Decreasing Phantom Limb Pain for Amputees with Phantom Limb Pain and Brachial Plexus Avulsions Through Various Therapy Interventions: A Systematic Review

Devin Stuckwisch, OTS, Haylee Barker, OTS, Kylee Martin, OTS, Martina Kramer, OTS, Niki Hoseinpour, OTS, Sydney Stevens, OTS
Occupational therapy doctoral students at Indiana University; iuot@iupui.edu

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This rapid systematic review of the literature discusses the evidence of studies related to effective occupational therapy interventions in reducing phantom limb pain (PLP) due to amputations and brachial plexus avulsions (BPA). This review provides a comprehensive overview and analysis of 30 studies that addressed many of the interventions commonly used in phantom limb pain rehabilitation. Phantom limb pain is a painful sensation perceived in the absence of a limb or in a deafferented limb. Suffering from acute or chronic pain can decrease engagement and performance in meaningful occupations. Overall, we found moderate evidence to support the effectiveness of various therapy interventions for decreasing PLP in individuals with amputations and BPAs.

Focused Clinical Question

The purpose of this rapid systematic review was to search the literature and critically appraise findings to address the following focused question: What is the evidence of rehabilitation interventions for reducing phantom limb pain (PLP) in amputees and brachial plexus avulsions (BPAs)?

Statement of Problem and Background

Approximately 75% of amputees develop pain within a few days after limb removal surgery and 70% of phantoms remain painful several years after amputation (Tilak et al., 2016). Many phantom limb pain (PLP) treatment options are invasive, expensive, and must be performed in a clinic or alongside a medical professional. As for BPA, it has been found that nearly all patients experience persistent, throbbing

pain after injury that is associated with decreased quality of life and participation in occupations (Ciaramitaro, et al., 2017). Like PLP, BPA treatment options need to be explored to determine an effective method to reduce pain.

Mirror therapy is one of the only treatments that is non-invasive, cost effective and can be self administered in the home; however, emerging treatments such as virtual reality, nerve stimulation, non-invasive brain stimulation, and other imagery methods are becoming viable options to treat pain experienced due to PLP and BPA. Currently, there is limited research on the effectiveness of these interventions in the reduction of pain to increase occupational engagement and participation. A rapid systematic review was conducted to research the effectiveness of various non-invasive, cost effective interventions in the management of PLP and pain after a BPA injury. The purpose of this rapid systematic review topic is to assist OT practitioners in using evidence based interventions in their practice to address treatment of PLP and BPA.

Method for Conducting the Evidence-Based Review

This rapid systematic review examined studies that assessed the effectiveness of occupational therapy interventions for improving phantom limb pain for amputees. Decreasing Phantom Limb Pain was chosen by a research group of occupational therapy students who felt that phantom limb pain is a critical factor that impacts overall quality of life in amputees, as well as occupational participation and performance.

During the process of selecting articles for this systematic review, reviewers initially chose articles based on the article being published within the last sixteen years between 2006 and 2021. Further, studies that took place in the United States and countries with healthcare systems that are predicted to transfer well to the United States such as Italy, Australia, Canada, UK, Sweden, Germany, Turkey, Cambodia, Netherlands, and Japan were included.

Other specific inclusion criteria were as followed:
- Participants were community-dwelling, all genders, present with phantom limb pain, and between the ages of 15-90 years.
- The interventions and outcomes described in the study were embedded in the domain of occupational therapy.
- The article was Level I, II, or III evidence.

The following articles were excluded: meta-analysis', systematic reviews, articles that provided Level IV and V evidence, articles not in English, amputees with bilateral amputations, studies not in the desired countries, and studies that do not meet outcome measure criteria.

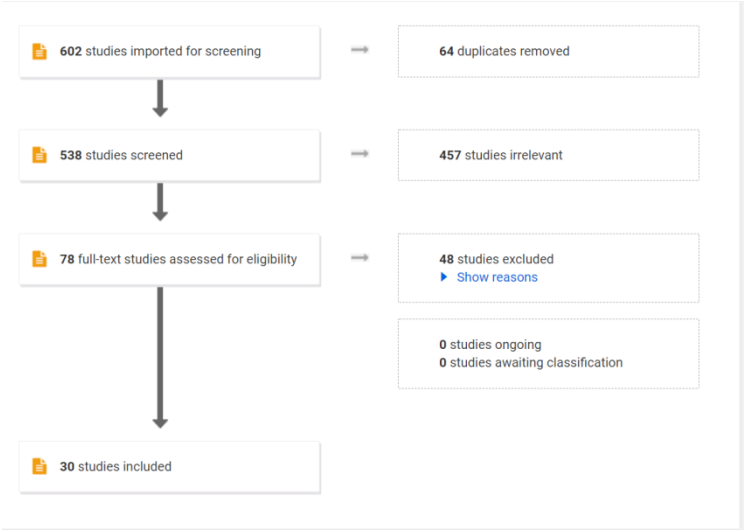
This review used the Level of Evidence criteria based on study design and group assignment:

Level I - Systematic reviews, meta-analysis, randomized controlled trials
Level II- Two groups, nonrandomized studies (e.g. case control)
Level III- One group, nonrandomized (e.g. cohort, before and after, pretest and posttest, longitudinal)
Level IV- Descriptive studies that include analysis of outcomes (single subject design, case series)
Level V- Case reports and expert opinion that include narrative literature reviews and consensus statements

The articles that were determined to be within the appropriate Level of evidence and which met the inclusion criteria were further categorized into six main treatment themes which improve phantom limb pain.

Theme 1: Virtual Reality
Theme 2: Traditional Mirror Therapy
Theme 3: Traditional Mirror Therapy Combined with Additional Intervention
Theme 4: Non-Invasive Brain Stimulation
Theme 5: Nerve Stimulation
Theme 6: Other Imagery and Reprocessing Methods

Figure 1
PRISMA Diagram



Note. PRISMA diagram generated from Covidence

Results

This review includes a total of 30 studies— 13 Level I, 2 Level II, and 15 Level III studies. From these studies, the findings have been clustered into 6 areas that represent treatments administered or potentially administered by occupational therapists treating phantom limb pain. The treatment categories were virtual reality, traditional mirror therapy, traditional mirror therapy combined with additional intervention, non-invasive brain stimulation, nerve stimulation, and other imagery and reprocessing methods. The results are as followed:

Virtual Reality

Virtual reality interventions have the potential to alleviate acute phantom pain, due to the nature of using 3D representations of the affected limb. Of the studies reviewed, one Level II study and seven Level III studies addressed the efficacy of virtual reality interventions on reducing phantom limb pain through movement representation.

A Level III cohort study (Rutledge, T., Velez, D., Deep, C., McQuaid, J.R., Wong, G., … Giap, H., 2019) showed that a single or multiple treatment session of a virtual reality bicycle ride, for both upper and lower amputation patients, provided significant reductions in acute unpleasant phantom sensations, along with high ratings for helpfulness, immersion, realism, and satisfaction of the game.

A Level II case control (Sano, Y., Wake, N., Ichinose, A., Osumi, M., Oya, R., … Kuniyoshi, Y., 2016) demonstrated a comparison of a virtual reality arm manipulation treatment with tactile feedback to no tactile feedback. A larger analgesic effect was produced for the tactile group, but the results were not statistically significant due to the effect only lasting a few minutes indicating no-long term intervention effect.

A Level III cohort study (Perry, B., Armiger, R., Wolde, M., McFarland, K., Alphonso, A., Monsoon, B., Pasquina, P., Tsao, J., 2018) found that according to the Visual Analog Scale and Short Form - McGill Pain Questionnaire phantom limb pain was decreased with significant improvements through virtual reality intervention techniques.

A Level III cohort study (Ichinose, A,. Sano, Y., Osumi, M., Sumitani, M., Kumagay, S., Kunivoshi, Y., 2017) phantom limb pain was significantly reduced through the combination of virtual visual feedback and somatosensory to the cheek. Participants participated in a virtual reality environment with cheek stimulation given if participants correctly used the “affected” virtual limb. R values were reported at 0.68 and the experimental group showed that pain reduction rates were significantly lower than the control groups.

A Level III cohort study (Osumi, M., Iomatata, K., Inoue, Y., Otake, Y., Morioka, S., Sumitani, M., 2018) found that through virtual reality environments, participants could control their virtual phantom limb through intact limb movements. The feeling of producing intentional movements of the virtual/ phantom limb significantly correlated with a decrease in phantom limb pain associated with kinesthesia related pain.

A Level III cohort study (Osumi, M., Ichinose, A., Sumitani, M., Wake, N., Sano, Y., … Morioka, S., 2017) found that a virtual reality rehabilitation treatment for the forearm and hand displaying a 3D computer graphic for the affected arm, controlled by the intact arm, alleviated acute phantom limb pain, while enhancing movement representation of the phantom limb, but no long-term follow up was studied.

A Level III Cohort Study (Ortiz-Catalan, M., Guomundsdottir, R.A., Kristofferson, M.B., Zepeda-Echavarria. A.,Caine-Winterberger, K., Kulback, K., Widehammer, C., Eriksson, K., Stockselius, A.,Ragno, C., Pihlar, Z., Burger, H., & Hermansson, L., 2016) assessed changes in intensity, duration, frequency, quality, and intrusion of PLP during a augmented and virtual reality decoding of phantom motor execution intervention. It was found that pain intensity, quality, duration, and intrusion had clinically significant improvements after the intervention and provided moderate strength as an effective intervention.

A Level III Cohort Study (Mercier, C., & Sirigu, A., 2009) provided evidence that after 16 training sessions, participants reported an average 38% decrease in background pain, with 5 participants out of 8 reporting a reduction greater than 30%. Interestingly, this decrease in pain was maintained at 4 weeks post intervention in 4 of these 5 participants (except for one participant who decreased his morphine dose by 80% during that period).

There is overall moderate evidence to support the use of virtual reality therapy interventions to reduce phantom limb pain in the amputation and BPA population.

Traditional Mirror Therapy

The traditional use of mirror therapy has demonstrated a strong ability to improve phantom limb pain amongst amputees. In this review, two level I articles, one level I article, and three level III articles discussed the efficacy to use traditional mirror therapy for reducing phantom limb pain.

One Level I randomized control trial (Finn, S. B., Perry, B.N., Clasing, J. E., Walters, L. S., Jarzombek, S. L., Curran, S., … & Tsao, J. W., 2017) provided evidence that mirror therapy compared to covered mirror therapy demonstrated a statistically significant decrease in phantom limb pain as well as a decrease in the total daily time participants experienced pain.

A Level II randomized single crossover study (Ramaduga, S., Nagabushanam, S., Katuwal, N., Chatterjee, K., 2017) provided evidence of significant reductions in phantom limb pain as a result from traditional mirror therapy

treatment. Significant reductions were recorded compared to the control group ($P < 0.0001$).

One Level III uncontrolled prospective treatment outcome cohort-based pilot study (Darnall, B., Li, H., 2012) provided evidence showing a significant reduction in mean phantom limb pain intensity after month 1 and month 2 of the intervention. The overall median reduction in phantom limb pain intensity after the second month of treatment was 15.4%. The participant's level of education was found to be a confounding factor that impacted results.

A Level III cohort study (Imaizumi, S., Asai, T., & Koyama, S., 2017) assessed agency and ownership over PLP before and after a short-term mirror therapy session. There was a clinically significant change seen in agency indicated increased quickness and accuracy and decreased difficulty when performing movements immediately after the session; however, no significant change was observed for ownership in bodily shape and incorporation of phantom limb. There was an ownership change that was significant for the presence of the phantom limb. Weak evidence was also found for pain intensity and unpleasantness.

A Level I randomized control trial (Brodie, E.E., Whyte, A.,& Niven, C.A., 2007) demonstrated the effects of mirror conditioning, in which the unaffected intact limb was placed in a mirror box and viewing this limb within the mirror image while aligning the amputated phantom limb with this image, in comparison to placing the amputated phantom limb and intact limb on either side of the mirror while covering it, in order to see the intact limb itself but not the mirror image of the intact limb. The results indicated statistical significance to reduce phantom limb pain in both interventions based on visual analogue scale (VAS) outcomes. However, neither of the interventions diminished PLP more than another.

A Level III cohort study (Yıldırım, M., & Kanan, N., 2016) showed that there was a statistically significant decrease in average PLP scores every week of the study period and for 1-month total score ($p<0.01$). It was also found that patients who did not use a prosthesis had greater effect from mirror therapy ($p<0.05$), and prosthesis usage explained 30.6% of the change in average PLP scores before and after mirror therapy (Adjusted $R2=0.306$, $p<0.05$)

Overall, the results display that the use of traditional mirror therapy to reduce phantom limb pain provides moderate to strong evidence for amputee individuals.

Traditional Mirror Therapy Combined with Additional Intervention

These studies all researched the effectiveness of traditional mirror therapy combined with an additional intervention. Studies have shown that traditional mirror therapy has a statistically significant impact on phantom limb pain. Therefore, studies were conducted to determine if combining other interventions with mirror therapy would have the same effect.

A Level III cohort-based study (De Nunzio, A. M., Schweisfurth, M. A, Ge, N., Falla, D., Hahne, J., Godecke, K., … & Farina,. D., 2018) showed a significant reduction in phantom limb pain intensity as well as decreased sensory characterization of phantom limb pain through the use of a differential electromyography band and mirror therapy.

A Level III cohort-based study (Foell, J., Bekrator-Bodmann, R., Diers, M., & Flor, H., 2013) showed mirror therapy combined with neural activation in both the somatosensory cortex and primary motor cortex monitored by fMRI had a medium-sized effect on pain reduction. Researchers discovered that a participant's ability to relate the mirrored movement to their phantom had a large impact on the reduction of pain. Researchers found no statistical correlation between the time since amputation and the benefit from treatment.

A Level III pilot study with a cohort cross sectional repeated-measure study (Houston, H., & Dickerson, A. E., 2016) showed both acute and subacute groups had decreased interference from phantom limb pain affecting self-care, walking ability, car transfers, and low chair transfers. The study showed positive improvements from pretreatment to post treatment as well as post treatment to maintenance period. The researchers also determined a statistically significant reduction in phantom limb pain interference with sleep for both groups. A statistically significant improvement in mood and quality of life during the treatment and maintenance periods for both groups
A Level I randomized controlled trial (Ol, H. S., Van Heng, Y., Danielsson, L., & Husum, H., 2018) provided evidence that in their first round of treatment, which included mirror therapy alone, tactile therapy alone and combined mirror and tactile therapy, led to a mean reduction in VAS ratings for phantom and stump pain greater than 50%. Moreover, in the second round of treatment which was comprised of those who did not experience pain relief in the first round of treatment, found pain relief in the combined mirror and tactile therapy intervention where the reduction in VAS ratings was greater than 90% for phantom and stump pain.

A Level I Randomized Control Trial (Rothgangel, A., Braun, S., Winkens, B., Beurskens, A., & Smeets, R., 2018) assessed changes in intensity, duration, and frequency of PLP after a mirror therapy with augmented reality teletreatment. In comparison to a traditional sensomotor exercise group, as well as a self-delivered mirror therapy group, it was found that intensity of PLP had clinically significant improvements in the mirror therapy with augmented reality teletreament group. However frequency and duration of PLP improved more in the mirror therapy with augmented reality teletreament group, but it was not significant.

A Level I Randomized Control Trial (Külünkoğlu, B.A., Erbahçeci, F., & Alkan, A, 2019) showed statistical

significance to reduce the intensity of phantom limb pain based on pain scores from the visual analog scale (VAS) through the practice of mirror therapy with conducted exercises and movements for the lower limb in comparison to standard phantom exercises.

There is overall moderate evidence to support the use of occupational therapy interventions to decrease phantom limb pain in individuals with amputations. The combination of mirror therapy and additional interventions including but not limited to augmented reality, tactile therapy intervention, and fMRI neural activation all demonstrated a significant decrease in phantom limb pain.

Non-Invasive Brain Stimulation

Of the 4 studies that reviewed for non-invasive brain stimulation, there were 3 Level I studies, and 1 Level III study. Non-invasive brain stimulation has shown to target the part of the brain dedicated to the missing or nonresponsive limb. The aim of these studies was to determine if non-invasive brain stimulation could be an effective treatment in decreasing PLP in participants with BPA or amputations.

A Level I randomized controlled trial (Segal, N., Pud, D., Amir, H., Ratmansky, M., Kuperman, P., Honingman, L., & Treister, R., 2021) provided evidence that transcranial direct current stimulation (tDCS), given everyday over a 2-week span, when combined with mirror therapy (MT), produces a large long-term analgesic effect on patients suffering with PLP after a unilateral amputation in the acute stage.

A Level III Case-Control study (Chan , A.W., Bilger, E., Griffin, S., Elkis, V., Weeks, S., Hussey-Anderson, L., Pasquina, P.F., Tsao, J.W., & Baker, C.I., 2019) assessed phantom limb pain through visual representations found in the sensorimotor cortex through the use of fMRI scans during mirror therapy. Statistical significance ($p<0.001$) was indicated for visual mirror therapy, where PLP decreased during increased exposure time in response to visual responsiveness within the sensorimotor cortex.

A Level I randomized controlled trial (Kikkert, S., Mezue, M., O'Shea, J., Henderson Slater, D., Johansen-Berg, H., Tracey, I., & Makin, T. R., 2019) provided evidence that PLP relief is significantly correlated with reduced activity in the S1/M1 missing hand cortex after intervention stimulation. More specifically, a single 20-minute session of task-concurrent NIBS (anodal tDCS) over the S1/M1 missing hand cortex caused both short-and longer-term PLP relief when compared to the sham.

A Level I randomized control trial (Bolognini, N., Spandri, V., Ferraro, F., Salmaggi, A., Molinari, A. C., Fregni, F., & Maravita, A., 2015). Provided evidence that a 5-day treatment of anodal tDCS of the motor cortex induces a persistent reduction of chronic postamputation PLP, stable up to 1 week, as compared to a 5-day treatment with sham tDCS. Furthermore, participants reported an average of 41% decrease in background PLP, with 4 out of the 8 participants reporting a reduction greater than 30% after the active tDCS week. Frequency of PLP paroxysms decreased at an average of 33%, with a reduction greater than 30% in 4 out of 8 patients. Interestingly enough, 1 participant even showed a complete (100%) PLP relief on both measures and was maintained the week after the treatment. The study also found as soon as each daily session of active tDCS was completed, participants reported an instant reduction of PLP intensity; in contrast, after sham tDCS, their responses were variable. No change in nonpainful sensations was found following either active or sham tDCS.

There is overall moderate to strong evidence in the use of non-invasive brain stimulation as an intervention to provide short term and long term PLP relief in amputees and persons with BPA.

Nerve Stimulation

Of the studies reviewed for nerve stimulation, there were 2 Level I studies and 1 Level II study that assessed the effectiveness of nerve stimulation on the management or reduction of PLP or BPA. The aim of these studies were to determine if nerve stimulation could be an effective, yet affordable treatment for individuals experiencing PLP or BPA in comparison to other treatment methods.

A Level I randomized controlled trial (Tilak, M., Isaac, S. A., Fletcher, J., Vasanthan, L. T., Subbaiah, R. S., ... Tharion, G., 2016) provided evidence that a transcutaneous electrical stimulation (TENS) intervention, when compared to traditional mirror therapy, for unilateral amputee patients, provided similar reductions in phantom limb pain and is an affordable, easily accessible, and effective treatment option.

A Level III Cohort Study (Mulvey, M.R., Radford, H.E., Fawkner, H.J., Hirst, L., Neumann, V., & Johnson, M.I., 2013) assess intensity of pain and non-painful sensations before, during, and after a 2 - hour TENS intervention. TENS was found to have statistically significant improvements for pain intensity during the intervention ($p<0.05$); however, these results did not stay consistent after the intervention was completed. Non-painful sensations were not found to improve, but overall, all participants tolerated the session well.

A Level I randomized control trial (Brede, E., Metter, E.J., & Talbot, L.A. (2017) demonstrated that the utilization of neuromuscular electrical stimulation (NMES) in combination with a military amputee rehabilitation program (MARP) for lower extremity amputees, was overall statistically significant to reduce phantom limb pain. However, results are not as statistically significant to demonstrate consistent improvements for phantom limb pain

over time due to the amount of participants who reported more phantom limb pain at the beginning of the study.

Overall, the use of nerve stimulation proved to have moderate strength on the effectiveness of managing or reducing PLP or pain experienced in BPA. Nerve stimulation, overall, does not have long term impacts; however, immediate improvements can be seen, indicating nerve stimulation could be applied to alleviate pain when an individual experiences discomfort or disruption to their daily lives.

Other Imagery and Reprocessing Methods

The articles within this subtitle focus on interventions related to mental imagery and reprocessing methods to decrease phantom limb pain and increase function. With non-traditional methods of treating phantom limb pain, the articles in this section provided statistically significant positive effects in treating phantom limb pain through Eye Movement Desensitization and Reprocessing therapy and motor imagery interventions.

A Level I randomized control trial (Brunelli, S., Morone, G., Iosa, M., Ciotti, C., De Giorgi, R., Foti C., & Traballesi, M. (2015) demonstrated that the SAIPAN protocol, which includes mental imagery of the phantom limb, muscle relaxation throughout the body, and phantom exercises, is statistically significant in reducing the rate, duration, intensity, and bother of phantom limb pain. Results also demonstrated reduction in PLP 1 month after interventions were conducted.

A Level I Randomized Control Trial (Moseley, G.I., 2006) assessed pain and function/disability before, during, and after a graded motor imagery intervention which focused on limb laterality recognition, imagined movements, and mirror movements. In comparison to a standard care control group, the graded motor imagery intervention was found to have a significant change in pain intensity and function, which also continued throughout the follow up sessions.

A Level I Randomized Control Trial (Rostaminejad, A., Behnammoghadam, M., Rostaminjad, M., Behnammoghadam, Z., Bashti, S., 2017) found that Eye Movement Desensitization and Reprocessing therapy where clients replayed and identified previous traumatic experiences along with bilateral stimulation from therapists resulted in significant decreases in phantom limb pain up to twenty-four months following up.

Of the three articles reviewed under "Other Imagery Methods", all three articles provided strong evidence in reducing phantom limb pain through randomized control trials. Mental and motor imagery techniques, along with EMDR therapy all work to decrease phantom limb pain.

Discussion and Implications for Practice

The results from this rapid systematic review shows moderate evidence supporting therapy interventions that reduce PLP due to amputations and BPA. The evidence includes interventions that fall under the themes of virtual reality, traditional mirror therapy, traditional mirror therapy combined with additional intervention, non-invasive brain stimulation, nerve stimulation, and other imagery and reprocessing methods.

Overall, there is moderate evidence for the effectiveness of therapy interventions for decreasing PLP due to amputations and BPA. As clinicians, we need to consider our client's individual differences and how they might impact the successfulness of interventions. We should tailor our interventions to meet our client's individual goals and practice meaningful occupations in regards to reducing phantom limb pain. Clinicians should focus on these kinds of interventions and determine which interventions are most meaningful to the client to reduce phantom limb pain and to increase their occupational performance in their daily lives.

The feasibility to implement many of these interventions may also be affected by the resources in which the individual has access to. Some of these interventions can be performed at home with household items after one educational session while others have to be performed in a hospital with expensive technology and equipment and alongside competent staff.

Limitations

This rapid systematic review included 30 articles of which 50% of them were Level III evidence, indicating that the evidence is of moderate quality. Numerous studies within this review had small sample sizes, wide range of publishing dates, self-reported measures, lacked long-term follow up, and a wide variety of interventions. Most of the studies were single blinded because the therapist providing interventions could not be blinded, due to the nature of the interventions they were providing. Though the best articles were chosen for this rapid systematic review, many articles were excluded due to the specific criteria for a rapid systematic review. Lastly, as studies had to be chosen outside of the United States, the translation of this research to the United States can be limited by differences in other culture's classification and perception of pain and overall health.

Conclusions

With moderate evidence supporting the use of various interventions for alleviating pain in amputees and brachial plexus avulsion patients, future Level I studies should be conducted to determine the long term improvements of interventions for alleviating phantom limb pain. Virtual reality, mirror therapy, brain stimulation, nerve stimulation,

and other imagery interventions are shown to have an impact on a patient's pain level. Numerous studies reported significant reductions in acute pain, but lack long-term follow up to report the effects on chronic pain. For future research, it would be beneficial to study these interventions under randomized controlled trial protocol and within the United States to give a better picture of the effectiveness of these interventions in our healthcare system.

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Table 1. Evidence Table

Theme 1: Virtual Reality				
Author/Year	**Level of Evidence/Study Design/Participants/Inclusion Criteria**	**Intervention and Control Groups**	**Outcome Measures**	**Results**
Akimichi Ichinose, MSc, Yuko Sano, PhD, Michihiro Osumi, PhD, Masahiko Sumitani, MD, PhD, Shin-ichiro Kumagaya, MD, PhD, & Yasuo Kuniyoshi, PhD, 2017	**Level of Evidence:** III Cohort Study **Participants**: 9 patients suffering for PLP. **Inclusion Criteria:** Experiencing Phantom Limb Pain due to Brachial plexus avulsion or arm amputation. No participant was in the acute stage. All participants were outpatients in the Anesthesiology and Pain Relief Center at The University of Tokyo.	Participants were asked to "touch" virtual target objects within the Virtual reality environment with the virtual affected limb. The test group included a "cheek" condition where vibrating motors were placed on the cheek. If a person touched a target object with the virtually affected hand, a synchronous tactile stimulus was applied to the cheek. For control groups, the motors were placed on the intact hand and then had "no condition". In this case, the stimulus was applied directly to the virtual intact hand as a source for a control group.	The study looked to measure pain relief in participants previously experiencing PLP.	Pain was significantly reduced in the Cheek ($P = .004$) and Intact Hand ($P = .016$) conditions. . Statistical analyses showed that the pain reduction rates differed between conditions (Friedman test, $\chi 2 = 14.8$, $P = .0006$). Pairwise comparisons showed that the pain reduction rate in the Cheek Condition was significantly higher than in the Intact Hand ($P = .018$) and No Stimulus ($P = .0006$) conditions. R values reported were 0.68.
Briana N. Perry, Robert S. Armiger, Mikias Wolde, Kayla A.	**Level of Evidence:** III Cohort Study	The study placed 8 electrodes around the residual limb with a 9th ground electrode. The input through the	The study used the VAS and SF-MPQ as means to measure the occurrence, severity, and symptoms of	Overall according to the VAS, 7/8 participants had a decrease in PLP across the study of 1-2 months. According to the SF-MPQ,

McFarland, Aimee L. Alphonso, Brett T. Monson, Paul F. Pasquina, & Jack W. Tsao, 2018	**Participants**: 9 total **Inclusion Criteria:** Recruited from Walter Reed National Military Medical Center. Participants must be within 18 months of sustaining an UE amputation. Criteria also consisted of a normal neurological examination, the presence of three weekly PLP episodes, and no prior history of vertebral disk disease/condition, sciatica, or radiculopathy.	electrodes was characterized as surface EMG signals. Through the virtual environment participants were instructed to follow limb movements of a virtual avatar within the system during sessions. At the end of the sessions, participants were able to "move" virtual limbs during a period of "free play". There were no controls in this study as all 9 participants were tested using the Virtual Environment.	pain.	7/8 subjects also reported decreased PLP with significant improvement, (B= -0.096, p= 0.003). Results suggest that VIE is a viable PLP and RLP therapy option for the majority of individuals with UE amputation.
Mercier, C., & Sirigu, A. (2009)	**Level of Evidence:** III **Study Design:** single case multiple baseline (cohort) N= 8 **Inclusion Criteria**: PLP due to complete BPA resulting in a deafferentation and paralysis of the hand,	Prior to the intervention, the participants intact arm was filmed while performing the following motor tasks: flexion/extension of the elbow, pronation/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	The outcome measured was PLP. PLP was assessed before and after each session as well as daily through a diary.	The results were that after 16 training sessions, participants reported an average 38% decrease in background pain, with 5 participants out of 8 reporting a reduction greater than 30%. Interestingly, this decrease in pain was maintained at 4 weeks post intervention in 4 of these 5 participants (except for one participant who decreased his morphine dose by 80% during that period). Paired *t* tests showed a significant group difference between

	traumatic above-elbow amputation that occurred 1 to 16 years before, right handed prior to lesion **Exclusion Criteria:** medication change <1 month prior, surgical procedure <3 months prior	object (such as a glass), precision grip with small objects, and dialing a phone number. These images were then flipped to depict the participants missing limb performing the movements. The actual movements chosen for the intervention were different for each participant due to the movements being chosen based on if they could perform the task with visual feedback. Also, 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. In each session, 10 movements were each presented to the participant 10 times for a total of 100 movements. Each movement was 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 participant was asked to report on their ability to follow the movement and sensations felt. The experimenter used only open-ended questions to avoid cueing the participant to the kinds of sensations that he		pretreatment and posttreatment pain both at 1week (P=0.02) and at 4weeks (P=0.03). No difference was found between week 1 and week 4 of the follow-up period (P = 0.44)

		might encounter. Each session lasted between 30 and 60 minutes, depending on the speed of the phantom movements. All participants underwent 2 treatment sessions per week for 8 weeks (16 treatment sessions; 1600 phantom limb movements with virtual visual feedback).		
Michihiro Osumi, Kazunori Iomatata, Yuji Inoue, Yuko Otake, Shu Morioka, & Masahiko Sumitani, 2018	**Level of Evidence:** III Cohort Study **Participants:** 19 Patients **Inclusion Criteria:** Experiencing PLP with amputation or brachial plexus avulsion injury. All patients were outpatients at University of Tokyo Hospital.	Movement of the intact arm, hands, and fingers was detected and captured via infrared video cameras. The mirror reversed the image and that was visually fed back to the patients via an immersive head-mounted display. Using the VR system, the participants were able to go into the virtual environment and control their virtual phantom limb with intact limb movements. The feeling of producing intentional movements of their phantom limb was induced when simultaneously moving their bilateral hands.	PLP intensity and phantom limb movements were evaluated using the SF-MPQ and Bimanual circle-line coordination task.	R rehabilitation significantly restored movement representation ($P < 0.0001$) quantified using the bimanual coupling effect and significantly alleviated PLP intensity ($P < 0.0001$). The factor analysis revealed that PLP characteristics could be divided into two factors: “somatosensory-related pain characteristics” and “kinesthesia-related pain characteristics.” PLP alleviation via VR rehabilitation was significantly correlated with “kinesthesia-related pain characteristics” (r ¼ 0.47, P ¼ 0.02) but not “somatosensory-related pain characteristics” (r ¼ 0.22, P ¼ 0.17).

Ortiz- Catalan, M., Guomundsdottir, R.A., Kristofferson, M.B., Zepeda-Echavarria. A., Caine-Winterberger, K., Kulback, K., Widehammer, C., Eriksson, K., Stockselius, A., Ragno, C., Pihlar, Z., Burger, H., & Hermansson, L. (2016).	**Level of Evidence:** Level III **Study Design:** Cohort study **Participants:** Patients were recruited from 3 clinics in Sweden and Slovenia who had noted that traditional clinical treatment was not reducing PLP or had not reported pain changes for a month. Participants' average age was 50.3 years and PLP was experienced, on average for 10.3 years. **Inclusion Criteria:** *male or female *required to have a controllable portion of the biceps and triceps *reported that PLP was not being reduced with standard care *reported there was no reduction in pain in the past month **Goal:** The primary goal of this study was to introduce a non-invasive treatment for PLP in patients with upper extremity (UE) amputations, both unilateral and	Each participant received the same intervention and completed 12 sessions and 3 follow-ups at 1, 3, and 6 months. The intervention was given twice per week, except one patient who received treatment daily. Each session was 2 hours long and included 5 steps: 1 - pain evaluation, 2 - placement of electrode and fiducial marker, 3 - practiced motor execution in augmented reality, 4 - gaming by racing care using phantom movements, and 5 - matching random target postures of virtual arm in virtual reality. For steps 3-5, there were three different levels of difficulty: 2 movements with 1 degree of freedom (DOF), 2-4 DOF, and 2+ DOF.	The primary outcomes were changes in **intensity, duration, frequency, quality, and intrusion of PLP**. Each outcome was measured before, during, after, and at each follow-up. **Intensity:** A pain intensity scale was used to determine frequency. **Duration:** A weighted pain distribution scale was used to determine the duration of PLP. **Frequency:** This was measured using a study-specific scale, rating the occurrence of PLP per week. **Quality:** This was assessed by using the numeric rating scale (NRS), components of the McGill Pain Questionnaire, and the pain rating index. **Intrusion:** This was determined by answered questions asked by the investigators and score on a NRS. This looked at how often PLP decreased engagement in ADLs and sleep.	Pre to post intervention, the average weight pain distribution saw a 56% improvement (p=0.001), showing an improvement in duration for 12 patients, and the NRS saw a 55% improvement (p=0.004), showing improvement in pain intensity for 9 patients. The pain rating index saw a 51% improvement (p=0.0001), indicating that all patients experienced decreased intensity and quality of PLP. Pain such as stabbing and tiring-exhausting pain decreased after the intervention (p=0.016). Intrusion was improved by 43% (p=.004), 8 reported less interference with ADLs and 11 reported less interference with sleep. Overall, outcomes presented with moderate strength in statistically significant correlations ranging from 0.43 to 0.62) for duration/intensity, quality/intensity, present intensity, and intrusion. **Interpretation:** This a novel study that has the potential to be an effective intervention with more research that includes a larger sample size. Implications for this intervention can also be used outside of PLP, such as strokes, nerve injuries, and hand surgery, as it aims to increase the neural drive to muscle and increase recruitment for proper brain circuitry to produce a movement.

	bilateral, through the use of augmented and virtual reality decoding of phantom motor execution. Another goal was to increase patient engagement at a low cost and incorporate those with PLP with bilateral amputations.			
Osumi, M., et al., (2017)	**Level of Evidence:** Level III **Study Design:** Cohort **Participants**: BPA patients with perceived phantom upper limb and pathological pain recruited from the University of Tokyo Hospital *age 43-64 **Inclusion Criteria:** *chief complaint of PLP **Goal**: assess whether neurorehabilitation with a VR system would be effective in producing two outcomes	The participants underwent a VR rehabilitation treatment where a head mounted display was worn. The intact forearm and hand were converted symmetrically as 3D computer graphics. The participants controlled their affected arm by moving their intact arm to "feel" that they were moving both by looking at a virtual screen.	Outcomes assessed were restoring movement representations of the phantom limb and improving PLP. Outcome measured used: *VR Measurement *11-point NRS to assess pain reduction *Short- Form McGill Pain Questionnaire to measure pain intensity *Bimanual Circle-Line Coordination Task (BCT) to assess phantom movements	There was a strong association between the VR treatment and alleviating PLP while enhancing movement representation of the phantom limb. There were significant effect sizes: McGill = 0.84 and NRS = 0.85 suggesting large-scale treatment effects. There was an average decrease on the SF-MGQ (pre 8.3 +/- 7.6, post 2.5 +/- 3.2, p = 0.015; 61.5% relief). NRS scores decreased: pre 5.2 +/- 2.4, post 3.0 +/- 2.1, p=0.015, 39.1 % relief. Interpretation: There was no long term follow up for this study to determine analgesic effect for chronic pain. Also, treatment time was only 10 minutes. Future research is needed to study long term effects and a longer observational period is needed to fully understand the analgesic effect of a VR treatment.
Rutledge, T., et al., (2019)	**Level of Evidence:** Level III	The VR environment was made to model MT treatment for PLP: experience limbs as intact through	Quantitative data accessed: realism, usability, satisfaction, side effects, and	The pre to post treatment reduction in PLP was statistically significant (t=2.7, P=0.02, d=0.53).

	Study Design: Cohort **Participants**: 14 veterans recruited from the Veterans Affairs San Diego Healthcare System *predominantly male *low levels of depressive symptoms *low to moderate levels of PTSD *good to very good health **Inclusion Criteria:** *age 21-80 *upper or lower amputation with PLP for 6 months *PLP intensity >4/10 *English speaking *able to operate a VR headset *ability to use prosthetic limb **Goal**: describe the development of a virtual reality (VR) treatment for chronic PLP and unpleasant phantom sensations in high-risk veterans	appearance and movement of their VR avatar. The VR equipment was made for both upper and lower amputation participants to stimulate a bicycle ride on a pedaler at the participants own pace through an avatar. The VR could be completed at home or in the laboratory. 10 of the participants only completed 1 VR treatment, while the other 4 completed multiple sessions: 5, 12, 14, or 28 treatments.	effects on PLP and phantom sensations. Outcome measures used: *Phantom Limb Pain Questionnaire (PLPQ) *Trinity Amputation and Prosthetic Experience Scale (TAPES) *Short Form-12 (SF-12) *The Patient Health Questionnaire-9 (PHQ-9) *Post-Traumatic Stress Disorder Checklist-Military Version (PCL-M) Outcomes assessed included intensity of PLP, characteristics, sensations, general health, depression, PTSD, helpfulness of VR, positive and adverse reactions.	There was a significant reduction in pre to post treatment of phantom sensations (t=4.4, P=0.001, d=1.7). There was a >75% reduction in unpleasant sensations after VR treatment. No adverse effects were reported via any participants. Participants rated VR treatment highly (>75%) for helpfulness, immersion, realism, and satisfaction for both the multiple and single treatment sessions. Although there were significant findings from this article, the sample size is very small with no long term follow up or equal treatment among all participants.
Sano, Y., et al., (2016)	**Level of Evidence:** Level II **Study Design:** Case Control **Participants**: 7 arm amputation or brachial plexus	Cases: participants represent the BPA and amputation population in Tokyo over a wide age span Controls: recruited from same place, same inclusion criteria, and same population	Outcomes measured included pain reduction, ownership, and agency of the virtual affected arm. Questionnaires used: *Short Form McGill Pain Questionnaire	The average reduction rates under the two groups were significantly different ($p = 0.047 < 005$. All participants reported the analgesic effect which declined rapidly but only lasted a few minutes,

	avulsion patients with presenting pain recruited from the Department of Pain and Pallative Medicine at the University of Tokyo Hospital *in the chronic stage of pain *right hand dominant **Inclusion Criteria:** *diagnosis of upper limb deafferentation pain ipsilateral to injury after BPA or PLP after arm amputation *mean pain intensity in the past week of >4 on 11-point scale *pain duration >3 months *age between 20-80 years **Goal**: relieve pain by neurorehabilitatio n using a VR system with sensory feedback	The participants were not randomly assigned, but the two groups differed in terms of: Cases: received tactile feedback during the VR treatment Controls: received no tactile feedback during the VR treatment Participants' movement was detected by gloves, head displays, and mirror-reversed images in a virtual environment. Participants were asked to reach and touch objects with an intact arm which virtually operated the affected hand. When the arm reached the target, a collusion sound was played for auditory stimulus. For the cases (tactile feedback group), vibrators were placed on fingertips which vibrated when the participant touched the object to apply tactile feedback. Each group had an exposure time of 5 minutes with a 2 second break between each round. Intervention lasted over 3 weeks.	*Ownership vs Agency Questionnaire Participants answered subjectively, and then answers were compared via standardized scales.	indicating no long-term intervention effect. The overall result was that pain was significantly alleviated under the tactile feedback group compared to the no tactile feedback group, which shows that tactile feedback might be effective for pain relief during neurorehabilitation using VR. The overall reduction rates for the McGill pain score were significant ($P<0.05$), meaning tactile feedback and VR strengthens pain reduction. Interpretation: Sample size was very small and treatment time was 5 minutes, which resulted in only a few minutes decrease in pain. This would not be an effective treatment for patients experiencing chronic pain post BPA or amputation.
Theme 2: Traditional Mirror Therapy				
Brodie, E. E., Whyte, A., and Niven, C.A. (2007).	**Level of Evidence:** Level I **Study Design:** RCT **Participants:** 80	<u>Intervention Group:</u> Participants in the mirror condition group were to put their unaffected limb into a	Phantom **limb pain (PLP),** phantom limb sensation (PLS), phantom limb awareness (PLA),	For PLP, participants in both studies reported decreased PLP after interventions were conducted. Although there was a statistical significance

	participants mirror conditioning group (intervention) = 41 participants; 35 male and 6 females; age range: (20-83 years old) Non-mirror condition group (control) = 39 participants; 28 males and 11 females; age range= (25-80 years old) **Inclusion Criteria:** lower limb amputees, presence of phantom limb, right or left side amputee, experienced 1-50 years since amputation, ages 20-83	mirror box and looked into the mirror where they saw their intact limb. The intact limb and the phantom limb were aligned. Control Group: participants aligned their phantom limb and their unaffected limb next to each other on either side of the mirror. In doing so, participants would see their unaffected limb and not the mirror image. Both groups conducted 10 exercises for 10 times each for both phantom and unaffected limbs	and phantom limb movement (PLM)	in PLP for both groups, power failed because it did not reach 80% as a result of large variability. Both groups showed statistical significance in the reduction of PLP. For the mean results of the VAS intensity score for mirror condition group, pre-intervention VAS score was 57 and post-intervention VAS score was 40. For the control group, the pre-intervention VAS score was 33 and the post-intervention VAS score was 29. For PLS, results were statistically significant for both groups however power failed to reach 80% as well due to large variability. For PLA in the mirror condition group, 12 participants reported no PLA prior to interventions and for the control group, 9 participants reported no PLA. Results display that not all participants had PLA. For PLM, there was more statistical significance in the mirror conditioning group, as a result of more responses in relation to movement in comparison to the control group.
Darnall, B., Li, H. (2012).	**Level of Evidence:** III **Study Design:** Uncontrolled Prospective Treatment Outcome Pilot Study **N=** 31 41.9% Female, 58.1% Male *M* age=61 years old **Inclusion**	**One group:** The method used in this study was a cohort-based pilot study. All participants of the study engaged in the same home-based self-delivered mirror therapy program. The participants did include those who lived in-state and out-of-state. After researchers found participants who met the	The primary outcome was **reduction** of **phantom limb pain intensity** which was measured using an 11-point numeric rating scale (0-10) per patient-report. 0= no pain and 10= worst pain imaginable. The secondary outcomes were **depressive**	Phantom Limb Pain Intensity: There was a significant reduction in mean phantom pain intensity at month 1 (n=31, p=0.0002) and at month 2 (n=26, p=0.002). The study's overall median reduction in phantom limb pain intensity after the second month of the study was 15.4%. The study showed those with higher education (>16 years) had a greater reduction in pain

	criteria: community-dwelling adults aged 18-75 years, reported phantom limb pain >3 on a 0-10 numeric rating scale, complete amputation surgical healing.	inclusion criteria, subjects were screened over the phone and then if they were eligible they either enrolled remotely or in-person. After enrollment, each participant signed an informed consent form, researchers administered baseline measures, and provided a demonstration of mirror therapy and gave participants any needed equipment. Those who were out-of-state were given a stipend to purchase a mirror for study purposes.	**symptoms and daily mirror therapy diary** which were measured using the Centers for Epidemiologic Studies Depression Subscale (CES-D) and self rating of phantom pain intensity (0-10 scale), quantification of mirror therapy in minutes, and a brief description of specific mirror therapy exercise session. The participants received weekly phone calls during the first month from the study coordinator to address any questions about study procedures. Each participant was given a study binder that included an information sheet on mirror therapy, a set of self-addressed, postage paid envelopes, and daily mirror therapy diaries and study questionnaires. Participants were asked to complete and post back at the 1 and 2 month time points. Every participant was given a 7-minute DVD explaining and demonstrating home-based self-delivered mirror therapy. All data was analyzed using the SAS software release 9.2.	intensity (p=0.01). The participant's level of education was found to be a confounding factor that impacted the results.
Finn, S. B., Perry, B.N.,	**Level of Evidence:** I	**Mirror Therapy Group:** Each	The **primary outcome** was	**Phantom Limb Pain:** Eight participants reported a

Clasing, J. E., Walters, L. S., Jarzombek, S. L., Curran, S., Rouhanian, M., Keszler, M. S., Hussey-Andersen, L. K., Weeks, S. R., Pasquina, P. F., & Tsao, J. W. (2017).	**Study Design:** Randomized control trial **N=** 15 100% Male **Inclusion Criteria:** Active duty United States Military Service members, beneficiaries, or retirees, ages 18 to 70, unilateral upper extremity amputation, and any gender	participant, with a research assistant or study investigator at Walter Reed and Brooke Army Medical Centers, completed 15 minutes of mirror therapy each day for 5 days out of the week for 4 weeks. They also completed pain surveys each day. Participants were asked to perform hand movements while looking at their intact limb in the mirror. They performed numerous movements including but not limited to abduction/adduction of the thumb and fifth finger, flexion/extension of the thumb, and pronation/supination of the hand. Participants were asked to use the visual analog scale to report pain levels as well as the number of episodes of pain each day and the duration in minutes per day. Measurements were taken at baseline and after treatment sessions. **Covered Mirror Therapy Group:** Each participant, with a research assistant or study investigator at Walter Reed and Brooke Army Medical Centers, completed 15 minutes of mirror therapy each day for 5 days out of the week for 4 weeks. They also completed pain surveys each day. Participants were asked to perform hand movements while looking at their intact limb in the mirror. The mirror, however, was	decreased phantom limb pain related to amputation.	decrease in phantom limb pain while one participant reported an increase in phantom limb pain. The group's mean pain score decreased from 41.4 to 27.5mm on a 100-mm visual analog scale. The covered mirror therapy group did not experience a statistically significant decrease in pain. There was an estimated large effect size of the initial and final visual analog scale scores with Cohen's *d* of 0.971. The researchers also found a significant change in total daily time that participants were experiencing phantom limb pain. There was a decrease from 1,022 to 448 minutes. The covered mirror therapy participants did not experience a significant decrease in the daily amount of minutes they experienced phantom limb pain; mean of 743 to 726 minutes.

		covered using an opaque sheet so they could not see their reflection. The participants who were assigned to the covered mirror therapy group had the opportunity to switch to the other group after 4 weeks. All participants were switched to mirror therapy group after 11 treatment sessions. Participants were asked to use the visual analog scale to report pain levels as well as the number of episodes of pain each day and the duration in minutes per day. Measurements were taken at baseline and after treatment sessions.		
Imaizumi, S., Asai, T., & Koyama, S. (2017).	**Level of Evidence:** Level III **Study Design:** Cohort study **Participants:** A total of 9 male, adult upper limb amputees averaging 64.78 years of age completed this intervention and received monetary reward. PLP was experienced, on average, for 39.87 years. **Inclusion Criteria:** *no current medical treatment for pain *relatively good health	Each participant received the same intervention. Each participant performed a 15-minute, short-term MT session individually without their prosthetic device. To begin, patients completed the following movements while looking in a mirror: moving intact limb away/toward the mirror, moving the intact limb forward/backward, and opening/closing hand in no particular order, speed, or range. Patients were asked to relate the intact limb movements to their phantom limb.	A subjective questionnaire was used to determine changes in primary outcome measures before and immediately after the short-term MT session: **agency and ownership.** To measure these outcomes, the questionnaire consisted of a 5-point scale and 8 questions relating to presence of phantom limb, incorporation of phantom limb, bodily shape, quickness, accuracy, difficulty, pain intensity, and unpleasantness.	It was found that the sense of agency increased after the short-term MT session by 3.813, indicating substantial evidence for quickness, accuracy, and difficulty. As for ownership, there was only a slight increase in feelings of ownership by 1.867, indicating weak evidence. Presence of the phantom limb was the only ownership component that saw a clinically worthwhile increase (2.378). Incorporation, bodily shape, pain intensity, and unpleasantness were all also found to have weak evidence (0.897, 0.340, 0.376, and 0.333, respectively). **Interpretation:** This study has good implications for agency, but not enough to apply this intervention solely based on this study. This study had a small sample size and

	*could perform everyday tasks with or without their prosthetic **Goal:** This study had 3 primary goals: 1) Determine if and how senses of agency and ownership over PLP were affected by mirror therapy (MT). 2) Determine if PLP is reduced due to MT. 3) Determine the relationship between agency, ownership, and PLP after a short MT intervention			performed no follow-up. Though authors did an excellent job accounting for and mediating the effects of confounding factors such as depression, interoceptive accuracy, and schizophrenia, the study does not provide enough beneficial evidence to be used in OT practice.
Shashikumar Ramaduga, Satish C Nagabushnam, Nagendra Katuwal, Kaushik Chatterjee 2017	**Level of Evidence:** II Randomized Single Crossover Study **Participants:** 28 in Control Group and 32 in	Participants were spit into a control group and experimental group. For the entire length of the study the experimental group participated in traditional mirror therapy for 15 minutes a day. The control group began exercises with the	All were assessed using the VAS and Short-From McGill Pain Questionnaire at the 4^{th}, 8^{th}, and 12^{th} week during intervention to assess levels of pain.	Clients were tested every four weeks for follow-up intervals. Significant reductions in PLP were recorded in the first four weeks in the test group compared to the control ($P < 0.0001$). After the switchover, the control group also recorded significant

	Experimental group **Inclusion Criteria:** Amputees with PLP. Age above 15 years and below 75 years. Ability to communicate in English/Hindi.	mirror covered for the first four weeks and then "crossed over" to traditional mirror therapy for the remaining part of the study.	Official measures were severity of pain, the duration, and frequency of pain.	reductions once beginning traditional mirror therapy. It was concluded that mirror therapy significantly reduced PLP.
Yıldırım, M., & Kanan, N. (2016)	**Level of Evidence:** III **Study Design:** quasi-experimental (cohort) N= 15 **Inclusion Criteria:** > age of 18, unilateral upper or lower extremity amputation and having PLP, able to read and write Turkish, and having a calm environment at home/ hospital to practice mirror therapy **Exclusion Criteria:** visual impairment or severe hearing loss, having any condition that prevents movement of opposite extremity (such as plaster cast, paralysis in the intact limb), being diagnosed	All participants were first taught the process of the treatment before being responsible for performing the treatment independently at home. The participants were also given the Mirror Therapy Practice Follow-Up Booklet which they were to document daily PLP scores before and after each treatment. The treatment rules are as followed: eyes focused on reflection in mirror; both limbs performing symmetrical movements (forward and back, rotating wrist/ankle joint, moving the fingers, opening and closing hand) practicing everyday-at least once a day (more if they want), and lasting a minimum of 20 minutes. The participants did this for 4 weeks. Researchers called participants 2x/wk. to check up and answer any questions.	The outcome measured was PLP. The 0-10 Numeric Pain Intensity Scale was used to measure PLP before and after each treatment session. It was also administered a month after the end of treatment.	The results of this study were that there was a statistically significant decrease in average PLP scores every week of the study period and for 1-month total score ($p<0.01$) It was also found that patients who did not use a prosthesis had greater effect from mirror therapy ($p<0.05$), and prosthesis usage explained 30.6% of the change in average PLP scores before and after mirror therapy (Adjusted $R2=0.306$, $p<0.05$) There was no significant relationship between effect of mirror therapy and demographic, amputation or PLP-related characteristics of the patients ($p>0.05$). No significant difference was found in correlation analysis between average PLP score before and after mirror therapy, the average number ($rs=0.178$) and duration ($rs=-0.315$) of mirror therapy sessions practiced for 4 weeks ($p>0.05$).

	with a mental disorder that could diminish ability to concentrate during therapy			
Theme 3: Traditional Mirror Therapy Combined with Additional Intervention				
De Nunzio, A. M., Schweisfurth, M. A, Ge, N., Falla, D., Hahne, J., Godecke, K., Petzke, F., Siebertz, M., Dechent, P., Wiess, T., Flor, H., Graimann, B., Aszmann, O. C., Farina,. D. (2018).	**Level of Evidence: III** **Study Design:** Cohort Study **N= 10** 50% Female, 50% Male *M* age= 57.7 years old **Inclusion Criteria:** Major unilateral upper-limb amputation, PLP at least twice a week with an average peak intensity of 3 on a visual analog scale, and amputation more than two years from the enrollment.	**One Group:** After the participants were enrolled in the study, they were asked to report their phantom limb pain and the pain intensity on a visual analog scale as well as the characteristics of the pain and any pharmacological interventions they were using. The participants were asked to report four times a day two weeks prior to training, during training, and six weeks after training. Researchers also administered the two-point discrimination test to determine the participant's somatosensory sharpness on their amputated limb. The phantom limb treatment protocol included measuring muscle activation using a differential electromyography band that was placed over each amputee's stump. The band also contained eight micro-vibrators that produced sensory feedback. The participants conducted ten movements including five wrist movements, three hand movements, and two	The **primary outcome** was reducing phantom limb pain. The **secondary outcome** was determining the sensory characterization of pain using a pain perception scale.	**Phantom Limb Pain:** The researchers observed a significant reduction in the intensity of phantom limb pain experienced by the participants. Participants experienced a 21.6% decrease in phantom limb pain directly after treatment concluded. However, a 32.1% decrease in phantom limb pain intensity was recorded at follow-up which was 6 weeks after treatment had stopped. The researchers concluded based on the reduction of pain at follow-up the treatment has clinical effectiveness for chronic pain reduction. **Sensory Characterization:** The study showed there was a reduction in the sensory characterization of phantom limb pain between during the training period and immediately after the training period. There was no statistical difference between during the training period and six weeks after treatment. These results showed that improvement in the sensory characterization of phantom limb pain lasted only until after treatment had ended.

		finger movements. Participants also underwent a sequence of fMRI measurements to determine if a cortical reorganization in the brain happened after amputation.		
Foell, J., Bekrator-Bodmann, R., Diers, M., & Flor, H. (2013).	**Level of Evidence: III** **Study Design:** Cohort Study **N= 13** 30.8% Female, 69.2% Male *M* age= 50.6 years old **Inclusion Criteria:** major unilateral upper limb amputation, experience phantom limb pain regularly at least once a week with an average intensity of at least 20 on a visual analogue scale ranging from 0 to 100, amputated for more than 2 years to rule out acute phantom limb pain	**One Group:** Each participant was required to give daily reports of pain using the visual analog scale starting 2 weeks before treatment began, after 4 weeks of training, and then after 2 weeks of no treatment. The researchers made sure they had baseline measures for pain for each participant before treatment began and then made sure to measure pain rating 2 weeks after treatment was stopped to determine if there were any long-term effects from the treatment. Throughout the pre-phase, training phase, and post-phase each patient was followed up with about any pain medications they were currently taking, any that they stopped taking, or any that they started taking. Each participant participated in 4 weeks of mirror therapy exercises. The first exercise included opening and closing of fingers while repeatedly converging the fingertips and starting with a loosely opened hand, palm towards the mirror, but without any of the fingers to touch each other or the palm. The second exercise was	The primary outcome was to **decrease phantom limb pain** after amputation. The secondary outcomes were determining **brain changes** tied to **mirror therapy** and specific **lip** and **hand movements**. and how the location of neural activity in the primary **somatosensory cortex** during specific tasks changes based on movements.	Phantom Limb Pain: The study showed a medium-sized effect on pain reduction with a Cohen's *d* of 0.52. Overall, the treatment produced a 27% decrease in pain in participants. Neural Activity: With the lip movement task, the fMRI showed significant bilateral activation in the primary motor cortex, primary somatosensory cortex, and the insular cortex. With the hand movement task, the fMRI also showed increased bilateral activation in the primary motor cortex, insular cortex, and primary somatosensory cortex before and after the treatment. There was also increased activation in the inferior parietal cortex and thalamus at the first time point. The fMRI showed less intense activation before and after treatment in the somatosensory cortex on the side of the amputation. After treatment there was an average reduction shift of 2.9 mm for the primary somatosensory cortex and a 1.5 mm for the primary motor cortex. These shifts in neural activation are not statistically significant. The study showed that there was no significant correlation between the time since amputation and the benefit from treatment. The researchers found that a

		stretching of the fingers with palm towards the mirror. The third exercise was turning the hand switching between palm facing upward and palm facing downward. The fourth exercise was ordered convergence of the fingertips and thumb with the participant's palm toward the mirror but avoiding touching the fingertips to the thumb. The final exercise was tracing figures with the index finger. The fMRI measurements were taken at the beginning of the 4 weeks and the end of the 4 weeks. Participants were given specific instructions and demonstrations on the lip and hand movement they were to perform during the MRI. A mirror was attached to the MRI machine so participants could view their hand and lips as they were making the specific movements. During the MRI, an auditory signal was presented and participants were expected to perform the lip or hand movement once they heard the signal.		participant's ability to relate the mirrored movement to their phantom had a large impact on the reduction of pain. A confidence interval of 95% was used with time being the main effect and the individual participants as the blocking effect.
Houston, H., & Dickerson, A. E. (2016).	**Level of Evidence: III** **Study Design:** Pilot study used as a cohort cross sectional repeated-measure **N=** 14 43% Female,	**Acute Group:** Participants were recruited to this group before their amputation surgery. Once their amputation was completed, the researchers measured their residual limb and	The **primary outcomes** were activities of daily living interference and well-being. **Secondary outcomes** included time required before prosthetic fitting and	**Activities of Daily Living:** Between the two groups, there was a noticed decrease in phantom limb pain interference with self-care, walking ability, car transfers, low chair transfers, and sleep. The mean value collected from pretreatment

	57% Male *M* age= 58.2 years old **Inclusion Criteria:** English speaking adults with a unilateral lower extremity vascular amputation, amputation had to have enough femur or tibia bone remaining to use an amputee cover, and participants who had not yet had their amputation prior to being admitted to surgery and participants who had surgery more than 8 months previously.	then gave them two amputee limb covers that used Farabloc technology. They wore the limb cover for 23 out of 24 hours per day. Within the first 2 days after amputation, the researchers took pretreatment measurements. Participants receiving instructions on how to don and doff as well as care for the Farabloc amputee limb cover. They received a plexi-glass mirror that was used for mirror therapy exercises. They were expected to perform one set of 15 repetitions of bilateral active range of motion exercises for each joint while looking at the nonamputated limb in the mirror. The participants were asked to complete these exercises for 15 minutes per day. **Subacute Group:** Participants were recruited to this group if their amputation was at least 8 months before enrollment in the study. Once enrolled, the researchers measured the participant's residual limb and recorded that number. Then the participants were issued two amputee limb covers that used Farabloc technology. They were expected to wear the cover whenever they removed their prosthesis. The researchers took pretreatment measures on the participants either at the Amputee Support	wearing tolerance of prosthetic.	to posttreatment and between the posttreatment and maintenance period demonstrated a positive improvement. The researchers also discovered a statistically significant reduction in phantom limb pain interference with sleep for both groups. **Well-Being:** Between the two groups, the researchers measured statistically significant improvements in mood and quality of life during the treatment and maintenance periods. For the acute group, there was no statistical significance for their satisfaction with how things had worked out since the amputation.

		Group or at the prosthetic clinic. Participants receiving instructions on how to don and doff as well as care for the Farabloc amputee limb cover. They received a plexi-glass mirror that was used for mirror therapy exercises. They were expected to perform one set of 15 repetitions of bilateral active range of motion exercises for each joint while looking at the nonamputated limb in the mirror. The participants were asked to complete these exercises for 15 minutes per day.		
Külünkoğlu, B.A., Erbahçeci, F., and Alkan, A. (2019)	**Level of Evidence:** Level I **Study Design:** RCT **Participants**: 40 subjects 23 males, 17 females Mirror therapy group (experimental): 20 participants, average age=32.60 years, 12 males and 8 females, right side amputees = 12 and left side amputees = 8 Phantom exercise group (control): 20 participants, average age= 29.60 years, 13 males and 7 females, right side amputees = 9 and left side amputees = 11 **Inclusion Criteria**: males and females, ages	Intervention Group (mirror therapy group): participants in the mirror therapy group, placed their amputated limb within a mirror box and moved their toes and ankle (of non-affected limb) by flexing/extending and inverting/everting their foot, adducting and abducting toes, and rotating ankle 10 times for 15 minutes. They would watch these exercises and movements through the mirror. Control Group (phantom exercise group): participants conducted exercises with 15 repetitions and were able to stop these exercises before reaching 15 repetitions if PLP disappeared. Participants conducted toe adduction and abduction, foot	Phantom limb pain (PLP) [VAS score], QoL [SF-36 from physical problems, social functioning, physical functioning, role limitation, mental health, vitality, pain, and general health perception] and psychological status stress (BDI)	For the mirror therapy group, PLP significantly decreased based on the VAS scores in comparison to the phantom exercise group. In the mirror therapy group, baseline results for VAS scores, the median was at 70.5 and by week 4, VAS score was 0. For the phantom exercise group, baseline results of the VAS scores for PLP was at a median of 67.5 and by week 4, the median for the VAS score was 6.5. These scores indicated a significant reduction in VAS scores and favored the mirror therapy group. For QoL scores of the mirror therapy and phantom exercises groups based on the SF-36 scores and mental health, as well as psychological stress from the BDI, both groups improved QoL and psychological status. However, results from the mirror therapy group showed a higher significance in comparison to the

	18-45 years old, unilateral transtibial amputees, experiencing PLP at least once a week, and score at least 40 on the visual analogue scale (VAS)	inversion and eversion, and ankle flexion and extension. Participants moved their phantom limb and unaffected limb in opposite directions and were also positioned the same, specifically in the position where PLP was present. Participants also conducted knee flexion and extension, as well as hip flexion and extension until PLP disappeared.		phantom exercise group.
Ol, H. S., Van Heng, Y., Danielsson, L., & Husum, H. (2018)	**Level of Evidence:** I **Study Design:** Open, randomized, semi-crossover N= 45 **Inclusion Criteria:** >16 years old, unilateral trans-tibial amputation after landmine trauma no more than 12 months before entering study, PLP with or without stump pain **Exclusion Criteria:**amputation stump anomalies requiring surgical reconstructions such as chronic infections, neuroma or major soft tissue deformities, chronic alcoholism or drug abuse, loss	Mirror therapy group:participant sat on a chair with bare legs visible. A mirror measuring 30 cm x 80 cm was placed between the legs along the amputation stump so that the participant could see the uninjured limb in the mirror while the amputated limb is hidden behind the mirror screen. For 5 min every morning and night for 4 weeks the participant fully concentrated on performing slow repeated movements of the foot from a neutral position to maximum dorsal flexion while closely observing the reflected image of the uninjured limb in the mirror. Tactile therapy group: The participant lies on a bed, not watching the stump, just concentrating on feeling the tactile stimuli, while for 5 min every morning and evening for 4 weeks, a close family	The outcomes measured were PLP and stump pain and were mere measured using a 10 cm VAS scale after each treatment round and 3 months post experiement.	After the first round of treatment, the mean reduction in VAS ratings for phantom and stump pain was >50%. No significant differences were observed between the 3 subsamples. 9 out of 45 participants did not respond to the first round of treatment and therefore were crossed over for a second round of treatment. Only 7 participated in the second round and reacted to the second-round treatment with a reduction in VAS ratings >90% for phantom and stump pain. There was a tendency toward better effect of combined mirror-tactile treatment compared to the monotherapies as estimated by percentage reduction in VAS scores. The 95% CI for the difference in percentage PLP reduction between T and M + T was 2.8–20.3; between M and M + T 10.0–8.6; and between M and T −11.5–31.0. Also regarding stump pain the combined treatment had a slightly better effect than the monotherapies as estimated by percentage VAS reduction, the 95% CI for the difference between T and M

	or deformities of limbs other than the present amputation, mental and/or cognitive disorders rendering self-rating of health unreliable	member carefully exposes the skin of the medial, frontal, lateral, and dorsal parts of the amputation stump to five different stimuli: a stone, a wooden stick, a soft brush, a soft cloth, and a soft feather. The same sequence of tactile stimuli is applied in all treatment sessions. Mirror and tactile (combined) therapy group: The mirror and the tactile treatments go on serially, with 5 min for each treatment. The process for each is the same as above. If the participant has the mirror therapy before the tactile treatment in the morning, the tactile treatment is done before of the mirror therapy at night. After the 4 weeks, non-responders to mirror therapy were crossed over to the tactile therapy group, non-responders to tactile therapy were crossed over to the mirror therapy group and non-responders to combined mirror and tactile therapy were excluded from further treatment.		+ T being 5.0– 15.7; between M and M + T 4.9–22.8. No significant difference was found between the monotherapies, the 95% CI for the difference between the M and T subsample regarding percentage VAS reduction being −10.0–17.0. None of the study participants applied tactile or mirror therapy during the post-treatment observation period. All forty- four study participants estimated the levels of pain 3 months after the conclusion of the treatment by VAS scales. The end-point ratings demonstrated that the intervention had a sustained effect. The changes in VAS rating from the end of the last intervention to evaluation 3 months later were minimal: for PLP the mean difference in rating was 0.9 (SD 0.8), for stump pain the mean difference was 1.0 (SD 0.9). No significant differences between the three treatment arms were observed regarding how long the treatment effects lasted.
Rothgangel, A., Braun, S., Winkens, B., Beurskens, A., & Smeets, R. (2018).	**Level of Evidence:** Level I **Study Design:** Randomized Control Trial **Participants**: All 68 participants were	There were 3 groups for this study, each of which received different interventions for 10 weeks total. During the first four weeks, all patients received 10 individual session with a therapist, each session lasting 30 minutes.	The primary outcomes were changes in **intensity, duration, and frequency** of PLP. Each outcome was measured before, during, and after the intervention and at the 6-month follow-up.	The frequency of PLP improved for all groups, 22 in the MT groups and 6 in the control group. The duration improved for 17 patients in the MT group and 3 in the control. There was found to be significant effects in intensity improvement (p=0.26). However, the treatment

	adults with a unilateral lower limb amputation. Each had an average pain intensity for PLP of 3 on the Numeric Rating Scale (NRS), with one or more episodes of PLP per week. They were recruited through their treating physician. **Inclusion Criteria:** *male or female *sufficient cognitive, motor and communication skills for teletreatment, following instructions, and filling out questionnaires *no comorbidities, such as stroke or severe mental disorders *must live in reasonable distance to treatment site *did not receive mirror therapy (MT) in the last 3 months **Goal:** The goal of this study was to determine the difference between traditional MT to sensomotor exercises without a mirror. Authors	**Group A:** This was a 4-week intervention for traditional MT performing exercises in observation of different positions, basic motor exercises, exercises using sensory stimuli, motor exercises using various objects and mental practice of phantom limb exercises. This was then followed by 6 weeks of teletreatment using augmented reality MT, which included monitoring of PLP, digital exercise programs using traditional MT, augmented reality MT using the tablet-integrated camera, audio-visual instruction of mental practice, limb laterality recognition training, communication with the personal therapist and others, and background information. **Group B:** This was a 4-week intervention for traditional MT given the same treatment as Group A. This was then followed by 6 weeks of self-delivered MT with no training material provided. **Group C:** This was a 4-week sensomotor exercise intervention, given the same exercises as Group A and B, but without a mirror. This was then followed by 6 weeks of	**Intensity:** This was measured using the NRS for PLP intensity for the week prior to beginning the study. **Duration:** This was measured by using a 7-point scale. **Frequency:** This was measured by using a 6-point scale. Secondary outcomes consisted of **different dimensions of PLP, intrusion in ADLs, quality of life, and self-efficacy.** **Different Dimensions of PLP:** This was assessed using the German version of the Neuropathic Pain Symptom Inventory. **Intrusion:** This was assessed using the German version of the Patient-Specific Functional Scale, allowing the client to identify 3 important daily activities. **Quality of Life:** This was assessed using the using the German version of the 5-dimensional EuroQol questionnaire, as well as a Visual Analogue Scale. **Self-Efficacy:**	effects for both frequency and duration were not significant. It was found that women saw significant treatment effects for intensity, for patients who received telescoping, and for those perceiving a motor component. At 10 weeks, all groups saw an improvement in frequency, and it was found duration was likely to improve more in patients with longer pain episodes or constant pain. At 6 months, patients in all groups (27 total) saw a decrease in the duration of PLP episodes; however, in comparison, the MT was found to have more significant treatment effects than the control ($p=0.019$) and teletreatment ($p=0.050$) groups. Both experimental groups saw a significant effect in decreased intrusion in PLP. **Interpretation:** The effect size did not reach clinical significance. Overall, this article provides moderate evidence to support the use of mirror therapy, as not all outcomes were found to have a significant, clinically worthwhile improvement. Future studies should have a larger sample size, stricter inclusion criteria, set individualized plans for each participant, possibly different outcome measures, and be applied to populations within the United States.

	also aimed to assess the effects of teletreatment through the use of augmented reality MT in comparison to sensor motor exercises without a mirror.	self-delivered exercises without training materials.	This was assessed using the German version of the Pain Self-Efficacy Questionnaire.	
Theme 4: Non-Invasive Brain Stimulation				
Bolognini, N., Spandri, V., Ferraro, F., Salmaggi, A., Molinari, A. C., Fregni, F., & Maravita, A. (2015).	**Level of Evidence:** I **Study Design:** crossover, double-blind, sham- controlled treatment (randomized controlled trial) **N=** 8 **Inclusion Criteria:** age 18 to 90 years old, normal score (>24) on the Mini-Mental State Examination, limb amputation at least 2 months before study enrollment, stable presence of PLP for at least 2 months, and written informed consent. **Exclusion Criteria:** coexistence of major neurologic, neuropsychological, and psychiatric diseases, being actively enrolled in a separate	Group 1: 1 week of treatment with tDCS (5 days, Monday to Friday) and 1 week of sham tDCS (5 days, Monday to Friday) Group 2: 1 week of sham tDCS (5 days, Monday to Friday) and 1 week of treatment with tDCS (5 days, Monday to Friday) During active tDCS, a constant current of 1.5 mA was applied for 15 minutes, with a ramping period of 10 seconds both at the beginning and at the end of the stimulation (ie, fade-in and fade-out phases, respectively). The current density (.043 mA/cm2) was maintained below the safety limits. The sham tDCS was applied with the same parameters and electrode montage as active tDCS but the current only lasted for 30 seconds.	The outcome measured was PLP. Participants were asked to rate their current pain state on a 10-cm visual analog scale (VAS) immediately before and immediately after each daily tDCS application. throughout the 2 weeks of treatment. VAS scores were used to assess PLP intensity at the moment of assessment, nonpainful phantom limb sensation and phantom limb movement. This last VAS rating was only included in the evaluation starting from the third patient treated. Participants also completed a daily diary in which they made 3 separate VAS ratings, assessing PLP back-ground intensity (ie, pain felt in the phantom limb constantly or most of the day, frequency of PLP paroxysms and stump pain intensity.	The results of this study were that a 5-day treatment of anodal tDCS of the motor cortex induces a persistent reduction of chronic postamputation PLP, stable up to 1 week, as compared to a 5-day treatment with sham tDCS. Participants reported an average of 41% decrease in background PLP, with 4 out of the 8 participants reporting a reduction greater than 30% after the active tDCS week (a 30% pain relief can be considered as a clinically significant difference, being superior to the maximal placebo effect (<25%) observed in nonpharmacologic randomized double-blind clinical trials conducted). Frequency of PLP paroxysms decreased at an average of 33%, with a reduction greater than 30% in 4 out of 8 patients. Interestingly enough, 1 participant even showed a complete (100%) PLP relief on both measures and was maintained the week after the treatment. The study also found as soon as each daily session of active tDCS was completed, participants reported an

	study targeting pain relief, and, any contraindication to noninvasive brain stimulation		These measurements were obtained during the week prior to the treatment (baseline), during the first week and the second week of the treatment, and during the first week after the end of the intervention (follow-up). For each week, patients were required to complete the diary every day, from Monday to Sunday.	instant reduction of PLP intensity; in contrast, after sham tDCS, their responses were variable. No change in nonpainful sensations was found following either active or sham tDCS. Also, participants who had an immediate increased feeling of motor control over the phantom limb brought about by active tDCS: The phantom limb moved more easily at the end of active tDCS, whereas no change, or even a decrement, of phantom motor control took place after sham tDCS, showing that an increased ability to move the phantom limb was shown to reduce PLP, whereas amputees with greater PLP are less able to move their phantom limb.
Chan, A.W., Bilger, E., Griffin, S., Elkis, V., Weeks, S., Hussey-Anderson, L., Pasquina, P.F., Tsao, J.W., & Baker, C.I. (2019).	**Level of Evidence**: Level III **Study Design**: Case-Control Study **Participants:** 18 participants <u>Intervention group</u>: unilateral lower-limb amputees, 9 participants, 5 males and 4 females, 3 L and 3 R lower limb amputees, age range: 30-75 years old <u>Control group:</u> healthy, non-lower limb amputees, 9 participants, age range: 24-58 years old, 5 males and 4 females	Both groups participated in 3 MRI sessions, where cortical responses of the feet and hands were recorded and measured in response to visual exposures. Both groups received the block design experiment for visual representations and localization of sensorimotor regions, imaging acquisition of the brain, and fMRI scans with the same time intervals. **Intervention Group**: participated in mirror therapy sessions and reported PLP. The VAS was utilized to measure PLP for this group. **Control Group**: Participants of this group were not amputees. Sensorimotor	Phantom limb pain, visual responsiveness in sensorimotor cortex	**PLP** is reduced at longer periods of time in response to visual responsiveness during visual mirror therapy. VAS scores displayed statistical significance at $p < 0.001$ to reduce PLP, where VAS scores were reduced by 46% from session 1 to session 3 based on the fMRI interventions. Results also indicated atypical responsiveness at times and only certain parts of the brain were enhanced. Visual responsiveness to images within the sensorimotor cortex is related to phantom limb pain over an extensive period of time during mirror therapy.

	Inclusion Criteria: males and females, ages 24-75 years old for both groups, and corrected to normal eye vision For intervention group: lower limb amputees, experiencing on going PLP For control group: no lower limb amputation, matching age and gender of amputee participants	cortex was identified. Functional and anatomical markers for this were identified.		
Kikkert, S., Mezue, M., O'Shea, J., Henderson Slater, D., Johansen-Berg, H., Tracey, I., & Makin, T. R. (2019).	**Level of Evidence:** I **Study Design:** double blind, within-subject, counterbalanced design **N=** 17 **Inclusion Criteria:** unilateral upper limb amputees who experienced PLP episodes at least once a week **Exclusion Criteria:** contraindications for magnetic resonance imaging (MRI) and transcranial direct current stimulation, the usage of drugs that affect the concentrations of the inhibitory neurotransmitter gamma-	**Intervention:** 17 amputees participated in 4 consecutive experimental sessions (3 real, 1 sham), spaced at least 1 week apart. Each experimental session lasted about 4 hours and consisted of behavioral testing prior to and post MRI, MRI pre and post tDCS stimulation, and simultaneous tDCS and MRI. Participants performed phantom hand movements under these 3 active tDCS conditions: 1-anodal tDCS to primary sensorimotor missing hand cortex (i.e. contralateral to the amputation side), 2-anodal tDCS to primary sensorimotor intact hand cortex (i.e. ipsilateral to the amputation side), and 3-cathodal tDCS to primary missing hand sensorimotor cortex. One amputee did not complete testing for the active tDCS session	The outcomes measured were transient PLP intensity, transient non-painful phantom sensations vividness, and transient residual arm/stump pain as well as ratings of state anxiety. These outcomes were obtained at several time points in each testing session to investigate tDCS effects, outside the scanner using VAS, and through automated text messages sent twice a day requesting to provide subjective PLP intensity ratings when the participants were done with the study.	Immediately after stimulation offset, PLP significantly increased in the sham condition (1-sample $t= 4.81$, $p < 0.001$, $d = 1.29$. However, in the intervention condition, there was no increase in PLP (1-sample Wilcoxon $Z = -1.73$, $p = 0.084$, $r = -0.46$). This resulted in a significant difference in PLP modulation between the intervention and sham conditions immediately following stimulation (Wilcoxon $Z = -2.73$, $p = 0.006$, $r = -0.73$) At the end of the experimental session (approx. 90 minutes after stimulation offset), PLP remained significantly increased in the sham condition (1-sample $t= 2.77$, $p = 0.016$, $d = 0.74$). Conversely there was significant PLP relief in the intervention condition (1-sample $t= -6.20$, $p < 0.001$, $d = -1.60$), leading to a significantly different PLP modulation between the intervention and sham

	Aminobutyric acid, and active enrolment in another brain stimulation experiment	where anodal tDCS was applied to primary sensorimotor intact hand cortex. **Control:** Control participants were tested once without NIBS to enable baseline comparisons with the amputees. Amputees' phantom hand was matched to controls' nondominant hand.		conditions (paired t = 8.18, p < 0.001, d = 2.19). To assess longer-term PLP effects of intervention stimulation, first, PLP ratings were assessed in the following session, (taken at least 1 week after each stimulation condition). Results showed no PLP change was observed for the sham condition (1-sample Wilcoxon Z = 0.00, p = 1.00, n = 11, r = 0), yet PLP remained significantly reduced following intervention stimulation (1-sample Wilcoxon Z=−2.80, p=0.005, r=−0.89, n=10). However, statistical analysis showed no significant difference between the intervention and sham conditions (Wilcoxon Z = −1.36, p = 0.173, d = −0.56). This may be due to the reduced number of participants (n = 6) that could be included in this across-stimulations analysis, as a result of the counterbalancing of session order. The longer-term PLP effects of intervention stimulation were secondly assessed using daily PLP ratings obtained throughout the week following each stimulation condition from all participants. Results were the average PLP was significantly lower in the week after intervention stimulation compared to sham (paired t = 2.65, p = 0.019, d = 0.68). Overall, this study found that PLP relief significantly correlated with reduced activity in the S1/M1 missing

				hand cortex after intervention stimulation. More specifically, a single 20-minute session of task-concurrent NIBS (anodal tDCS) over the S1/M1 missing hand cortex caused both short- and longer-term PLP relief.
Segal, N., Pud, D., Amir, H., Ratmansky, M., Kuperman, P., Honingman, L., & Treister, R., (2021)	**Level of Evidence:** Level I **Study Design:** Randomized Controlled Trial **Participants**: 30 patients suffering with PLP due to recent amputation (23 males and 7 females) aged 21-82 who were hospitalized in Lowenstein rehabilitation Hospital **Inclusion Criteria:** *man or women *age > 18 *amputation performed within the past 8 weeks *average daily PLP score of at least 4 on the numerical pain scale (NPS) from 0-10 during the past week *no change in consumption of medication in the past week excluding analgesics per requestion *able to understand the purpose and	Participants were randomized to one of three groups: Group 1: MT alone *20-minute treatment sessions in a quiet room alternating between plantarflexion/dorsiflexion and inversion/eversion movements Group 2: MT and sham tDCS *22-minute treatment sessions with 20 minutes of active treatment time Group 3: MT and real tDCS *22-minute treatment sessions with 20 minutes of active treatment time All groups received 10 sessions performed over a 2-week span with a study nurse present.	NPS used at baseline. Short Form McGill Pain Questionnaire (SF-MPQ): assess qualities of pain using 15 descriptors of sensory and emotional aspects of pain on a scale of 0-3 Brief Pain Inventory (BPI): 15 items to assess lowest, highest, and average pain intensity on a scale 0-10 Subjective benefit of treatment: scale 0-100% Primary outcome measure: change in pain intensity at 1 week compared to baseline and at 4 weeks post treatment Secondary outcome measure: changes in total and sensory scores using SF-MPQ, changes in worst and average pain scores via BPI, and change in subjective benefit from baseline to 4 weeks post treatment. Assessments were completed at	A combination of MT and tDCS produces a large analgesic effect on patients with PLP following unilateral amputation in the acute stage. The largest reduction in pain was observed 4 weeks following the end of treatment. At the 3 month follow up, pain intensity significantly reduced ($P<0.001$) in the MT and real tDCS group when compared to the other two groups. Overall, there was an analgesic effect of >80% that was seen and maintained for 12 weeks post treatment. Interpretation: MT alone has modest and temporary effects on PLP, but when combined with tDCS a bigger magnitude in pain reduction and an analgesic effect is shown.

	instructions of the study *agreed to participate and to provide written informed consent Goal: assess if a combination of mirror therapy (MT) with transcranial direct current stimulation (tDCS) results in a superior analgesic effect as compared to mirror therapy alone		baseline, 1- and 2-weeks during intervention, and 1 week, 1 month, and 3 months	
Theme 5: Nerve Stimulation				
Brede, E., Metter, E.J., & Talbot, L.A. (2017).	**Level of Evidence:** Level I **Study design**: Randomized Control Trial (RCT) **Participants**: N=44; NMES+MARP group = 23 participants, average 25.7 years old, 96% males MARP only = 21 participants; average 26.1 years old, 100% males **Inclusion Criteria**: active-duty military participants, reporting decrease pain in PLP, PLS, and all pain related symptoms, experiencing	Intervention Group: Group: Participants received both the Neuromuscular Electrical Stimulation (NMES) and the Military Amputee Rehabilitation Program (MARP). Subjects participated in a 12-week program where participants were prepared for a prosthetic and practicing using a prosthetic for functional mobility following the MARP protocols. The MARP was delivered by a physical therapist. Subjects were also given a home-treatment of NMES during the 12 weeks for 15 minutes a day for 5 times a week. The NMES was used to stimulate the quad. muscles to create contractions within the legs.	The primary outcome measure was **phantom limb pain.** Other outcome measures included phantom limb sensation, pain within the week, and Pain rating index, # of words chosen, and present pain intensity from the McGill Pain questionnaire.	Phantom limb pain: Both groups demonstrated PLP to be statistically significant ($p=0.004$). However, MARP-only group was more likely to not report daily PLP while NMES+MARP group reports for daily PLP was not significantly different and PLP did not change in comparison to baseline results. Phantom Limb sensation: Overall daily PLS was statistically significant for both groups, $p<0.001$. Pain within the week: Pain for the past week was presented to be statistically significant for both groups however MARP-only group was more likely than NMES+MARP group to report pain at week 7. McGill Pain Questionnaire: Pain Rating index: Both groups improved overtime

	post-amputation pain, unilateral transtibial amputation	Control Group: Participants received only the MARP protocol, where the first 6 weeks focused on prosthetic use and the second 6 weeks focused on using the prosthetics for functional mobility. Both intervention and control groups reported levels of PLP, PLS, pain within the week, and completed the McGill Pain Questionnaire for present pain intensity, pain rating index, and # of words chosen.		and therefore, it is statistically significant with $p<0.001$. # of words chosen: Both groups improved and statistically significant, $p<0.001$. Present pain intensity: NMES+MARP only group reported lower levels of pain and MARP only group reported similar levels of pain intensity in comparison to baseline results. Subjects from NMES+MARP reported less pain than subjects from the MARP only group. However, overall results were statistically significant with $p<0.001$.
Mulvey, M.R., Radford, H.E., Fawkner, H.J., Hirst, L., Neumann, V., & Johnson, M.I. (2013).	**Level of Evidence:** Level III **Study Design:** Cohort study **Participants:** There was a total of 10 transtibial amputees who participated, all of which experienced PLP, stump pain, or both. Patients were recruited from a local rehabilitation center. **Inclusion Criteria:** *average pain of 3 on the NRS during the last month *uses prosthetic for at least 2 hours at a time, 2 times per week	All participants received the same 2- hour intervention. Each participant selected one movement they perceived to the most painful and occurred almost daily. The TENS unit was then used and electrodes were placed according to the identified movement for optimal location. The TENS unit was then turned on for 60 minutes while patients remained in a seated position. Outcomes were measured at rest, 30 minutes into the session, and after 60 minutes. A follow-up was then conducted to gather further information in outcome changes.	The primary outcome was **intensity of pain**, and the secondary outcome was **intensity of prosthetic limb awareness/nonpainful sensation**. Each were assessed using the NRS on an 11-point scale.	It was found, in comparison to the baseline, that pain intensity at rest ($p<0.05$) and at movement ($p<0.05$) were statistically significant while the TENS was on; however, after receiving the intervention of the TENS, these outcomes were not found to be significant. Nonpainful sensation intensity was also found to have no improvement due to the use of TENS. However, all subjects did tolerate the TENS unit well. **Interpretation:** This study began to show that TENS has the potential to be an effective treatment, as it could be used as an aid for perceptual embodiment of the prosthetic limb. It also shows the potential to reduce pain. However, due to a small sample size and intervention dosage, this study presents with moderate evidence supporting the use of TENS as an intervention.

	*no recent changes in medications **Goal:** The goal of this study was to determine whether a TENS intervention produced changes in pain intensity at rest and during movement, perceptional embodiment of the prosthetic limb, and tolerability.			
Tilak, M., et al., (2016)	**Level of Evidence:** Level I **Study Design:** Single Blinded, Randomized Controlled Trial **Participants:** 26 participants who were registered through the Amputee Clinic in Physical Medicine and Rehabilitation *23 were men *average of 45 days post amputation **Inclusion Criteria:** *present with PLP *unilateral amputation *age 18-60 *have no visual or sensory impairment, bleeding disorders, or	Participants were randomized to one of the following groups: Group 1: MT *13 participants *1 dropped out, leaving 12 participants who received this treatment *12 male and 1 female *9 lower limb amputees and 4 upper limb amputees Group 2: TENS *13 participants *11 male and 2 females *10 lower limb amputees and 3 upper limb amputees The duration for the study was 4 consecutive days and participants received 1 treatment session per day.	The primary outcome measure was pain intensity via the visual analogue scale (VAS) and universal pain score (UPS). The VAS is a 10 cm line that indicates no pain on one end and severe pain on the other end. The UPS includes 6 hand draw faces with scores 1-10 which represent happy for no pain and sad for levels of pain.	The MT group has a reduction from 5.46 to 2.08 on the VAS scale ($p = 0.003$) and a reduction from 5.50 to 1.93 on the UPS ($p=0.003$). The TENS group had a reduction on the VAS scale from 5 to 2.46 ($p = 0.001$) and a reduction on the UPS from 5.69 to 2.08 ($p=0.002$). There was no reported significant difference between the two groups. Both intervention types are effective, easily accessible, and can be self-administered by the participants at home.

	bilateral amputation **Goal**: evaluate and compare how MT and TENS improves PLP in amputees by measuring pain intensity pre and post intervention			
Theme 6: Other Imagery and Reprocessing Methods				
Brunelli, S., Morone, G., Iosa, M., Ciotti, C., De Giorgi, R., Foti, C., & Traballesi, M. (2015).	**Level of Evidence**: Level I **Study Design**: RCT **Participants**: 51 participants total (after randomization) but **40** participants analyzed due to drop out; <u>SAIPAN protocol group (experimental):</u> average age = 58.75 years, 14 males and 6 females, 27 participants total after allocation but 20 analyzed. <u>Control group</u>: average age = 65.25, 13 males and 7 females, 24 participants total after allocation but 20 analyzed. Standard physical therapy & exercise group (control): **Inclusion Criteria**: 18+ years and older, female and males,	Intervention Group: Participants received the experimental intervention, where they participated in the SAIPAN protocol. The SAIPAN protocol includes combining progressive muscle relaxation throughout the body, mental imagery of the phantom limb, and utilizing phantom exercises. Phantom exercises were conducted at least 15 minutes or until PLP/PLS was no longer present. If PLP/PLS appeared again, phantom exercises would be restarted with up to 5 new exercise. The intervention group participated in the intervention for 4 weeks and conducted in the intervention 2 times per week for 50 minutes. Control Group: participants received general physical therapy and were part of a general exercise program that focused on various strengthening and stretching exercises, as well as isometric and	Phantom limb pain (PLP) and phantom limb sensation (PLS) based on the intensity, rate, duration, and bother	Intervention group showed significant improvements in all pain factors of rate, duration, intensity, and bother of **PLP** and PLS in comparison to the control group. Intervention group with SAIPAN protocol demonstrated to reduce pain measures in rate, intensity, duration, and bother for **PLP** and PLS within 1 month after interventions were conducted. For **PLP**, the statistical significance of the experimental group showed that the rate duration, intensity, and bother were $p=0.002$, $p=0.006$, $p=0.036$, and $p=0.012$ respectively. For the control group, statistical significance for **PLP** rate, duration, intensity, and bother were, $p=0.307$, $p=0.290$, $p=0.254$, and $p=0.331$ respectively. For PLS, the statistical significance of the experimental group for rate, intensity, and bother are $p<0.001$, $p=0.031$, and $p=0.011$ respectively. For the control group, the statistical significance of the control group for rate, intensity, and bother are $p=0.673$, $p=0.703$, and $p=0.814$ respectively.

	prosthetic users and non-prosthetic users, unilateral lower limb amputees, experiencing phantom limb pain (PLP) or phantom limb sensation (PLS)	dynamic exercises. The exercises were created to work on the residual limb for 2 times a week and over a period of 4 weeks. Both experimental and control groups also received occupational therapy and received prosthesis training.		
Moseley, G.I., (2006)	**Level of Evidence:** Level I **Study Design:** Randomized Control Trial **Participants:** Patients were contacted through a hospital physiotherapy department, neurology, and pain clinic waiting lists. A total 69 were eligible, but after inclusion criteria was assessed, 51 participated, 9 with a brachial plexus avulsion, 9 amputees, and 37 CRPS, detecting a sample size of 0.80. **Inclusion Criteria:** *male or female *no neurologic, psychopathology, motor disorders, or dyslexia *could perform a rapid name test *no visual impairments	There were 2 groups for this study, each of which received different interventions for 6 weeks: **Experimental Group:** There were 25 participants randomly assigned to the experimental group that received a graded motor imagery intervention. No participants withdrew from this group. For the first 2 weeks, participants completed limb laterality recognition. The next 2 weeks focuses on imagined movements. The last 2 weeks consisted of mirror movements. **Control Group:** There were 26 participants randomly assigned to the control group. Individuals in the control group received standard medical and physiotherapy care. One participant withdrew from this group. All 6 weeks consisted of a standard physiotherapy program, and participants maintained usual medical care. One treatment per week was	The primary outcomes measured in this study included **pain** and **function/disability** and were measured before and immediately after the interventions, as well as at a 6-month follow-up. **Pain:** Pain was also assessed using the McGill Pain Questionnaire (MPQ) to determine present pain levels, whereas the Visual Analogue Scale (VAS) measured pain over the last 2 days. **Function/Disability:** Function and disability were assessed by using a Numerical Rating Scale (NRS). This gave patients the opportunity to identify 5 activities/tasks that typically performed daily prior to their injury, but no longer engage in due to pain.	Pain assessed with the use of the VAS and function assessed with the NRS showed positive effects ($p=0.001$, $p=<0.001$, respectively) overall. The experimental group saw a main effect for pain intensity through the VAS ($p=0.002$), as well as for function through NRS ($p=0.001$). At the 6-month follow-up, there was a main effect seen in the control group for pain VAS ($p=0.001$) and function NRS ($p=0.001$). It was found that duration of symptoms does not related to change in VAS ($p=0.224$). At follow up, it was found that all participants in the control group sought care for pain, while only 11 had in the experimental group. **Interpretation:** Though this study was relatively sound, it did bring about a few limitations. When it comes to diagnoses, this type of intervention may be more beneficial to individuals with less traumatic injuries but has the potential to be effective for PLP or BPA, as researchers did mention that the abundance of CRSP1 diagnoses may have concealed strong effects.

	*no other limb pathology or pain *lived too far away from location of intervention **Goal:** The goal of this study was to determine if graded motor imagery would be a more effective treatment method than standard medical and physiotherapy care for individuals with PLP due to previous research on this method being effective for individuals with CRSP1, less traumatic form of PLP.	completed with a physiotherapist, and participants were given HEP.		
Rostaminejad, Akbar; Behnammoghadam, Mohammad; Rostaminejad, Marzieh; Behnammoghadam, Zargham; Bashti, Somaye 2017	**Level of Evidence:** I Randomized Control Trial **Participants**: 60 total participants **Inclusion Criteria:** Patients reporting with PLP at the Clinical Rehabilitation Unit in the city of Yasuj, Iran. Must have amputation.	Groups were split into an experimental group (30) and a control group (30). The intervention included EMDR therapy which is an 8 part therapy that works to identify and address previous experiences that were traumatic and overwhelmed the brain's natural coping capacity. Participants were asked to think of the disturbing image and then in addition, simultaneous bilateral stimulation was performed by the therapist, including alternating eye	Levels of pain were measured through the Subjective Units of Distress Scale and the Pain-rating scale.	The EMDR therapy was administered through 12 one-hour sessions within one month while the control group received daily care. Participants were measured with the Subjective Units of Distress Scale and the Pain-rating scale. It was determined that in the experimental group the PLP decreased between the first and last sessions and remained so at the 24 month follow-up. Differences between the two groups were deemed statistically significant ($P<0.001$).

		movements left and right. The client then reflects on what came to mind. The control was allocated to routine care.		