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Pain and the Brain: A Systematic Review of Methods, EEG Biomarkers, Limitations, and Future Directions (Protocol)

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 February 2025 and was last updated on 7 February 2025.

INTRODUCTION

Review question / Objective We formulated three research questions using the Population, Interest, and Context (PICo) structure. The desired population was people in or subjected to pain state conditions. The interest was pain biomarkers, while the context was for EEG signals. Three constructed research questions were answered to gain insight into the existing studies' methodologies, analysis, and limitations.
1. What experimental approaches are being used to study pain states in humans compared to pain-free control states using EEG?
2. How do electrical brain signal responses differ between chronic and experimentally induced pain states?
3. What are the limitations of current methodologies for studying human pain states in the literature?

Rationale To the best of our knowledge, there is no current systematic review that highlights the EEG responses of pain states while encompassing both chronic pain and experimentally induced pain methods, allowing for the comparison of signals from inducted pain states and chronic pain.

Condition being studied This systematic review examines the methods, participant characteristics, types of pain states, associated pain biomarkers on the brain's electrical activity, and limitations of the current pain studies. The review aims to identify what experimental methods researchers implement to study human pain states compared to human control pain-free states; if electrical brain signal responses of those who experience pain states differ from those in pain-free states.

METHODS

Search strategy A literature search was conducted using PubMed, Web of Science, and Google Scholar following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines to obtain relevant studies

between 2008 and 2023. The two keywords were "Electroencephalography" or "EEG" and "Pain Biomarkers" or "Pain Biomarker."

Participant or population The participants were not limited to a certain population. The review includes a variety of different chronic pain participants (including chronic lower back pain and osteoarthritis). Additionally, healthy cohorts used as controls or those subjected to experimental pain stimulation were investigated.

Intervention Resting state EEG for chronic pain conditions were assessed along with experimentally induced pain for both chronic pain and pain-free individuals.

Comparator Neural activity of participants experiencing pain in comparison to those in pain-free states will be assessed.

Study designs to be included Only original studies were included in the systematic review.

Eligibility criteria Our set of criteria included: (1) the study must focus on collecting EEG data for some variation of pain state, (2) the study must investigate at least one of the research questions this review asks, and (3) the study must have a very low bias presence. The included studies presented significant additions in answering the research questions. Studies were excluded if they did not address the research questions, did not involve human subjects, did not utilize EEG, did not assess pain states, or failed to report on neuro-biomarkers of pain. Additionally, studies lacking demographic information, details on the participant population, pain type, or study design were not included in this review.

Information sources Only electronic databases were used.

Main outcome(s) This review presents the variety of experimental setups, participant populations, pain stimuli methods, lack of standardized data analysis methods, supporting and contradicting study findings, limitations, and future directions.

Quality assessment / Risk of bias analysis Bias levels are determined considering study limitation concerns presented in the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) and the Newcastle-Ottawa Scale. Examples from GRADE include selective outcome reporting, recruitment bias, stopping the study early for benefit, inappropriate eligibility criteria, and flawed outcome measurements. Perspectives outlined in the Newcastle Ottawa Scale also guide when deciding on bias ratings, including the selection of the study groups, comparability of the groups, and outcome assessments.

Strategy of data synthesis Data was collected by both reviewers independently. The analysis of study data included assessing participant demographic information, study materials and methods, study features, reported results, and limitations. This information was used to compare the characteristics of different studies and the results between studies.

Subgroup analysis N/A.

Sensitivity analysis Bias for each study was considered. Additionally, the exclusion criteria did not limit types of pain stimulation or participant populations.

Country(ies) involved United States of America.

Keywords Pain; Brain; EEG; Biomarkers; Review.

Contributions of each author

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