

Examining the Mechanisms of Phantom Limb Pain

Benjamin Clark, Anne Austin, Rachelle Denman, Kent McCuistion, Stacey Smith
Faculty: Dr. Ken Pitteti

Department of Physical Therapy

Abstract. Phantom limb pain (PLP) is pain (shooting, stabbing) emanating from the missing limb(s) and is the most prevalent amputee-related pain. Therefore, it is important for clinicians who treat amputees to understand the underlying mechanisms of PLP. The purpose of this study was to review the literature on PLP and collaborate with amputees to identify its possible origins. Potential sources involved both peripheral and central locations within the nervous system. Our findings suggest multilevel neuroplasticity primarily located in the peripheral nerves, spinal cord and/or thalamocortical networks, indicating the need for diverse methods of treatment.

1. Introduction

Phantom limb pain (PLP) is commonly referred to as “pain in the missing part of the limb” or “painful sensations referred to the absent limb”. Phantom pain is described as shooting, stabbing, boring, squeezing, throbbing and burning [1]. In the United States, there are approximately 1.7 million people living with limb loss and it is estimated that one out of every 200 people in the U.S. has an amputated appendage. Phantom pain has been reported as high as 80-85% in persons with limb loss. Although it may be constant, PLP is usually intermittent, with the majority experiencing pain weekly. It can be extremely debilitating in that 50% of American veterans experienced PLP sufficiently severe to hinder their lifestyle on more than 6 days each month [2]. Therefore, it is important for clinicians treating persons with limb amputations to understand the underlying mechanisms that contribute to phantom pain and therefore, approaches to treating PLP.

2. Experiment, Results, Discussion, and Significance

Recent literature (1990-present) on PLP was reviewed and compared to interviews involving a recent (< 6 months post) and two long standing (> 30 years) traumatic amputees. The interviews involved questions addressing precipitating and mitigating events, the quality and frequency of pain and type of treatment for their PLP.

Pain enters the spinal cord via peripheral afferent C-fibers and alpha-delta fibers. Peripheral afferent fibers synapse within the dorsal horn of the spinal cord on second order neurons or projecting neurons. The projecting neurons are at the origin of two important ascending pain pathways, the spinothalamic and spinoreticular, which carry pain messages to the brainstem and thalamus. As these pain pathways ascend rostrally through the brainstem they will synapse with neurons in the periaqueductal gray and nucleus raphe magnus. Synapsing in these nuclei will engage descending modulating pathways that will regulate pain output at the level of the spinal cord.

The projections of the spinothalamic pathway eventually end in the thalamus. Projecting fibers from the thalamus convey painful and thermal sensation to the primary somatosensory cortex (i.e., the homunculus). Input to the homunculus allows for localization of stimuli and intensity of the pain.

Within this pathway, the mechanisms thought to be the source of PLP involve peripheral nerves from the stump, the dorsal horn of the spinal cord, and central reorganization both in the spinal cord and homunculus [1]. Recent literature indicates that the amount of maladaptive cortical reorganization directly correlates to the intensity of PLP felt. We will begin discussing the mechanisms of PLP in the peripheral nervous system. [3].

Peripheral:

- Stump neuroma
 - Hyperexcitability of pain fibers originally from the amputated limb;
 - Formation of ephapses causing “cross talk” of stump pain fibers to pain fibers once originating from the amputated limb;
 - Cold enhanced reflexive norepinephrine release from sympathetic-efferent fibers within the neuroma stimulating novel expression of α_2 -adrenergic receptors on the terminal of pain fibers from the amputated limb.
- Dorsal horn of spinal cord
 - Loss of afferent input from the amputated limb leads to decreased inhibitory impulses from descending modulating pathways (i.e., periaqueductal gray and nucleus raphe magnus);
 - Absence of descending inhibition causes projecting neurons to send “painful epileptic discharges” rostrally.
- Central reorganization-dorsal horn of spinal cord:
 - Afferent fibers from stump “invade” inactive/silent regions of the dorsal horn;
 - Painful afferent information from stump interpreted as pain from the phantom limb.
- Central reorganization—somatosensory cerebral cortex/homunculus:
 - Arborizing fibers from adjacent areas (e.g., face, stump of upper arm) “invade” inactive/silent regions of the phantom limb (e.g., hand) in the somatosensory cortex;
 - Painful afferent information from face/stump of upper arm interpreted as pain from phantom hand.

Mechanism-based treatment modalities for phantom pain:

- Peripheral involves blocking initiation or conduction of action potential of pain fiber or utilization of “Gate control theory” according to Melzack [4]:
 - Local anesthetic injections (e.g., lidocaine) into stump;
 - Peripheral nerve stimulation (pulse radiofrequency, massage).
- Central treatment consists of pharmacological manipulation of pain pathways in spinal cord, brain stem, and cerebral cortex:
 - NMDA receptor antagonist (e.g. ketamine), opioids, anticonvulsants, and tricyclic antidepressants;
 - Deep brain stimulation.
- Complementary Therapies:
 - Cognitive behavioral therapy (i.e., changing maladaptive thinking leading to changes in affects and behavior);
 - Hypnosis and visualization of imaginary limb (i.e., limbic or emotional behavior associated PLP);
 - Mirror box therapy (i.e., utilizing visual stimulus to reverse incongruent sensorimotor feedback loops to what is actual and what is seen)[5].

3. Conclusions

To date, PLP is likely caused by a combination of the above mechanisms in that treatment modalities have at best yielded mixed, short term benefits. Therefore the interactions between peripheral, spinal, and supraspinal (e.g., brain stem, limbic system, and homunculus) phenomena are all thought to contribute to PLP, and should be considered when planning treatment.

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5. References

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