

Modulation of Neuronal Activity in Neuropathic Pain Following Repetitive Motor Cortex Stimulation in Rats

Myeounghoon Cha¹, Seong-Karp Hong², Sun Joon Bai³, Bae Hwan Lee¹

¹Department of Physiology, Yonsei University College of Medicine
Seoul 03722, Republic of Korea

²Division of Bio and Health Sciences, Mokwon University
Daejeon 35349, Republic of Korea

³Department of Anesthesiology and Pain Medicine, Yonsei University College of Medicine
Seoul 03722, Republic of Korea

mhcha@yuhs.ac; karp@mokwon.ac.kr; sjbae@yuhs.ac; bhlee@yuhs.ac

Extended Abstract

When the sensory nervous system is affected by injury or disease, it often leads to a sense of numbness or lack of sensation. Neuropathic pain is thought to be associated with these types of abnormal peripheral and central nerve problems, which can lead to the development of a chronic neuropathic pain state [1]. Pain is known to change brain oscillation in humans and animals [2, 3]. Electroencephalography (EEG) is an electrophysiological monitoring method to record electrical activity of the brain. EEG measures voltage fluctuations resulting from ionic current within the neurons of the brain [4]. EEG studies in patients with chronic pain show increased power amplitude in widespread areas, including prefrontal cortex (PFC) and primary somatosensory cortex (S1) [5]. In the early ninety, motor cortex stimulation (MCS) was initially applied to central pain secondary to thalamic stroke, but, over time, its usage expanded to various types of chronic neuropathic pain. The clinical literature reveals that repetitive MCS shows approximate 45 to 75% of pain control rate [6]. Although several studies have used event-related EEG potentials evoked by phasic noxious stimuli as biomarkers of pain [7, 8], few have investigated the effect of pain lasting minutes or days on spontaneous EEG waveforms. Here, we investigated that nociceptive states in rat model of neuropathic forms of pain correlate with increased EEG power over the cerebral cortex.

In this study, we hypothesized that pain enhances EEG power and rhythmical oscillations. We further hypothesized that the changes in EEG power and rhythmical oscillations are reversed to normal following repetitive daily MCS treatment. In order to quantify the EEG signal changes, EEGs were recorded in chronic neuropathic pain rats and compared with EEGs in individuals with pain relief by repetitive cerebral MCS method. Our results show increased brain rhythmical oscillations in awake, freely behaving rat models of chronic neuropathic pain. We found that in rats with neuropathic pain, ongoing activities were increased. However repetitive MCS modulated these EEG power and brain oscillations when it relieved pain. In the EEGs of MCS treatments, the delta- and theta-frequency band decreased, while activities at alpha- and beta-frequency bands did not significantly change. These data suggest that quantitative EEG might be a valuable predictor of pain and analgesia in rodents. This study was supported by the Basic Research Program through the National Research Foundation (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2015R1C1A1A01053484 and 2017R1A2B3005753).

References

- [1] M. Cha, S. W. Um, M. Kwon, T. S. Nam, and B. H. Lee, "Repetitive motor cortex stimulation reinforces the pain modulation circuits of peripheral neuropathic pain," *Sci Rep*, vol. 7, pp. 79-86, 2017.
- [2] R. T. Canolty, E. Edwards, S. S. Dalal, M. Soltani, S. S. Nagarajan, H. E. Kirsch, et al., "High gamma power is phase-locked to theta oscillations in human neocortex," *Science*, vol. 313, pp. 1626-1268, 2006.
- [3] G. Buzsaki, C. A. Anastassiou, and C. Koch, "The origin of extracellular fields and currents--EEG, ECoG, LFP and spikes," *Nat Rev Neurosci*, vol. 13, pp. 407-420, 2012.
- [4] F. Ernst Niedermeyer, *Electroencephalography : Basic principles, Clinical applications, and related fields*, 2005.
- [5] J. Sarnthein, J. Stern, C. Aufenberg, V. Rousson, and D. Jeanmonod, "Increased EEG power and slowed dominant frequency in patients with neurogenic pain," *Brain*, vol. 129, pp. 55-64, 2006.

- [6] M. C. Lima and F. Fregni, "Motor cortex stimulation for chronic pain: systematic review and meta-analysis of the literature," *Neurology*, vol. 70, pp. 2329-2337, 2008.
- [7] A. Farajidavar, S. M. Athar, C. E. Hagains, Y. B. Peng, and J. C. Chiao, "Detection of thermal pain in rodents through wireless electrocorticography," *Conf Proc IEEE Eng Med Biol Soc*, vol. 2012, pp. 2535-2538, 2012.
- [8] S. C. Leiser, J. Dunlop, M. R. Bowlby, and D. M. Devilbiss, "Aligning strategies for using EEG as a surrogate biomarker: a review of preclinical and clinical research," *Biochem Pharmacol*, vol. 81, pp. 1408-1421, 2011.