INPLASY PROTOCOL

To cite: Zhao et al. Gamma-band Oscillations in Phasic, Tonic, and Chronic Pain. Inplasy protocol 202180072. doi: 10.37766/inplasy2021.8.0072

Received: 18 August 2021

Published: 18 August 2021

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Support: **NNSFC (No. 32071061, 31822025).**

Review Stage at time of this submission: **Data analysis.**

Conflicts of interest:
None declared.

Gamma-band Oscillations in Phasic, Tonic, and Chronic Pain

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Review question / Objective: **Researchers are concerned that gamma-band oscillations (GBOs) sampled using electroencephalogram (EEG) and magnetoencephalogram (MEG) could be relevant to a spectrum of pain, e.g., phasic pain, tonic pain, and chronic pain. However, lacking strong nor rejecting evidence, the above notion has been debated by researchers for decades. The current study aims to tap into the relationship between gamma-band oscillations and the three types of pain perception using Anatomic Likelihood Estimation (ALE) and Comprehensive Meta-Analyses (CMA). Specifically, the current authors will (1) examine the relationship between the amplitudes of GBO and intensity of pain perception using CMA; (2) evaluate the frequency range of GBO using CMA; (3) estimate the latency range of GBO using CMA; (4) explore scalp distributions of GBO through ALE; and (5) summarize the functions and significance of GBO.**

Condition being studied: **We studied the GBOs sampled by EEG and MEG under the circumstances of phasic and tonic pain in healthy subjects and clinical patients. In addition, we also included studies of GBOs that are associated with chronic or spontaneous pain in patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 August 2021 and was last updated on 18 August 2021 (registration number INPLASY202180072).

INTRODUCTION

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METHODS

Participant or population: Human, including participants from the general publications, health subjects, and patients suffering from acute or chronic pain.

Intervention: Studies of phasic and tonic pain induced by stimulation (e.g., laser or heat stimulation), as well as studies of chronic or spontaneous pain in patients (i.e., without intervention), were included in the current meta-analysis.

Comparator: 1. participants (e.g., participants suffering from chronic pain and healthy subjects); 2. pain stimulation method (e.g., laser and heat); 3. pain stimulation place (e.g., left or right side of the body, including hand or forearm); 4. pain stimulation duration (e.g., phasic or tonic).

Study designs to be included: Both cross-sectional and longitudinal studies could be included.

Eligibility criteria: We reviewed both EEG and MEG studies that discussed the relationship between GBO and pain perception, the frequency range of GBO, the latency range of GBO, and the scalp distribution related to GBOs. Our inclusion criteria were: (1) peer-reviewed publications in English; (2) studies with humans (i.e., health subjects or clinical patients suffering from pain); (3) using techniques of EEG and MEG; (4) studies reported statistical results for meta-analyses (e.g., 95%CI of the frequency range of GBO and the GBO related electrodes, such as Cz and C4); (5) the mean age of participants was equal or larger than 18 years old; (6) if studies reported results for both each subgroup of participants as well as for the overall participants, results for subgroups were included in the current meta-analyses; and finally, (7) all repeating publications using the same set of data were treated as one publication.

Information sources: We included peer-reviewed publications from electronic databases (e.g., PubMed and Web of Science). If any critical information was lacking from the publications, we contacted the corresponding authors for further details.

Main outcome(s): Our preliminary CMA and ALE results suggested that: (1) the amplitudes of GBO and intensity of pain perception were positively correlated (an estimated r = 0.52 based on the overall study set); (2) the 95%CI of the frequency range of GBO was 54.76 to 67.62 based on the overall study set; (3) the 95%CI of the wave range of GBO was roughly around 61.51 to 95.01 based on the overall study set; In addition, the ALE results suggested that: (4) the key electrodes of GBO that related to pain perception were Cz, C2, and adjoining electrodes based on the overall study set.

Quality assessment / Risk of bias analysis: The risk of publication bias will be evaluated using the funnel plot.

Strategy of data synthesis: We used CMA software to examine the correlation of GBOs and pain perception, the 95%CI of the frequency range of GBOs, and the 95%CI of the latency range of GBO. In

addition, we converted the electrodes code (e.g., Cz and C2) to Talairach coordinate system and located the key electrodes related to GBOs. We recorded the sample size, mean and SD (or equivalent information), as well as moderating information (e.g., handed and sex ratio of participants) for each study.

Subgroup analysis: We estimated the CMA results based on the overall studies, and conducted comparisons using the Grouping function of CMA. Similarly, we evaluated the ALE results based on the overall studies, and used the 'contrast datasets' process of ALE to conduct the subgroup analyses.

Sensitivity analysis: We used the "remove one" analysis of CMA to gauge the sensibility of the meta-analysis.

Language: English.

Country(ies) involved: China.

Keywords: pain, gamma-band oscillations, EEG, MEG, meta-analysis.

Contributions of each author:
Author 1 - Qing Zhao - 1. literature searching design; 2. data coding design; 3. CMA and ALE analysis design; 4. conducting ALE analyses; 5. supervising the literature searching, data coding, and data analyses; 6. drafted the manuscript; 7. final manuscript writing, result checking, proof-reading, and submission.
Author 2 - Zhenjiang Li - 1. literature searching; 2. data coding; 3. conducting CMA analysis; 4. data checking; 5. results checking; 6. drafted the manuscript; 7. final manuscript writing and proof-reading.
Author 3 - Yuxuan Zeng - 1. literature searching; 2. literature searching checking 3. drafted the manuscript; 4. final manuscript writing, data checking, and proof-reading.
Author 4 - Li Hu - 1. research topic design; 2. literature searching design; 3. data coding design; 4. CMA and ALE analysis design; 5. supervising the literature searching, data coding, data analysis; 6. drafted the manuscript; 7. final manuscript writing and final manuscript approving; 8. the overall meta-analyses project management.