The Anti-nociceptive Effects of Binaural Beats on Formalin-induced Inflammatory Pain

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INTRODUCTION

Binaural beats is an auditory phenomenon that occurs when two slightly different frequencies are presented to each ear. The superior medial olive, a structure responsible for sound localization, compares the difference between each ear and creates the perception of a third frequency. Through a process called frequency-following response, the brainwaves synchronize with the perceived third frequency resulting in neural entrainment. Recent studies indicate that low-frequency binaural beats may reduce both acute and chronic pain, however these results are based on subjective self report data.[1] By recording the local field potential (LFP) of brain structures responsible for auditory perception, the inferior colliculus (IC) and primary audio cortex (A1), and regions associated with pain perception, the anterior cingulate cortex (ACC) and amygdala (AMG), we can effectively track the binaural beat response through the auditory pathway and see how it influences formalin induced nociception.

METHODS

- Design
  I will have two separate groups. Group one will have no auditory stimulation, with the purpose of establishing the nociceptive formalin response in the implanted brain regions. The second group will be a within subject design with the intention of establishing the binaural beat response with and without formalin. Each rat will be exposed to every level of the binaural beats before the formalin injection, and again after the injection.
- Animals
  I will use 12 Sprague Dawley rats. 6 females and 6 males.
- Electrode Implantation
  The rats will undergo the electrode implantation surgery under 3% isoflurane, which will be dropped to 2% during the recording phase. Four electrodes will be intracranially implanted in four separate brain regions: IC, A1, AMG, ACC. Two screws will be screwed into the upper region of the skull, and a grounding cable will be wrapped around the right screw to reduce noise.
- Auditory Input
  In order to find the optimal anti-nociceptive frequency, I will use two frequencies, 800Hz and 900Hz, each consisting of a 10hz difference resulting in alpha binaural beats. Each trial we will switch which ears are exposed to each which frequency, and the order of each frequency to ensure each combination is met.
- Formalin Induction
  After the 50-minute pre-formalin phase at 2% isoflurane, 50µL of 3% formalin will be injected into the left hind paw.
- Data analysis
  The raw LFP data will be processed by power spectrum analysis through MATLAB. The power will be calculated in MATLAB every ten-seconds, we will then average the power intensity for every 5-minute interval. Finally, the power of each frequency band will be normalized by the average power of the baseline (first 10 min). An ANOVA in SPSS using the normalized power will be utilized to compare the treatment group with the control group.

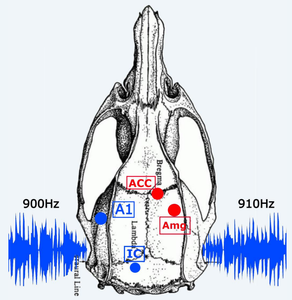


Figure 1. Electrode implantation sites.

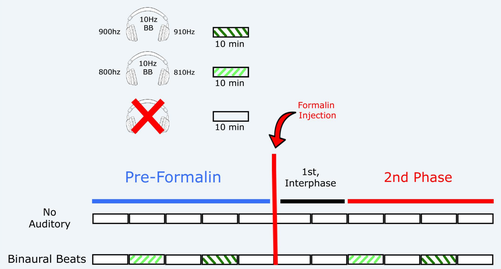
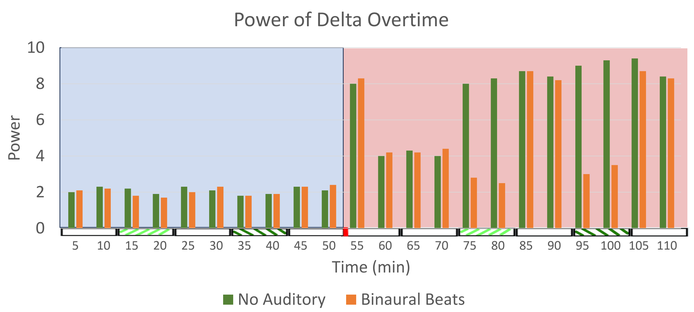
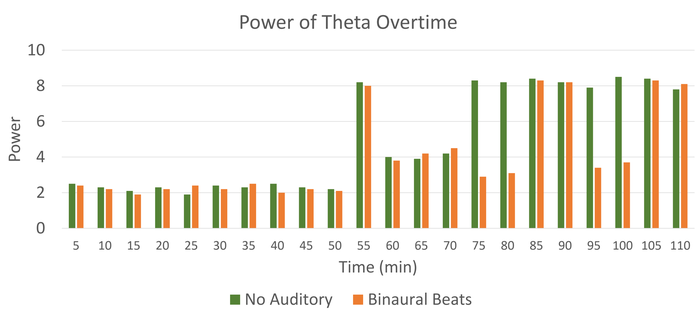
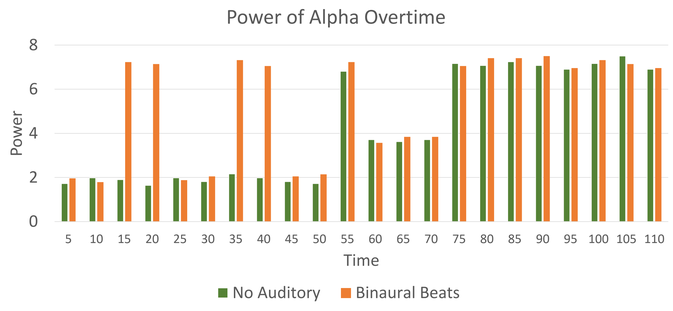


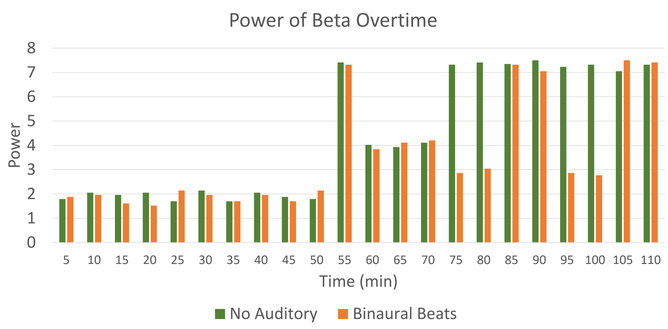
Figure 2. Experimental design.

EXPECTED RESULTS (Not Real Data)









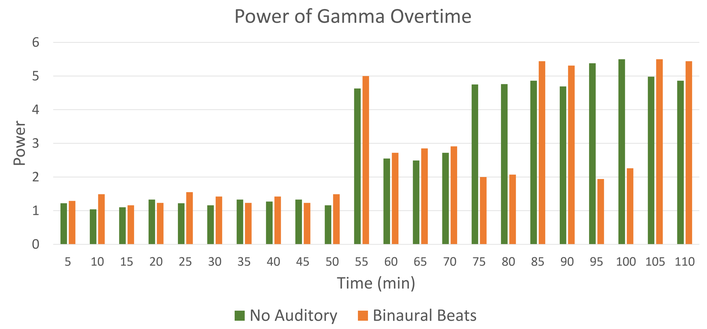


Figure 3. Bar graphs comparing the change in power across all five frequency bands between the no auditory group and the binaural beats group, with a clear division between the pre- and post formalin injection phases (2nd phase).

DISCUSSION

To establish the binaural beat response in the targeted brain regions, we will compare the normalized power of each frequency band during the pre-formalin phase across the no auditory group and the binaural beats group. We expect that alpha binaural beat stimulation will increase the power of alpha frequencies, indicating that the stimulation effectively resulted in neural entrainment.

To explore the effects of binaural beats on formalin induced nociception, we will compare the normalized power of each frequency band during the formalin phase (2nd phase) across the no auditory group and the binaural beats group. It has already been established that formalin increases the power of every frequency band in the targeted pain regions.[2] However, we expect that alpha binaural beat stimulation will increase the power of alpha frequency bands, causing a subsequent decrease in power of the other four frequency bands, possibly indicating a decrease in nociception.

CONCLUSION

In our hypothetical model, binaural beats will reduce pain induced by formalin. Future studies should explore the validity of the binaural beat response by utilized a control group that consists of a pure frequency presented to both ears.

Acknowledgments

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References

1. Shamsi, F., Azadinia, F., & Shaygan, M. (2024). Does brain entrainment using binaural auditory beats affect pain perception in acute and chronic pain?: a systematic review. *BMC Complementary Medicine and Therapies*, *24*(1). https://doi.org/10.1186/s12906-024-04339-y
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.