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What is This?
Phantom Limb Pain After Lower Limb Trauma: Origins and Treatments

Jens Foell¹, Robin Bekrater-Bodmann¹, Herta Flor¹, and Jonathan Cole²,³

Abstract
Phantom sensations, that is, sensations perceived in a body part that has been lost, are a common consequence of accidental or clinical extremity amputations. Most amputation patients report a continuing presence of the limb, with some describing additional sensations such as numbness, tickling, or cramping of the phantom limb. The type, frequency, and stability of these phantom sensations can vary immensely. The phenomenon of painful phantom sensations, that is, phantom limb pain, presents a challenge for practitioners and researchers and is often detrimental to the patient's quality of life. In addition to the use of conventional therapies for chronic pain disorders, recent years have seen the development of novel treatments for phantom limb pain, based on an increasing body of research on neurophysiological changes after amputation. This article describes the current state of research in regard to the demographics, causal factors, and treatments of phantom limb pain.

Keywords
Phantom limb pain, amputation, pathogenesis, treatment, neuroscience

Introduction
Phantom limb phenomena, that is, sensations in a body part that has been lost, have long been known in medicine and folklore. It is said that British war hero Admiral Lord Nelson, after losing his right arm in the Battle of Santa Cruz de Tenerife in 1797, continued to feel the fingers of this arm and believed that this provided "a direct proof of the existence of the soul,"¹ since part of his body continued to be felt even after its physical destruction. Even before this, in 1552, it had already been assumed that this so-called phantom limb pain (PLP) is physiological in nature, due to either peripheral factors or to a pain memory,² in modern terms.

Most amputees report some presence of the lost limb,³,⁴ with most of them suffering from PLP.⁵ In addition to amputations of extremities, phantom sensations and PLP have been reported after the loss of body parts such as teeth,⁶ internal organs,⁷ or genitalia.⁸ PLP can also occur when a limb is still present, but the afferent or sensory nerves are damaged, for example, after spinal cord injury⁹ or brachial plexus avulsion.¹⁰ Both PLP and nonpainful phantom phenomena have occasionally been reported in patients with congenital limb deficiencies,¹¹,¹² but it is unclear how those cases relate to PLP after amputation.¹³

PLP is a highly heterogeneous syndrome in terms of the development, frequency, intensity, and quality of pain, ranging from occasional slight painful sensations to constant severe pain. Some patients can determine the location of the perceived pain precisely, while others report diffuse pain that cannot be located with certainty. Both PLP and nonpainful phantom phenomena can first occur immediately after amputation or years later and can be alleviated or exacerbated by factors such as attentional focus, change in weather, or emotional distress.¹⁴,¹⁵

While the phantom limb usually resembles the somatosensory experience of the lost limb, it is notable that this is not always the case. Size and shape can be perceived differently to before and its posture can even be distorted into physically impossible positions.⁴ One particular distortion is "telescoping"¹⁶,¹⁷: here, the phantom arm or leg is perceived to shorten, with the hand or foot shifting closer to the residual limb. In arm amputees, this can lead to the phantom fingers being perceived as directly attached to the stump, say in the upper arm. After lower limb amputation, telescoping can lead to the phantom foot being perceived to be...
above floor level. The phantom limb can also be immobile or subject to voluntary or involuntary movements.

**Demographics**

Since the worldwide number of amputations is currently not tracked by any organization, it is difficult to determine the international prevalence of major limb amputations. In the United States, it is estimated that about 1.7 million people are currently living with an amputation. Due to demographic changes and higher rates of vascular diseases, this is likely to more than double in the mid-21st century.

The causes of amputations differ considerably for arms and legs. While vascular disease, secondary to diabetes, accounts for more than 40% of leg amputations, it is only the cause of about 5% of arm amputations. Injuries are more frequently the cause of arm (80% to 90%) than leg amputations. Cancer accounts for only a minority of amputations in both extremities. Lower limb amputations are therefore usually performed by elective surgery. Recent decades have seen a shift in the relative frequencies of above-knee and below-knee procedures, with the increasing rate of below-knee amputations improving patient mobility and rehabilitation, because in these patients, the preservation of the natural knee joint allows a higher functionality of the remaining leg.

A common side effect after an amputation is PLP. In epidemiological studies, prevalence rates of 51% to 80% were reported. In these studies, a total number of about 5700 amputees was surveyed, with an average PLP prevalence of 74.6%; children and adolescents suffer less often from PLP. The incidence of phantom pain in the first 6 months after the amputation is approximately 72% (54% to 82%) in the first 6 months after the amputation, although the incidence in arm amputations appears to be higher than in leg amputees. There are no differences between arm and leg amputations regarding pain intensity, although the probability of developing severe PLP is increased after leg amputation and is also associated with depressive symptoms. The prevalence of nonpainful phantom sensations lies between 70% and 90%. The presence of residual limb pain is positively correlated with PLP.

Beside the high prevalence of PLP, there is a remarkable amount of pain comorbidity in both leg and arm amputees: there are high rates (more than 20% each) of pain in the remaining leg, buttocks, neck, and shoulders, as well as arms and hands. Residual limb pain (45% to 74%) and back pain (about 50%) seem to be of particular clinical relevance. These complications in amputees go hand in hand with high rates of sleep disorders.

Prosthetic use is more common in leg amputees than in arm amputees, and they use the prosthesis longer per day. This use of the prosthesis depends on several factors, such as the type of amputation, age at amputation, and speed of rehabilitation. Older people use them less and have many more difficulties after amputation, which could be related to a higher overall morbidity. Factors that improve rehabilitation include an increase of muscle strength, flexibility, cardiovascular fitness, and balance and coordination.

PLP and phantom sensations were found to influence patients’ well-being after amputation. In lower limb amputees, PLP, together with factors such as residual limb pain and walking distance, reduced patients’ health-related quality of life. In a long-term survey of lower limb amputees, the presence of involuntary phantom movement was associated with lower physical health–related quality of life.

**Pathogenesis**

The large variation in prevalence, symptoms, and development described above suggests a multifactorial origin for PLP. The removal of an extremity, especially in a non-clinical context such as in an accident or during combat, is a severe disruption of the body’s integrity with negative effects on mechanical, peripheral, and central physiological as well as psychological levels. In an experimental attempt to investigate the relative influence of central and peripheral factors, the brachial plexus nerves of PLP patients were anesthetized. Since this method inhibits the transmission of nerve signals from the extremity to the central nervous system, it was assumed that the pain would be eliminated if produced primarily by the peripheral system but would be unaltered if the pain was generated in the central nervous system itself. It was found that this method alleviated pain in about 50% of the investigated patients, suggesting that both central and peripheral mechanisms contribute to the experience of PLP. Thus, both possible origins of this complex phenomenon will be discussed below.

**Peripheral Nervous System**

When a peripheral nerve is severed, the disconnected endings start growing toward each other. If successful, this bridges the gap between proximal and distal neural stump and repairs the damage. However, if one part of the nerve cell is too far away or even removed entirely, which is the case in a majority of amputations, this regrowth of the remaining nerve can lead to the formation of tangled knots of neural tissue. These neuromas are known to show spontaneous and unpredictable activity and might contribute to pain in some patients. Since they are located in the residual limb, neuromas are usually seen as a cause of residual limb pain rather than PLP. However, they have been reported to elicit both PLP and residual limb pain and there have been reports of alleviation of PLP after the removal of neuromas.
The individual differences in the type and location of nerve damage after a nonclinical amputation and the particular way that damaged neurons regrow in tangles in a specific patient could explain some of the large variation in the experience of PLP as well as residual limb pain. Apart from spontaneous ectopic discharges, neuromas can also display changes in transduction molecules for sensitivity to heat, cold, and mechanical stimulation. It is interesting to note that some patients report increased PLP as a consequence of external temperature change or nonpainful residual limb stimulation, which may be explained by this change in excitability. Since the formation of neuromas after nerve damage takes some time, this phenomenon may not fully account for the symptoms of those patients who report pain immediately after the amputation.

Ectopic discharges perceived as painful can not only originate in peripheral neuromas but also in the dorsal root ganglia (DRG), small nuclei of nerve cells that lie on the sensory dorsal root of each spinal segment and which contain the cell bodies of afferent sensory spinal neurons. These ectopic signals from the DRG can also be intensified by the interaction of neighboring cells and can summate with the signals from peripheral neuromas, leading to a higher nociceptive input. The finding that these signals can be created or intensified by sympathetic activation may contribute to the higher levels of PLP during emotional stress. There is evidence that the development of neuromas and DRG discharge may be influenced by a genetic disposition.

Spinal Cord

There are several mechanisms that can cause long-term hyperexcitability in spinal cord neurons after nerve damage and each of these may occur by itself, or in combination with the others, to enhance nociceptive input. It has been shown that neural injury can lead to a downregulation of opioid receptors, both on primary sensory nerve endings and on intrinsic spinal neurons. This may lead to a reduction of the inhibitory neurotransmitters γ-aminobutyric acid (GABA) and glycine, increasing the risk of spinal disinhibition. In addition, interneurons containing these substances may be destroyed by ectopic discharge or other consequences of axotomy or might change from an inhibitory to an excitatory effect under the influence of brain-derived neurotrophic factor (BDNF), which is released by microglia cells. At the same time, cholecystokinin, an inhibitor of opiate receptors, can be upregulated in injured neural tissue and thus lead to, or increase, the same effect. Another reaction to nerve tissue damage that might lead to long-term effects is the facilitation of N-methyl-D-aspartate (NMDA) receptor responses to glutamate, which can alter firing behavior in ascending projection neurons from the spine to supraspinal centers. The complex hyperexcitability caused by these processes has also been shown to spread as a result of functional reorganization, leading to an expansion of neighboring receptive fields in animals.

All these mechanisms influence the sensitivity of spinal neurons. However, there is also evidence that myelinated Aβ-fibers, which usually convey nonnociceptive touch and proprioceptive information, express substance P (a neuro-peptide associated with inflammatory processes and nociception) as a consequence of injured tissue. By this means fibers that are usually unrelated to nociception may turn into transmitters of nociceptive information after amputation.

That alterations at a spinal level can contribute to PLP is further supported by the finding that some pain-free amputees experience PLP during spinal anesthesia. However, the mechanisms of this effect are not fully understood at present.

Brainstem, Thalamus, Cortex

Even though the described alterations could account for some of the variations in PLP, the intensity and frequency of this type of pain has also been found to be connected to alterations in the anterior cingulate, somatosensory and motor cortices, brainstem, and thalamus. The latter 3 areas have strong connections to each other although it is as yet unclear how structures interact when one or more of them are altered after peripheral tissue damage. It is known, however, that in cortical as well as thalamic  and anterior cingulate areas, limb amputation can lead to reorganizational processes.

This reorganization occurs in several distinct stages. In the first stage, neural connections that are usually inhibited are unmasked. Unmasking is connected to an increased release of excitatory neurotransmitters, a higher density of postsynaptic receptors, an altered conductance of neural membranes, decreased inhibitory inputs, and the removal of inhibition from excitatory inputs and results in higher cortical excitability in those amputees that experience PLP. In the second, later stage, these biochemical alterations are enhanced by structural changes such as the creation of new axons (axon sprouting), and changes in synaptic strength even proposed a third stage of reorganization, in which receptive fields are refined according to their use. Such a use-dependent reorganization could be aided by the mechanisms of Hebbian learning and long-term potentiation. Additionally, it has been proposed that peripheral C-fibers have an inhibitory effect on cortical representation zones, which suggests that the loss of these fibers through amputation may facilitate reorganizational processes in these regions.

In the cortex, this reorganization refers to alterations in the representation of the body. A familiar depiction of this cortical body representation is in the form of a so-called homunculus, a humanoid figure that is stretched and...
distorted to demonstrate the differences between the actual size of a limb and the size of the brain area devoted to it. In somatosensory cortex, for example, lips and fingers, skin regions with a high sensitivity, have a large representation. Cortical reorganization of sensory representations, sometimes up to a shift of several centimeters, has been shown after limb amputation in animals \textsuperscript{69} and humans \textsuperscript{70,71}, here, the areas of primary somatosensory cortex (SI) that were representative for the lost body part are “invaded” by neighboring nerve cells and begin to represent other, remaining, body parts (see Figure 1). This type of reorganization may be a dysfunctional variation of a usually beneficial mechanism, sculpting cortical neurons according to body shape and activity: for example, cortical representation of the fingers is enlarged in string players \textsuperscript{71}, demonstrating how the areas of the cortex related to a specific body part within the sensorimotor cortex can come to represent its level of functional involvement.

Important for the understanding and treatment of PLP is that the magnitude of the shift in somatosensory cortex and to a lesser extent also in motor cortex that occurs after limb amputation is directly proportional to the intensity of PLP \textsuperscript{41,62,71-74}. This finding allows the evaluation of therapy methods at a neurophysiological level by assessing the reorganizational state of the patient’s cortex using neuroimaging techniques. Also, it helps understand the mechanisms behind PLP.

Earlier, it had been proposed that the cortical shift is primarily responsible for so-called referred sensations \textsuperscript{75}, in which a patient feels a touch on the phantom limb when a specific location on their skin is touched \textsuperscript{76}. However, the brain regions involved in this phenomenon seem to be more those involved in the integration of body signals (premotor cortex, parietal regions) rather than the somatosensory cortex \textsuperscript{77}.

The consequences of cortical reorganization after limb amputation have mostly been investigated in upper extremity amputees, although in general, the same mechanisms should apply for arm and leg amputation. A recent study by Kapreli et al \textsuperscript{78} investigated differences in the cortical organization of upper and lower limbs. Although knees, ankles, and toes are represented somatotopically in sensory area SI (just like elbows, wrists, and fingers), with the knee located more laterally and inferiorly than the other limb joints, Kapreli et al \textsuperscript{78} found differences in the amount of overlap between joint representations in the cerebellum. While the activation sites of fingers were clearly separated, the representations of the 3 lower limb joints (in the same subjects) displayed a large overlap. Accordingly, the somatopic representations of the lower limb parts were considerably closer to each other than those of the upper extremities. As of this time, it is unclear how this might influence a cortical reorganizational shift and its connection to PLP, although it is conceivable that such a difference in cortical body representation may be responsible for the recent finding of a lower odds ratio of PLP in lower limb amputees \textsuperscript{79}.

**Psychological Factors**

Individual differences in terms of cognition, affect, and behavior have been shown to influence the physiology and biochemistry that determines the generation and continuance of chronic pain \textsuperscript{80}. Recently, Vase et al \textsuperscript{81} investigated the phenomenon of pain catastrophizing, a possible psychological reaction in chronic pain patients. They found that this behavior, independently of other psychological factors such as anxiety and depression, explained 35\% of the variation in PLP. While most psychological responses to chronic pain are not unique to PLP patients, it seems
plausible that the special physiological and psychosocial circumstances present after extremity amputation may require further research into idiosyncratic emotional and behavioral reactions of amputees in relation to sufferers of other kinds of chronic pain.

Another factor may be the psychological ability to accept the limb affected by chronic pain or amputation as a part of one’s own body: it has been proposed that chronic pain in a body part is connected to ownership (ie, the subjective perception that a specific body part belongs to me) and agency (the sensation of being the initiator of certain acts of the body part), both of which are impaired in cases where the phantom limb is inconsistent, distorted, or cramped.82 This disruption of the feelings of ownership and agency may contribute to the generation of painful sensations and thus the recreation of these feelings is an element of several of the treatment methods described below.

**Pain Memory**

In many cases of clinical amputation, the affected limb has been painful for some time before the amputation, for example, because of vascular disease or a tumor. It has been found that this type of preoperative pain is a predictor for PLP,83 and there is some evidence for a similarity of pre- and postamputation pain.84 These phenomena suggest an influence of pain memory, that is, long-term changes in the central nervous system as a result of persistent nociceptive input.85,86 It is possible that neurons that used to be representative for the affected limb become strongly associated with painful sensations and become activated again after their cortical area is being invaded by neighboring regions. Because of their initial connection to the amputated limb, the painful sensation may be interpreted as originating from said limb, thus leading to PLP.87 However, against this, it has been argued that pre-amputation pain only predicts short-term PLP (up to 6 months after amputation) and may not be related to long-term postamputation pain.88

The possible contribution of pain memory brings peripheral anesthesia into focus: based on this concept, blocking nociceptive input from the affected limb before and during amputation might be expected to prevent the development of pain memory. The results on this approach have been controversial, with some researchers reporting pain relief,89 but others not.90

**Treatment**

PLP may depend on a multitude of factors as described above, including structural and functional alterations in the central and peripheral nervous systems as well as individual dispositions resulting from genetic, psychological, and experiential idiosyncrasies and is very resistant to treatment, with a gap between research and practice.90 About 3 decades ago, an extensive survey identified 68 therapeutic approaches to PLP, most of which were not even moderately effective.91 In the following section, we will discuss treatments that have been developed since that time and which have been proven to alleviate PLP in a clinical setting at least in some patients: pharmacological approaches, prosthesis use, sensory discrimination, mirror treatment, mental imagery, central stimulation, and behavioral chronic pain treatments that are not specific for PLP.

**Pharmacological Approaches**

One of the major causal factors for PLP, as described above, is cortical reorganization. Certain substances able to disrupt this process, such as NMDA receptor antagonists or GABA agonists, have been successfully used to prevent and reverse cortical reorganization in animals.92 Applying these substances during and after amputation may alleviate pain in human PLP patients.93,94 Further research relating to NMDA receptor antagonists revealed the short-term effectiveness of ketamine,95 although memantine was not effective.96,97 There has also been some success using substances not directly connected to cortical reorganization: patients with pain deriving mostly from neuromas seem to benefit from the application of lidocaine.98 Opioids, which are widely used for the treatment of neuropathic pain syndromes, have been used successfully in some patients with PLP,99 although the effect of gabapentin, which is also used in patients with neuropathic pain,100 is controversial in regard to pain in the phantom or residual limb.101,102

**Sensory Discrimination Training**

In a sensory discrimination paradigm, patients are instructed to report on the perceived location and frequency of tactile stimuli applied to the residual limb. It has been shown that after a number of 90-minute sensory discrimination training sessions with a steadily increasing difficulty level, patients’ ability to determine stimuli on the residual limb increases, and that with that, PLP intensity decreases up to 60% and dysfunctional cortical reorganization is reversed.103 Significant PLP alleviation was also reported after asynchronous stimulation of both the residual limb and the hip.104 In patients suffering from complex regional pain syndrome (CRPS), it has been shown that tactile stimulation only alleviates pain when patients are required to report on the location and type of the stimulus, indicating an effect of discrimination rather than passive tactile stimulation alone,105 in agreement with the previous reports. It is feasible to combine sensory discrimination trainings with other treatment options: one example would be a prosthesis that stimulates the residual limb in a way similar to the
training. One obstacle to this treatment is a loss of sensitivity in the residual limb, which can occur in some patients.

**Mirrors and Virtual Reality Applications**

Recent years have seen the application of mirror therapy for PLP in unilateral amputees. Here, a mirror is placed next to the patient's residual limb to create the illusion of a second intact limb, with the mirror image replacing the lost limb in the visual field.\(^{106}\) If set up correctly, repeated movements in front of the mirror of the intact limb will create the illusion of a controllable replacement limb (or, alternatively, a visualized phantom limb) in some patients. Ramachandran and Rogers-Ramachandran\(^{106}\) found that when patients saw and felt their amputated limb return, in and through the mirror, it relieved the painful cramps in the phantom reported by some patients. The treatment requires only very simple equipment and is free of side effects. It has led to pain alleviation in lower limb amputees with PLP after a 4-week controlled trial.\(^{107}\) However, about 40% of patients do not benefit from mirror treatment,\(^{108}\) and the pain reduction has not yet been correlated with other variables, such as a reduction of dysfunctional cortical reorganization. Furthermore, Casale et al.\(^{109}\) report high rates of treatment withdrawal even after few treatment sessions in a sample of lower limb amputees and recommend prior selection of the patients based on psychological and clinical factors. It has led to pain alleviation in lower limb amputees with chronic PLP after a 4-week controlled trial (as shown by our own data in Figure 2).

As mentioned earlier, chronic pain has been related to a lack of ownership and agency over the affected limb.\(^{82}\) It is conceivable that mirror training works by supplying a replacement limb that can be controlled and integrated into the body representation. At the moment, it is unclear who will benefit from this type of treatment and whether there are variations to the paradigm that may increase its effectiveness. One possibility may be the use of virtual reality or augmented reality setups, in which the mirror image is replaced by a computer-generated graphic representation of the lost limb. This technique provides increased flexibility, for example, for patients that have trouble controlling the residual limb because of paralysis or muscle damage or for patients with a severely deformed phantom limb. In the paradigms described above, the remaining limb has to be fully functional, so that its mirror image appears to be intact. A recent exploratory study\(^{110}\) circumvented this by using signals derived directly from the residual limb to control a virtual limb.

**Prosthesis Use**

Depending on amputation site and condition of the residual limb, there are several types of prostheses that amputees can use. Cosmetic prostheses recreate the lost limb visually and can be used as a support in several tasks, while myoelectric prostheses allow the user to control movements such as grasping or flexion of the elbow or knee by giving muscle commands. Unfortunately, on average most patients do not use their prostheses regularly, either because they do not consider them to be useful or because their use can cause or increases residual limb pain.\(^{23}\) Based on the results and proposed mechanisms of mirror therapy described above, it could be argued that a controllable
prosthesis is conceptually similar to a controllable mirror image of the intact limb, in that it can create sensations of agency and ownership. Therefore, it may be expected that patients with a myoelectric prosthesis report lower levels of PLP than those without. Indeed, Lotze et al. found that PLP, measured both by subjective reports and by the assessment of cortical reorganization, is lower in patients that use their myoelectric prosthesis for the most time of the day and use it to complete everyday tasks. This finding was supported by Weiss et al., who found a decrease of PLP (but not of non-painful phantom phenomena) in patients using prostheses with limited functionality versus patients using noneffective cosmetic prostheses. Additionally, lower limb amputees probably might have more benefit from regular prosthesis use than upper limb amputees in terms of less experience of PLP. However, these are cross-sectional studies and thus the causal connection between prosthetic use and pain intensity is not entirely clear.

Technological improvements in the quality of functional prostheses should help alleviate PLP further. Weiss et al. proposed that using the same muscles, and therefore the same nerve fibers, as before the amputation, might inhibit cortical reorganization by providing the cortex with consistent information about the limb. Current developments may soon allow tactile information to be received using the surface of the prosthesis and to relay this information to the patient via tactile or electrical stimulation of the residual limb. In patients not able to use a prosthesis or having difficulties adjusting to the use of an artificial limb, virtual reality environments may be used to simulate the use of a life-like functional prosthesis.

Another current approach is the improvement of prosthesis controllability using biorobotics. In a recent proof-of-concept study, upper limb amputees were instructed to perform movements with the missing limb mentally. These movement commands were recorded using electrodes implanted directly into the patients’ median and ulnar nerves and could be used to control a robotic limb.

Mental Imagery

In mental imagery paradigms, the missing limb is visualized using imagery of the limb and its movement rather than mirrors or virtual reality environments. Diers et al. compared cortical activity during both mental imagery and mirrored movement tasks and found that patients suffering from PLP reacted with activation in different cortical areas all related to body processing (primary somatosensory and motor cortices in mirror condition, and supplementary motor area in imagery condition). In a graded imagery paradigm, patients are required to perform specific movements in their minds, for example, by watching an image of a hand and imagining recreating the observed hand’s posture with their own hand. It has been shown that a regular training of this imagery reduces PLP as well as reducing cortical reorganization, although its effectiveness is disputed. The specific mechanisms behind these treatments, as well as the relative relevance of visual input or controllability of the simulated limb, have yet to be determined, with Sirigu and Duhamel suggesting that different sets of instructions cause participants to use different brain regions for mental imagery tasks, altering the outcome of the procedure.

Central Stimulation

The only nonbehavioral approach that tries to influence cortical reorganization is central stimulation. Here, electrical or magnetic pulses are used to alter the firing patterns of cortical neurons. This can be done invasively or noninvasively. In the former, electrodes are implanted directly above the motor cortex, which has been shown to be effective in some patients. Since invasive procedures always bear the risk of infection or other complications, recent efforts have aimed at stimulation through the skull in a noninvasive manner. Transcranial magnetic stimulation uses magnetic coils to create a magnetic field that induces electricity at a specific location on the cortex and has been shown to be effective in some PLP patients. Similar results have been found using transcranial direct current stimulation. For now, however, these methods can only be used in a laboratory setting.

Chronic Pain Treatments

Several behavioral treatment approaches have been used for PLP as well as for other types of chronic pain. Research on learned nonuse of a limb has led to the development of constraint-induced movement therapy, which has initially been used for stroke victims and has since been adapted for PLP. A pilot study on biofeedback approaches to PLP supports the use and further investigation of this method. A combination of biofeedback, progressive muscle relaxation, and psychological support has been effective in recent and chronic sufferers from PLP. Because of the correlation between preoperative and postoperative pain mentioned above, it has been proposed that, in addition to preoperative and perioperative analgesics, behavioral treatments applied before amputation may also have a beneficial effect on postoperative pain.

Conclusions

PLP is a frequent and persistent consequence of lower limb amputation and can significantly impede a patient’s quality of life. The development and the symptoms of PLP can vary widely among individuals and over time, and its causal and exacerbating factors are multilayered, including
several types of changes in the central and peripheral nervous system. These factors make the disorder difficult to understand or treat. Increasing knowledge of painful and nonpainful phantom sensations as well as peripheral and central reorganizational processes after amputation has facilitated the development of novel behavioral treatments such as mirror training, sensory discrimination, or mental imagery. Further investigations of perceptual changes after amputation and increased efforts in regard to prosthesis development and behavioral treatment methods will be needed as patients live longer and as diabetes becomes more frequent, leading to an expected higher frequency of lower limb amputations in the future.

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