International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Sleep Microstructural Alterations in Mild Traumatic Brain Injury: A Systematic Review and Meta-analysis Focusing on Sleep Spindles and Slow Wave Activity

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 December 2025 and was last updated on 21 December 2025.

INTRODUCTION

Review question / Objective The primary objective of this systematic review and meta-analysis is to quantitatively synthesize existing evidence regarding sleep microstructural alterations in patients with mild traumatic brain injury (mTBI). specifically, we aim to determine if spindle density and slow wave activity are significantly reduced in mTBI patients compared to healthy controls. A secondary objective is to explore potential sources of heterogeneity, such as time since injury (acute vs. chronic) and the presence of post-concussion symptoms.

Condition being studied Mild Traumatic Brain Injury (mTBI), commonly referred to as concussion, is an acute brain injury resulting from external physical forces. It is clinically characterized by a Glasgow Coma Scale (GCS) score of 13–15 upon initial assessment, often accompanied by transient loss of consciousness or post-traumatic amnesia.

Sleep disturbancess are among the most prevalent and persistent complaints in patients following mTBI, significantly impacting recovery and quality of life. While conventional polysomnography often reveals non-specific changes, emerging evidence suggests that mTBI may specifically disrupt sleep microstructure, particularly Sleep Spindles and Slow Wave Activity (SWA). These microstructural elements are critical bio-markers reflecting thalamocortical circuit integrity and are essential for sleep-dependent memory consolidation and neuroplasticity.

METHODS

Participant or population Patients of any age diagnosed with mild Traumatic Brain Injury (mTBI) or concussion, as defined by standard diagnostic criteria (e.g., Glasgow Coma Scale score of 13-15, loss of consciousness < 30 min, post-traumatic amnesia < 24 hours). Both acute and chronic

phases post-injury will be included. Studies involving moderate-to-severe TBI or penetrating brain injuries will be excluded.

Intervention Exposure to mild traumatic brain injury (mTBI) / Concussion.

Comparator Healthy controls (individuals with no history of TBI or significant sleep disorders).

Study designs to be included Cross-sectional studies ; Case-control studies ; Cohort studies.

Eligibility criteria
Inclusion Criteria:

Language: Only studies published in English will be included to ensure the quality and accuracy of data extraction.
Publication Type: Only full-text articles published in peer-reviewed journals will be considered.
Data Availability: Studies must report sufficient quantitative data (Means and Standard Deviations/ Standard Errors) for sleep spindle parameters (e.g., density, frequency) or slow wave activity (SWA) to allow for effect size calculation.

Exclusion Criteria:

Duplicate Data: If multiple publications report data from the same cohort of participants, only the study with the largest sample size or the most detailed data will be included to avoid duplication bias.
Co-morbidities: Studies involving participants with severe neurological disorders (other than TBI), prior history of psychiatric disorders, or severe pre-existing sleep disorders (e.g., typically diagnosed sleep apnea prior to injury) that could confound the results will be excluded.
Intervention Effects: For clinical trials investigating a drug or therapy, only the baseline (pre-intervention) data comparing mTBI patients and controls will be extracted.
Conference Abstracts: Conference abstracts, theses, and unpublished grey literature will be excluded due to the potential for incomplete data and lack of peer review.

Information sources To identify relevant studies, a comprehensive systematic search will be conducted across the following electronic bibliographic databases from their inception to the present:

PubMed / MEDLINE (National Library of Medicine);
Embase (Elsevier);
Web of Science Core Collection (Clarivate Analytics);
The Cochrane Library (Cochrane Central Register of Controlled Trials - CENTRAL);
PsycINFO (APA, particularly relevant for neuropsychological outcomes);
Scopus (Elsevier).
Additional Search Strategies:

Reference Lists: The reference lists of all included studies and relevant review articles will be manually screened to identify potential additional studies that may have been missed by the electronic search ("backward snowballing").
Contact with Authors: We will contact the corresponding authors of eligible studies via email to request missing data or clarification on study methodology if necessary.

Main outcome(s) Primary Outcomes: Quantitative EEG (qEEG) metrics of sleep microstructure obtained via Polysomnography (PSG). specifically:

Sleep Spindles: Including Spindle density (number/ min), amplitude, duration, and frequency (fast/slow spindles).
Slow Wave Activity (SWA): Including Delta power or Slow Wave Energy during NREM sleep.

Quality assessment / Risk of bias analysis Two independent reviewers will assess the methodological quality and risk of bias of the included studies. Any discrepancies will be resolved through discussion or consultation with a third reviewer if necessary.

The assessment tools will be selected based on the study design:

For Case-Control and Cohort Studies: The Newcastle-Ottawa Scale (NOS) will be used. This scale evaluates studies across three domains: (1) Selection of study groups; (2) Comparability of the groups; and (3) Ascertainment of exposure/ outcome. Studies will be awarded stars, with a score of ≥7 stars considered as high quality.
For Cross-Sectional Studies: The Agency for Healthcare Research and Quality (AHRQ) methodology (or a modified version of the Newcastle-Ottawa Scale adapted for cross-sectional studies) will be employed.
The results of the quality assessment will be presented in a table in the final review, and studies with high risk of bias will be subjected to sensitivity analysis.

Strategy of data synthesis 1. Statistical Software:

All statistical analyses will be performed using Review Manager (RevMan) software (Version 5.4, The Cochrane Collaboration) or Stata (Version 16.0).

2. Effect Measures:
Since sleep microstructural parameters (e.g., spindle density, frequency, SWA power) are continuous variables and may be measured using different recording montages or units across studies, the Standardized Mean Difference (SMD) (Hedges' g) with 95% Confidence Intervals (CIs) will be used to estimate the pooled effect size.

3. Assessment of Heterogeneity:
Heterogeneity among the included studies will be assessed using the Chi-square test (Cochran's Q) and the I^2 statistic.

If $I^2 < 50\%$ and $P > 0.1$, heterogeneity will be considered low, and a fixed-effects model will be applied.
If $I^2 \geq 50\%$ or $P \leq 0.1$, indicating significant heterogeneity, a random-effects model will be utilized to provide a more conservative estimate.
4. Sensitivity and Subgroup Analysis:
If significant heterogeneity is observed, sensitivity analysis will be conducted by removing one study at a time to assess the stability of the results. Subgroup analyses may be performed based on the severity of symptoms, time since injury (acute vs. chronic), or age groups, provided sufficient data is available.

5. Publication Bias:
If more than 10 studies are included in the meta-analysis, publication bias will be visualized using Funnel Plots and statistically tested using Egger's regression test.

Subgroup analysis If significant heterogeneity is observed (I^2>50%) and sufficient data are available (e.g., at least 2-3 studies per subgroup), we will conduct subgroup analyses to explore potential sources of heterogeneity based on the following pre-specified characteristics:

Time Since Injury (Phase of Recovery): We will stratify the analysis into Acute/Sub-acute phase (< 3 months post-injury) versus Chronic phase (≥ 3 months post-injury), as sleep architecture changes may evolve during the recovery process.
Age Group: Subgroups will be divided into Pediatric/Adolescent populations (< 18 years) versus Adult populations (≥ 18 years), given the natural developmental changes in sleep microstructure (e.g., spindle density and SWA) across the lifespan.
Mechanism of Injury: Comparison between Sports-related concussion (SRC) versus non-sports-related causes (e.g., motor vehicle accidents, falls, or blast injuries).
EEG Recording Methodology: Analysis based on different EEG lead locations (e.g., Frontal vs. Central vs. Occipital channels) if studies report region-specific data.

Sensitivity analysis To evaluate the robustness and stability of the pooled results, sensitivity analyses will be performed using the following strategies:

Leave-one-out Analysis: This involves sequentially removing one study at a time from the meta-analysis and recalculating the pooled effect size. This will help identify if any single study exerts a disproportionate influence on the overall results.
Quality-based Exclusion: We will repeat the analysis by excluding studies classified as having a "high risk of bias" (i.e., low quality, NOS score < 7) to ensure that the findings are not driven by methodologically flawed studies.
If the results remain consistent after these exclusions, the findings will be considered robust.

Country(ies) involved China.

Keywords Mild Traumatic Brain Injury; Concussion; Sleep Microstructure; Sleep Spindles; Slow Wave Activity; Quantitative EEG; Meta-analysis.

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