What is the Most Effective Non-invasive Non-pharmacological Treatment Mechanism for Reducing Phantom Limb Pain in Amputees?

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Introduction

In WRS 102, students develop writing skills in various disciplines. For instance, students may focus on scientific writing for their work in this course. **Sabrina Rivelazione** chose to research a scientific question, asking what treatment possibilities are possible for those suffering from phantom limb pain. This assignment required reviewing peer-reviewed research articles and formulating a persuasive argument.

Keywords: mirror therapy, phantom limb pain, reflexology, treatment, visual feedback therapy.

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Phantom limb pain (PLP) is characterized by pain felt in non-existent extremities.[4] Although present in those born without limbs, nearly 90% of amputees experience PLP.[1] Unfortunately, the causal mechanism of PLP is unknown, making it difficult to treat. Researchers are striving to find the most efficacious treatment, as 25% to 50% of patients report severe pain impairment reducing their quality of life.[5] Currently, there is a long list of treatments, all with various degrees of success. These include pharmacological treatments, non-invasive non-pharmacological strategies (such as visual feedback, brain stimulation, reflexology, and hypnosis), and invasive surgical strategies.[9] Recent studies have demonstrated that visual feedback therapies can revert cortical reorganization (a shifting of brain structure boundaries as a result of amputation); therefore, these treatments are promising for reducing PLP.[7,9,12] Considering the uncertainty of effective treatment mechanisms for PLP, the question arises, what is the most effective, non-pharmacological, and non-invasive treatment mechanism for reducing phantom limb pain in amputees?

Visual Feedback Therapies for Phantom Limb Pain

Recent studies provide significant evidence of visual feedback therapies reducing PLP, specifically virtual/augmented reality therapy (VR/AR) and mirror therapy (MT).[1,5,6,10,11] Modernized VR/AR therapies make use of computer-generated extremities, which provide functional, realistic, and intact visualizations of the affected limb.[5,10,11] Currently, MT is considered superior to VR/AR due to its visual realism and simplicity. MT involves using a mirror to observe the reflection of an intact limb as it moves, which activates the brain's primary motor cortex. The sensorimotor cortex is organized so sensory information is directed away from the wrong part of the brain (the part connected to the amputated extremity), thus reducing pain.[11] Visually observing the reflected limb creates a sense of ownership, tricking the brain into assuming the painful sensory signals sent to the phantom limb have been accounted for through motor movement. This promotes MT's efficacy over VR/AR, as the reflected limb replacing the phantom limb is highly realistic compared to computer-generated extremities. Furthermore, research has demonstrated the real-life timing of MT's visual feedback contributes to PLP relief, as reducing time delays increases a sense of extremity ownership.[11] Since the invention of MT by Ramachandran et al. in 1995, this classic treatment has proved effective in many amputees.[5,12] For instance, Chan et al. (2007) found 93% of their lower-extremity subjects responded to MT. When replicating the Chan et al. study, Finn et al. (2017) observed 89% of upper-extremity patients reporting declined PLP after a month; the daily time experiencing pain decreased from an average of 1022 minutes to 448 minutes, which illustrated the efficacy of MT.[6]

Despite MT's effectiveness, it requires an intact limb to operate and is therefore limited to unilateral amputees.[5,11] Bilateral amputees require VR/AR to induce artificial visual feedback.[1,10] The application of MT, VR, and AR therapies suggests kinaesthetic sensations of the phantom extremity reduce PLP.[10] VR provides an entire virtual environment, whereas AR adds virtual elements to an existing environment.[11] Both tactics provide technological graphics representative of missing extremities. Participants in a study by Ambron et al. (2018) reported immediate, sizeable declines in PLP after a few one-hour VR sessions.[1] This study, along with many others, provides evidence of substantially quick reductions of PLP using adaptable VR techniques specified to unique patient characteristics.[3,11] Researchers argue VR/AR therapies provide illusions of setting imaginary limbs to natural placements, away from biomechanically impossible (unnatural) positions, by deceiving the brain to believe the uncomfortable orientation is eliminated.[11] Additionally, transforming these therapies into gamification tactics motivates and engages patients to keep up their treatment, thus increasing their effectiveness. Overall, it seems VR/AR and MT therapies fill each other's gaps, making visual feedback therapies together to be quite promising for PLP reduction.

Visual Feedback Therapies Connected to Cortical Reorganization Theory

Visual feedback therapies are credited with reorganizing dysfunctional physical changes in the brain, and therefore appear to be highly valuable mechanisms for reducing PLP. One major theory connected to PLP is Cortical Reorganization Theory (CRT).[9,10] The basis of this theory relates PLP onset to neuroplastic changes.[9,11] Specifically, cortical reorganizations seem to occur in the somatosensory and motor cortices, with the degree of these dysfunctional arrangements relating to pain intensity.[5,7,9,10] Essentially, the area of the brain connected to the missing limb (as per the brain's cortical map, which represents corresponding neurons to anatomical actions) is taken over by a neighbouring area. This activates neurons that previously interpreted motor and sensory input from the now non-existent extremity and thus initiates pain.[5] Currently, visual feedback therapies are the main technique used to trigger sensations of phantom limb mobility and reverse these neuroplastic changes and reduce pain.[5,7,10,11] As visual feedback dominates control over intersensory conflicts in comparison to other senses, it appears these therapies reset brain circuits of the missing extremity, getting them back on track and decreasing PLP.[5,7,12]

Two recent studies have illustrated visual feedback therapies reducing cortical reorganization and PLP by manipulating brain structures back to their natural state.[7,12] In one study by Thøgersen et al. (2020), individualized AR training reduced both PLP and cortical reorganization.[12] Seven patients underwent eight 45-minute sessions of AR therapy, with personalized phantom visualizations created with 3D-modeling software to enhance sensations of phantom limb ownership. Prior to and after the AR therapy, fMRI neuroimaging scans were taken of a lip-pursing task to objectively measure cortical reorganizations. Results from the AR therapy found a significant 52% decrease of PLP, with post-treatment fMRI illustrating a significant cortical lip representation decrease and covariant PLP decline. Neuroimaging results indicated that lip representation reverted to its original place on the cortical map, thus supporting CRT.[12] Similarly, a second study by Foell et al. (2014) involved 11 subjects performing a similar lip-pursing task with fMRI scans done prior to and after four weeks of MT.[7] Results showed a similar conclusion to the Thøgersen et al. study, where MT seemed to reverse cortical reorganizations in the primary somatosensory cortex. There was a 27% pain reduction, as activity in the inferior parietal cortex (the brain region involved in pain perception) decreased.[7] Although these studies were limited by small samples, both experiments not only provide evidence for the effectiveness of visual feedback therapies but also demonstrate how PLP reduction is related to the CRT attribute. Therefore, results from both studies inevitably increase the credibility of visual feedback therapies as valuable treatment mechanisms.

Other Mechanisms for Phantom Limb Pain Reduction

Several researchers disagree with visual feedback as the most effective non-invasive, non-pharmacological treatment for PLP, believing other tactics are superior, such as non-invasive brain stimulation (NIBS) or reflexology.[5,8,9] For instance, Kikkert et al. (2019) demonstrated that NIBS, specifically transcranial direct current stimulation (tDCS), a treatment that delivers electric current to the brain, reduces PLP.[8] The researchers instructed 15 unilateral upper-extremity patients to perform phantom hand movements during a 20-minute session of tDCS applied over the primary somatosensory and motor cortex. Neuroimaging, used during and after stimulation, evaluated the neural mechanisms of PLP relief. Results illustrated decreased PLP as a result of stimulation, and neuroimages showed reduced primary somatosensory and motor cortex hand activity after stimulation, correlating with pain relief. However, NIBS techniques have previously been shown to only alleviate pain in the short-term (less than 90 minutes), with longer-term effects yet to be explicitly tested.[8]

Brown and Lido (2008) proposed that reflexology (a treatment that applies pressure to the feet and hands) could self-treat PLP.[2,9] They sent ten lower-extremity amputees into a five-phase, 30-week experiment. Patients recorded diaries regarding PLP duration and effects on sleep and life quality. The first two phases established individual pain patterns. The third phase consisted of weekly reflexology applied to the hands and remaining leg, followed by rest. The fourth phase implemented self-treatment teachings and more reflexology. The fifth (and final) phase involved asynchronous self-treatment.[2] Results showed relief from PLP symptoms, especially when reflexology was applied to the feet as compared to the hands. Unfortunately, most amputees find the feet difficult to reach, thus limiting self-treatment. As reflexology is a newer mechanism, there is little research available, revealing a credibility gap for this treatment.[2] Both reflexology and NIBS have the potential to be efficacious PLP treatments; however, the lack of explicitly tested research on longer-term relief using NIBS, and the immense difficulty of self-application in reflexology, lowers the convenience and attainability of these tactics.

Conclusion

Based on research, it seems the most effective non-invasive, non-pharmacological treatment for PLP is neither MT nor VR/AR therapy, but the combination of the two; VR/AR and MT fulfill each other's limitations.[1,3,5–7,9–12] MT adapts visual realism to phantom extremities, which is unattainable from VR/AR's computer-generated limbs.[11] However, VR/AR therapies are a more universal treatment, extending to bi- and poly amputees, and are not reliant on intact functional limbs.[3,5,11] It seems logical that combining these therapies would solve individual treatment constraints and increase amputees' quality of life, as there is evidence both treatments reduce PLP as theorized by CRT.[7,9,12] Although tactics such as NIBS and reflexology reduce PLP, the lack of evident long-term relief from NIBS and attainability issues of reflexology reduce their efficacy.[2,8] Therefore, using VR/AR and MT visual feedback therapies in synergy would create the most effective, achievable, and long-lasting phantom limb pain reduction in amputees.

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