for PTSD and prosthesis avoidance [69].

Possible Additional Therapeutic Uses

A variety of other impairments have been reported to respond to MVF [1], such as hemiparesis following stroke, complex regional pain syndrome /reflex sympathetic dystrophy (RSD), benign essential tremors, visual hemineglect following stroke, and weakness following hand surgery. The results are important for the MVF modifications described here because they further validate mirror treatment approaches, and because the neural mechanisms underlying hemiparesis, phantom limbs, and a host of other impairments may have underlying similarities. Future research into the perceived body (somatic fields) and its relationship to the physical body [70] will address whether the MVF methods described in the present paper improve the efficacy of treating these other impairments.

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