Alpha Oscillation in Phantom Limb Pain Patients: A Neuropathic Pain Signature

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Introduction:
People with acquired amputation face oftentimes the onset of chronic pain, which develops as either residual limb pain, neuroma or nociceptive phantom limb pain (PLP), or neuropathic PLP. (Ortiz-Catalan, 2018)
To date, the pathophysiology giving raise to PLP is still object of debate, with previous literature mainly focusing on whether and how reorganization takes place in the primary somatosensory and motor cortices (Flor et al., 1995; Makin et al., 2013). Striving to understand how changes in somatotopy and mototopy relate to PLP, brain imaging studies have traditionally been conducted with a task-based fMRI approaches which measure the neural activity in an indirect way (Jutzeler, Curt and Kramer, 2015). Yet, little is known about the effect of amputation on the global brain organization and electrophysiological techniques, such as EEG, have not been taken fully advantage of. In this study we analyse the power of spontaneous and ongoing EEG activity as a function of frequency. The rationale for this choice stems from the assumption that brain at rest, in opposition to task-based paradigms, allows to capture dynamics related to the processing of pain which would otherwise be masked by other sensory or cognitive functions processes.

Methods:
The study was approved by the ethical committee of Västra Götalandsregionen. A total of 7 adults subjects, 3 women and 4 men between 24 and 57 years of age, were enrolled on a voluntary basis and assigned to one of two groups based on the presence of PLP. The 'no PLP' group was composed of two able bodied subjects and one upper limb amputee. The 'PLP' group was formed by one subject with lower limb amputation and three with upper limb deficiency. During the recording of the EEG signals, subjects rested with their eyes closed sitting comfortably on a chair in a quiet room. EEG was recorded sampling at 2400 Hz in 2 sessions of 7 minutes each, with 63 active electrodes fixed in a cap at the standard 10-20 positions, using an ear-link reference and AFz ground (g.Hlamp, g.tec medical engineering GmbH, Austria).

Results:
Figure 1 shows grand average (plot in black) of the power spectra for the two groups (no PLP on the left and PLP on the right). As the spectra from different channels had similar scale and shape, the data was summarized by averaging all the electrodes for each channel. The averages for individual subjects are shown in blue. Figure 2 shows the topography of the power spectra of every channel averaged over the subjects.
Conclusions:

Due to the small size of the sample with only one amputee subjects without PLP, it is not possible to draw conclusions of statistical significance. It is however possible to appreciate, in an observational sense, that our results point in the same direction of literature on resting state EEG in various chronic pain conditions (Dos Santos Pinheiro et al., 2016). We observe continuous EEG dominated by alpha band oscillation (8-12Hz), widely distributed in the cerebral cortex (Fig.2). Sarnthein et al. (Sarnthein et al., 2006) related this spontaneous alpha
oscillation with the concept of thalamocortical dysrhythmia, which could also play a role in PLP. In the future, research on a larger sample while encompassing a more complete repertoire of time-frequency parameters is expected to bring conclusions of statistical valence. The ultimate interest is to identify biomarkers of chronic pain as a treatment target and diagnostic tool.

**Disorders of the Nervous System:**

Disorders of the Nervous System Other

**Imaging Methods:**

EEG ¹

**Neuroanatomy:**

Cortical Anatomy and Brain Mapping

**Perception and Attention:**

Perception: Pain and Visceral ²

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¹² Indicates the priority used for review