Effect of Graded Peripheral Electrical Stimulation on Brain Activity

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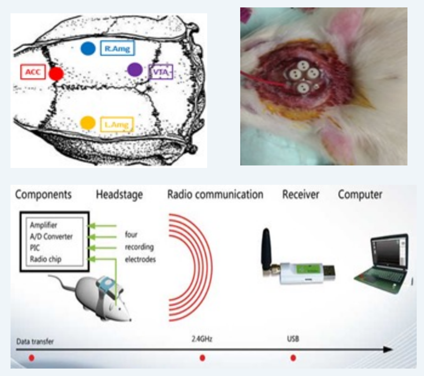
Introduction

Electrical stimulation (ES) is a valuable technique used for the intervention of pain, both in the peripheral or central nervous system. To investigate the efficacy of ES for acute pain relief, we utilize ES in the left ankle and local field potential (LFP) to observe alterations in power across frequency bands in four distinct rat brain regions: the anterior cingulate cortex (ACC), bilateral amygdala (AMG), and ventral tegmental area (VTA). The LFP can be subdivided into five frequency bands: delta, theta, alpha, beta, and gamma. Under isoflurane anesthesia, LFP was recorded in 2 separate conditions for each animal with 3 different parameters: 1ms duration, 11s at 5v, 10v, 50v, and 100v, delivered once, 3 minutes apart at 1, 50, and 100 Hz, before and after 50ul of 3% formalin injection in the left paw (nociceptive input). The results reveal that without formalin, under lower intensity stimulation, there was no change in power across the five frequency bands. However, administering a higher intensity stimulation tends to produce a transient suppression followed by a rebound phase. These findings suggest that the intensity and level of stimulation play a crucial role in modulating neural activity and highlights the complex dynamics of neural responses.

Methods

- **Animals:**
  Seven adult Sprague Dawley rats (N = 7, male = 2, female = 5), with an average weight of 357g±17g and a range of 301g-432g were utilized in this study. All procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Texas at Arlington. All animals were euthanized after the completion of this experiment.

- **Electrode Implantation:**
  The rodent was secured in place on a stereotaxic device under 3% isoflurane volatile anesthetic given via inhalation. Four 0.010-inch electrodes were separately intracranially implanted in four regions of the brain: ACC, RAMG, VTA, LAMG (Paxinos & Watson, 1998). Two screws were secured within the skull, one positioned in the upper right region and the other in the upper left region, affixed to a wire for grounding and reference purposes. The electrodes and screws were then secured with dental cement, acting as an adhesive bond.



- **Module setup and LFP recording:**
  The four electrodes and screw cable were connected to the wireless module (designed by SiChuan NeoSource BioTektronics Limited (http://www.neoscbio.com)) to receive the LFP signal from the brain. A USB dongle paired with the module was inserted into the computer to transmit the signal from the module to the recording software.

- **Formalin model induction:**
  The LFP signal was recorded under 2% isoflurane anesthesia for five-minutes as baseline for all rats. 50ul of 3% formalin was injected into the left hind paw of the rats after a five-minute baseline, after undergoing the first round of ES and before the second ES round.

- **Electrical stimulation model induction:**
  In two separate experimental conditions, the ES was administered in 3 separate parameters consisting of 1ms duration, 11s at 5v, 10v, 50v, and 100v, delivered once, 3 minutes apart at 1, 50, and 100 Hz. This was consistent throughout. This ES was delivered in the left hind paw of all rats.

- **Data analysis:**
  The raw data of LFP recorded from the module was processed by power spectrum analysis with the custom program of MATLAB. The power was calculated in MATLAB every ten-seconds, we then averaged the power intensity depending on the duration. Finally, the power of each frequency band was normalized by the average power of the baseline. The power of the five frequency bands was normalized by baseline average power. Next, the raw data was imported into Spike2 to analyze the data in power spectrogram and waveform graphs. Due to the ongoing nature of this project, an ANOVA test in SPSS will be later utilized to determine statistical results. All data are shown as the mean±SEM.

Results

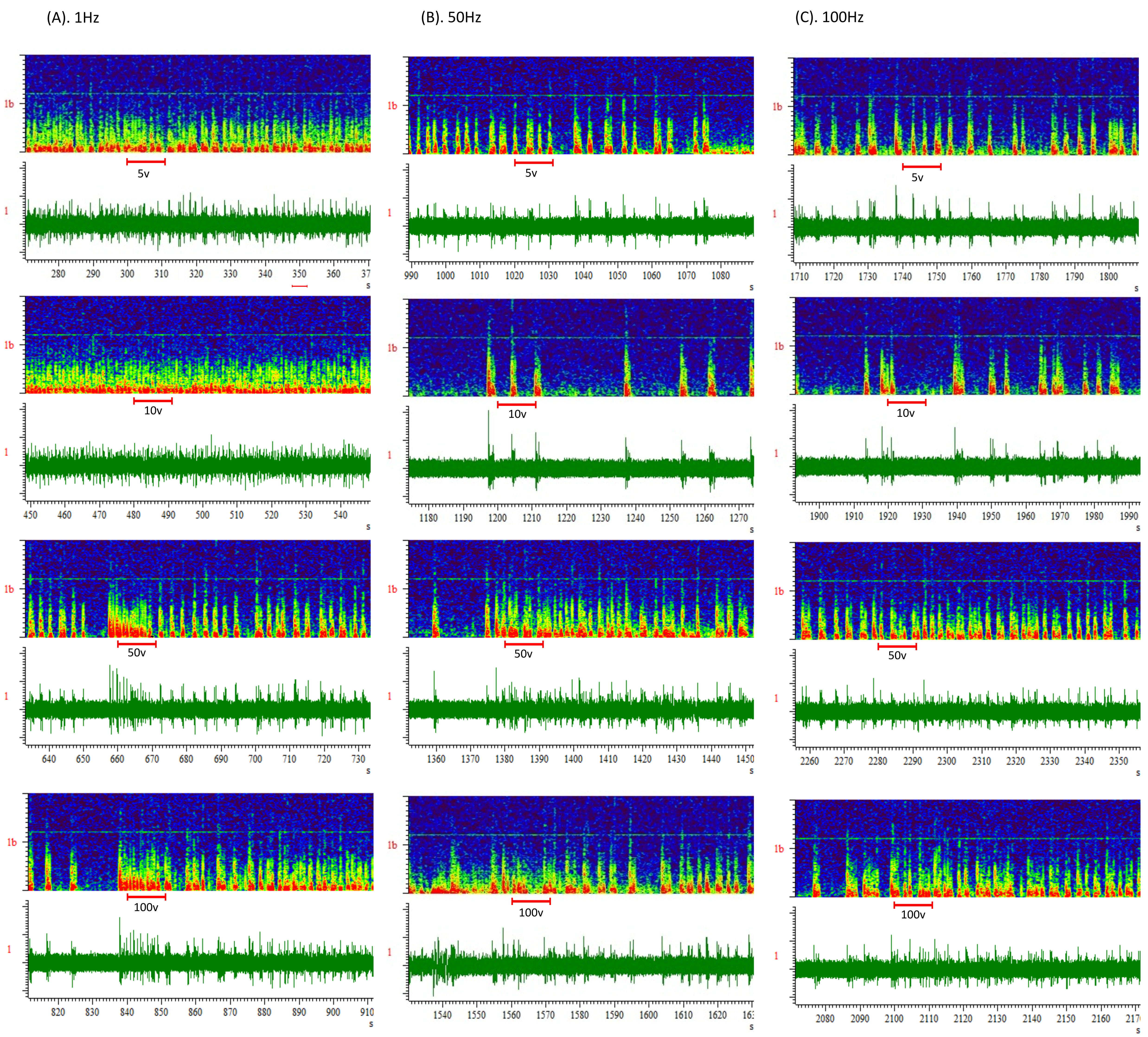


Figure 1. Representative traces of power spectrum analysis of ACC region in the pre-formalin ES condition. Note. Red bar indicates 11s of ES under different voltage parameters.

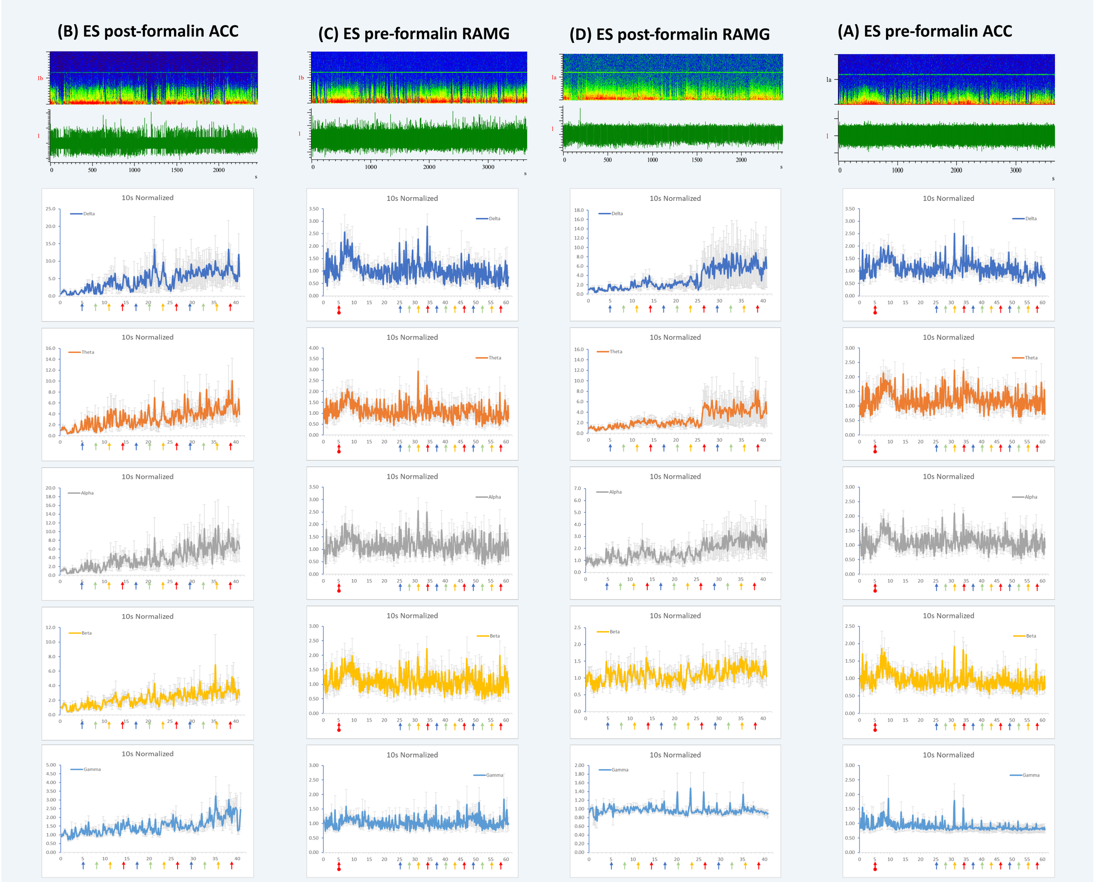


Figure 2. (A and C) Power spectrum analysis every 10 seconds for ES in the absence of formalin in the ACC and RAMG. (B and D) Power spectrum analysis every 10 seconds for ES after formalin. Note. Blue arrows indicate 5v, green arrows indicate 10v, yellow arrows indicate 50v, and red arrows indicate 100v. Red arrows with circles indicate when formalin was injected.

Discussion

Traditionally, data is analyzed every 5-minutes; however, we opted to analyze data at 1-minute intervals instead to better display the true temporal resolution. Despite our expectation of detecting changes, no significant differences were observed in either the pre-formalin or post-formalin conditions. We then conducted analyses at 10-second intervals for both conditions and noted instances of inhibition and excitation. These observed variations could be contributed by individual differences among the animals used in this study.

Pre-formalin ES condition:

- The findings indicate that in the absence of formalin, lower intensity ES produces little to no change across the five frequencies. However, higher intensity ES tends to produce an increase in power with a brief transient suppression followed by a rebound phase.

Post-formalin ES condition:

- After injection of formalin, there is an increase of power which reflects the first phase which usually occurs in the first 5 minutes. The second phase usually takes place 15 minutes after, but we did not see a clear significant phase. This is probably due to the electrical stimulation.

Conclusion

For the current set of data, we did not see the anticipated increase of different frequency power as the result of electrical stimulation in the periphery, either in pre- or post- formalin conditions. Therefore, our hypothesis was not supported. We will modify parameters for future studies.

References

1. Paxinos, G., & Watson, C. (1997). The rat brain, in stereotaxic coordinates. (6th edition) San Diego: Academic Press.
2. Wang, Zhen, and Yuan B. Peng. "Multi-Region Local Field Potential Signatures in Response to the Formalin-Induced Inflammatory Stimulus in Male Rats." Brain Research, vol.