

# Association of Non-Invasive Neuromodulation Techniques for Phantom Limb Pain Treatment

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## Background and Aims:

Phantom limb pain (PLP) is a chronic condition perceived in a limb that no longer exists<sup>1</sup>. Affects about 85% of amputated patients. Frequently, it can be overwhelming and challenging to manage, often necessitating a mix of treatments to improve patient pain and satisfaction, leading to poor quality of life<sup>2</sup>. Percutaneous Electrical Nerve Stimulation (PENS) is a therapy that involves inserting needles through the skin and accessing nerves to deliver electrical impulses to alleviate pain conditions<sup>3,4</sup>. Transcranial Direct Current Stimulation (tDCS) is a non-invasive form of neuromodulation that involves applying a low electrical current to specific cortex areas through electrodes over the scalp. It modulates brain activity and has shown potential in various neuroscience fields, including pain treatments<sup>5,6</sup>. This study aims to demonstrate the efficiency of the combination of peripheral and central neuromodulation therapies, such as PENS and tDCS, in amputee patients with PLP.

## Methods:

This series of cases comprise patients under treatment in an outpatient pain clinic of a tertiary university hospital in southern Brazil from January 2017 to February 2020. Eligibility criteria were: age  $\geq 18$  years old with phantom lower limb pain for at least 6 months already in pharmacologic treatment with anticonvulsants and/or tricyclic antidepressants. Patients underwent 10 sessions on a twice-a-week frequency of 20-minute tDCS with anodal stimulation over the primary motor cortex (M1) contralateral to the pain side, concurrently with PENS targeting the ipsilateral sciatic nerve, Figure 3, with alternate current at 2 Hz frequency, with current intensity set to stimulus perception at the phantom part of the member. Pain scores were evaluated before and after each section and compared during the first, fifth and last treatment sessions in the present study.

## Results:

Twelve patients (8 males and 4 females) were included, all of whom had lower limb amputations. Most were amputees due to vascular ischemic disease. The number of sessions ranged from 10 to 30. The evolution of the numeric pain rating (NPR) during the treatment period is shown in Figure 1. The media and standard deviation of the NPR are presented in Figure 2. Surprisingly, six patients (50%) reported no pain at all. The media and standard deviation of the NPR difference between the first and the last was  $6 \pm 3$ .

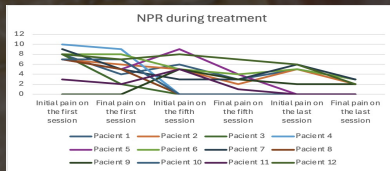


Figure 1- Numeric pain rating during treatment

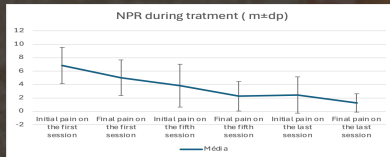


Figure 2- Media of NPR during treatment

## Conclusion:

To our knowledge, this is the first study to describe the combination of these neuromodulation techniques for treating PLP. The pathophysiology of PLP is not completely understood, but recent studies have shown ectopic discharges<sup>7</sup>, cortical reorganization<sup>8</sup>, and deafferentation<sup>9</sup> mechanisms may be interplaying to promote this complex phenomenon. It is hypothesized that PENS could stabilize ectopic discharge by creating an organized afferent current<sup>10</sup> which could also affect cortical reorganization<sup>11</sup>. Besides, it is proposed that tDCS on M1 can activate corticothalamic connections and influence brain areas such as the prefrontal cortex, the cingulate gyrus, and the periaqueductal gray matter, thus modulating both affective-emotional and sensory aspects of nociception, as well as producing endogenous opioids<sup>12</sup>. However, the magnitude of the clinical effect of this treatment surprised both us and the patients since phantom limb pain is known to be a refractory neuropathic pain condition.

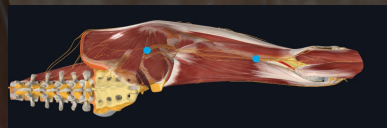


Figure 3- Needle placement over sciatic nerve

