

BRAIN-COMPUTER INTERFACES IN THE MANAGEMENT OF PHANTOM LIMB PAIN: CURRENT CONCEPTS AND EVIDENCE

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Abstract

Brain–Computer Interface (BCI) technology has rapidly advanced, offering promising applications in neuroscience, rehabilitation, and prosthetic control. This review synthesizes recent developments and ethical considerations in BCI, with a focus on motor imagery (MI)-based systems and their role in neurorehabilitation, particularly for stroke and amputee patients. MI-BCI enables users to control external devices through imagined movements, facilitating communication and motor recovery in individuals with motor impairments or paralysis [18, 1]. Rehabilitation systems integrating BCI with robotics and virtual reality have shown efficacy in improving motor function post-stroke, although challenges remain in system usability, clinical validation, and home implementation [7]. Additionally, BCI training has demonstrated potential in reducing phantom limb pain by modulating sensorimotor brain plasticity, offering novel therapeutic avenues for amputees [18, 20].

Ethical aspects of BCI technology encompass user safety, autonomy, privacy, informed consent, and justice, with emerging concerns related to psychological effects and animal research in commercial ventures [3]. The integration of AI and brain-to-brain interfaces further complicates the ethical landscape, necessitating ongoing discourse and policy development. Signal processing techniques, including feature extraction and classification algorithms, are critical for enhancing BCI performance, with deep learning methods gaining prominence [1]. Despite technological progress,



practical challenges such as electrode attachment, system portability, and real-time multi-intention prediction must be addressed to facilitate daily life applications [2].

In summary, BCI technology holds transformative potential for neuroscience and rehabilitation, yet requires multidisciplinary efforts to optimize technical performance, address ethical concerns, and ensure equitable access. Continued research is essential to refine BCI systems for clinical and commercial use, improve patient outcomes, and guide responsible innovation in this evolving field.

Introduction

Phantom limb pain (PLP) is a complex and debilitating neuropathic pain syndrome experienced by a significant proportion of individuals following limb amputation or severe deafferentation, such as brachial plexus root avulsion [20, 12]. Characterized by painful sensations perceived in the absent limb, PLP affects up to 80% of amputees and often persists chronically, substantially impairing quality of life [4, 16]. Despite its high prevalence and clinical burden, effective treatment options remain limited, with conventional pharmacological and surgical interventions often yielding insufficient relief [8, 12].

In recent years, brain-computer interfaces (BCIs) have emerged as a promising neurotechnological approach to managing PLP by leveraging neuroplasticity and providing real-time feedback to modulate maladaptive cortical representations associated with pain [16, 20]. BCIs enable direct communication between brain activity and external devices, bypassing peripheral neuromuscular pathways, thus offering novel therapeutic avenues for patients with severe motor impairments or amputations [15, 17]. This review synthesizes current evidence on the pathophysiology of PLP, principles of BCI technology, therapeutic protocols employing BCIs for PLP, clinical outcomes, and challenges in translating these approaches into clinical practice.

Pathophysiology of Phantom Limb Pain

PLP arises from complex neurobiological mechanisms involving peripheral, spinal, and central nervous system alterations. Peripheral mechanisms include abnormal spontaneous activity and increased sensitivity of neuromas and dorsal root ganglion neurons, with upregulation of sodium channels contributing to ectopic discharges that may trigger pain [4, 12]. At the spinal level, sensitization of dorsal horn neurons, reduced inhibitory interneuron activity, and enhanced excitatory neurotransmission via glutamate and NMDA receptors have been implicated [4, 12].

Central mechanisms involve maladaptive plasticity and reorganization within the sensorimotor cortex, particularly in the primary somatosensory (S1) and motor (M1) areas. Seminal studies demonstrated that cortical representations of adjacent body parts, such as the face, invade the deafferented hand area in amputees with PLP, correlating with pain intensity (6, 10, 10). However, more recent evidence suggests a nuanced relationship, with some patients exhibiting preserved phantom hand representations associated with pain, indicating that both maladaptive reorganization and residual representation may contribute to PLP [10, 4]. Functional neuroimaging and neurophysiological studies have further revealed increased excitability and altered connectivity in sensorimotor networks in PLP patients [6, 10].





Psychological and psychosocial factors, including anxiety, depression, and maladaptive coping, also modulate PLP severity and persistence, underscoring the multifactorial nature of the syndrome [4, 11]. The interplay between peripheral inputs, central plasticity, and psychological states forms the basis for targeted interventions aiming to restore sensorimotor integration and alleviate pain.

Principles of Brain-Computer Interfaces (BCIs)

BCIs are systems that decode neural activity to generate control signals for external devices, enabling communication and motor control without reliance on peripheral neuromuscular pathways [16, 19]. Signal acquisition modalities include non-invasive techniques such as electroencephalography (EEG), magnetoencephalography (MEG), functional near-infrared spectroscopy (fNIRS), and functional magnetic resonance imaging (fMRI), as well as invasive methods like electrocorticography (ECoG) and intracortical microelectrode arrays [12, 16, 19].

EEG remains the most widely used modality due to its portability, cost-effectiveness, and high temporal resolution, despite lower spatial resolution and susceptibility to artifacts [12, 16]. MEG offers improved spatial resolution and has been effectively used in decoding phantom hand movements for BCI control [18, 19]. fMRI and fNIRS provide hemodynamic measures with high spatial resolution, suitable for neurofeedback applications, though limited by cost and mobility [5]. Signal processing in BCIs involves preprocessing to enhance signal-to-noise ratio, feature extraction (e.g., common spatial patterns, wavelet transforms), and classification using algorithms such as support vector machines, linear discriminant analysis, and deep learning models [1, 17]. Feedback modalities include visual, auditory, and haptic signals, which are critical for neurofeedback-based therapies to induce cortical plasticity [9, 16].

BCI Protocols for Phantom Limb Pain

Therapeutic BCI protocols for PLP primarily utilize motor imagery (MI) paradigms, where patients imagine movements of the phantom or intact limb to modulate sensorimotor cortical activity [15, 19]. Real-time neurofeedback enables patients to observe and control representations of their phantom limb, often via virtual or robotic hand interfaces [18, 19].

Notably, training with a BCI decoder based on the intact hand representation, while patients attempt to move their phantom hand, has been shown to reduce pain and decrease the classification accuracy of phantom hand movements, suggesting attenuation of maladaptive cortical representations [18, 19]. Conversely, training with a decoder based on the phantom hand representation may increase pain by enhancing maladaptive plasticity [19].

Neurofeedback training without explicit phantom hand movements or hand-like visual feedback has also demonstrated feasibility in modulating pain and cortical representations, indicating that awareness or ownership of the phantom limb is not essential for therapeutic effects [20]. Hybrid BCIs integrating augmented or virtual reality environments provide immersive feedback that may enhance engagement and efficacy [7, 13].

Clinical Evidence and Therapeutic Outcomes

Randomized controlled trials and feasibility studies have reported significant reductions in PLP following BCI training protocols. For instance, a randomized crossover trial demonstrated a 32–





36% reduction in pain sustained for up to one week after three days of BCI training using an intact hand decoder [18, 19]. These effects are comparable to or exceed those observed with mirror therapy or augmented reality interventions, which typically require longer training durations [13, 15].

Neuroimaging studies confirm that BCI training induces plastic changes in sensorimotor cortical representations, with pain modulation correlating with alterations in classification accuracy of cortical activity patterns [18, 19]. These findings support a causal relationship between sensorimotor cortical plasticity and PLP.

Clinical applications of BCIs extend beyond pain reduction to include functional rehabilitation, as demonstrated in stroke patients using MI-based BCI systems coupled with functional electrical stimulation (FES), robotic assistance, or virtual reality feedback, which promote motor recovery through neuroplasticity [9, 7, 14].

However, many studies are limited by small sample sizes, heterogeneity in patient populations (e.g., amputation vs. brachial plexus injury), and short follow-up periods, necessitating further large-scale, longitudinal trials to establish efficacy and optimize protocols [7, 15, 18].

Challenges and Limitations

Technical challenges in BCI applications for PLP include low signal-to-noise ratios, variability in cortical representations, and the need for individualized calibration and training protocols to address user-specific neurophysiological and psychological factors [9, 16]. BCI illiteracy or inefficiency, where users fail to generate consistent control signals, remains a significant barrier [9, 16].

The complexity of PLP pathophysiology, involving both maladaptive and preserved cortical representations, complicates the design of targeted BCI interventions [6, 10]. Moreover, the high cost and technical demands of BCI systems, particularly those employing MEG or fMRI, limit accessibility and scalability compared to simpler approaches like mirror therapy [15, 18].

Ethical considerations include ensuring informed consent, especially in patients with communication impairments, safeguarding privacy and security of neural data, and addressing potential psychological impacts of BCI use [3, 15]. The need for interdisciplinary collaboration among neuroscientists, clinicians, engineers, and ethicists is paramount to address these challenges and facilitate clinical translation [3, 14].

Discussion

This review underscores the potential of brain-computer interface (BCI) systems, particularly those utilizing motor imagery (MI), as innovative tools for alleviating phantom limb pain (PLP) through modulation of maladaptive cortical plasticity. Several randomized trials and feasibility studies have demonstrated significant reductions in PLP following BCI interventions. Notably, Yanagisawa et al. [18, 19] reported a 32–36% pain reduction sustained for up to one week after only three days of BCI training using a decoder based on intact hand representation. These findings suggest that MI-based BCIs can induce clinically meaningful changes with relatively short intervention durations, potentially surpassing traditional approaches like mirror therapy or augmented reality, which often require longer periods [13, 15].

A central insight emerging from these studies is the importance of decoder selection in therapeutic outcomes. Training with an intact hand decoder was associated with decreased pain and a reduction





in classification accuracy of phantom hand movements, indicating a disruption of maladaptive cortical representations. In contrast, training with a phantom hand decoder increased pain levels, likely due to reinforcement of pathological activity patterns [18, 19]. This reinforces the critical role of targeted neuroplasticity modulation in BCI design for PLP treatment.

Furthermore, newer paradigms have shown that explicit visual representation or awareness of the phantom limb may not be essential for therapeutic efficacy. Neurofeedback protocols that omit hand-like visual feedback or even phantom hand movement still yield positive results, indicating that sensorimotor feedback alone is sufficient to induce cortical changes and reduce pain [20].

Despite these promising results, important limitations must be acknowledged. Many studies are constrained by small sample sizes, short follow-up durations, and heterogeneous populations, including both amputees and patients with brachial plexus injuries [7, 15, 18]. These factors limit generalizability and hinder the formulation of standardized clinical protocols.

Moreover, several technical barriers remain. BCI performance can be hindered by low signal-to-noise ratios, inter-individual variability in cortical representations, and BCI inefficiency—where some users fail to generate consistent control signals despite training [9, 16]. Additionally, high costs and limited portability of advanced imaging modalities such as MEG and fMRI restrict the scalability of certain systems [15].

From an ethical perspective, the use of neural data and patient autonomy presents new challenges. Informed consent, especially in patients with severe communication impairments, as well as the psychological impact of engaging with BCI systems, must be carefully considered [3, 15]. Furthermore, the integration of AI and virtual environments into BCI raises questions about transparency, accountability, and long-term effects.

In conclusion, BCI-based interventions hold substantial promise for treating PLP by leveraging cortical plasticity through real-time feedback and motor imagery paradigms. However, to transition from experimental to routine clinical use, larger, longitudinal trials, standardized protocols, adaptive algorithms, and ethical safeguards are essential. The path forward lies in developing cost-effective, user-friendly, and clinically validated BCI systems that can improve quality of life for individuals suffering from phantom limb pain.

Conclusion

BCI technology represents a promising and innovative approach to managing phantom limb pain by modulating maladaptive sensorimotor cortical plasticity through neurofeedback and motor imagery paradigms. Empirical evidence supports the efficacy of BCI training in reducing PLP and inducing beneficial cortical reorganization, with effects comparable to established therapies such as mirror therapy.

Advances in signal acquisition, processing, and classification, alongside immersive feedback modalities like virtual and augmented reality, enhance the potential of BCIs for both pain management and functional rehabilitation. Nonetheless, significant challenges remain, including technical limitations, user variability, cost, and ethical concerns, which must be addressed through rigorous clinical trials and interdisciplinary efforts.

Future research should focus on optimizing BCI protocols, expanding sample sizes, extending follow-up durations, and integrating adaptive algorithms to overcome BCI inefficiency. The





development of cost-effective, user-friendly, and scalable BCI systems will be critical for broader clinical adoption and improving the quality of life for individuals suffering from phantom limb pain.

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