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Stress as a seizure trigger in epilepsy and functional/ dissociative seizures: A scoping review protocol

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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 18 January 2026 and was last updated on 18 January 2026.

INTRODUCTION

Review question / Objective What are the commonalities and differences in FDS and epilepsy in terms of stress, specifically regarding:
- Stressful events as potential seizure triggers;
- Subjective and objective markers of stress as possible seizure triggers.

Background Epilepsy and functional/dissociative seizures (FDS) are neurological disorders that can have a significant impact on patients and families. Although associated with distinct underlying mechanisms, both conditions often involve the unpredictable occurrence of seizures, that can be related to psychological influences. In both conditions, stress can play a role in seizure occurrence.

Epilepsy involves recurrent seizures resulting from abnormal brain electrical activity1, with varied causes including genetic and structural factors2,3. Anxiety and depression commonly co-occur with the disorder4,5 while stress and sleep deprivation can trigger episodes6. FDS present as seizure-like events related to a complex interaction of biopsychosocial predisposing, precipitating or perpetuating factors including traumatic experiences, physical illness, and altered cognitive processing7-11. FDS are not caused by structural brain lesions or abnormal electrical discharges. Potential pathophysiological mechanisms include elevated autonomic reactivity9,12,13, altered emotional processing14-19, 20, 21, disrupted interoceptive awareness and dissociation22,23.

There are various approaches to the definition of stress. For the purpose of this review, stress will be defined as the physiological and psychological reaction to a real or perceived threat (stressor) and the process of its management until homeostasis is restored24,25. Nervous, immune, and endocrine systems are involved in physiological stress

responses25, while cognitive, emotional, behavioural and perceptual changes are part of psychological stress reactions26. This scoping review will focus on studies that assessed subjective and objective markers of stress in patients with FDS and epilepsy. As such, subjective stress scales (e.g., perceived stress scale, standard stress scale), mood and emotional state reports, will be used as subjective markers of stress. Neuroendocrine (e.g., cortisol levels, catecholamines), cardiovascular (e.g., heart rate variability, blood pressure, resting heart rate), immunological (e.g., pro-inflammatory cytokines levels), autonomic (e.g., skin conductance, pupil dilation, temperature regulation), and behavioural markers (e.g., COPE inventory, behavioural checklist for coping with stress) will be used as objective measures of stress. In addition to these physiological markers, studies that have reported on self- or observer reported stressful events/ actual stressors will be included as well.

A seizure trigger is any internal or external factor, stimulus, or condition that precipitates or provokes the onset of a seizure in individuals with seizure disorders27. Importantly, triggers do not cause seizures themselves but rather provoke seizures in individuals who are already predisposed to having them due to an underlying seizure disorder. Triggers demonstrate individual variability. There is typically a clear temporal relationship between exposure to the trigger and seizure onset, ranging from minutes to hours, and true triggers tend to consistently provoke seizures in susceptible individuals upon repeated exposure.

Rationale Epilepsy and functional/dissociative seizures (FDS) are neurological disorders that can have a significant impact on patients and families. Although associated with distinct underlying mechanisms, both conditions often involve the unpredictable occurrence of seizures, that can be related to psychological influences. In both conditions, stress can play a role in seizure occurrence.

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METHODS

Strategy of data synthesis The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews.

The scoping review research strategy will be as follows:
Databases: PubMed/Medline, Embase, PsychInfo, Web of Science, Cinahl

Search terms: (Epilep* OR seizur*[MeSH Terms] OR Functional seizure* OR Dissociative seizure* OR Psychogenic seizure* OR Non-epileptic seizure* OR Pseudoseizure* OR Conversion seizure* OR Psychogenic non-epileptic seizure* OR Functional neurological disorder* OR Somatoform seizure* OR Hysterical seizure*) AND (Trigger* OR Caus* OR Generat* OR Activat* OR Precipita* OR Mechanism* OR Start* OR Initiat*) AND ((Stress physiological [MeSH Terms]) OR (Stress, psychological [MeSH Terms]))
We will perform hand searches of the reference lists of relevant articles, including previous reviews, as well as examining reference lists in grey literature such as PhD theses and other unpublished sources.

Eligibility criteria Eligibility criteria are used based on PICO framework:
Population inclusion criteria:
- Adult patients (18 years+) with epilepsy or FDS; any gender. Population not restricted to any country.
- Diagnosis of FDS made by a neurology/neuropsychiatry specialist. Diagnosis of epilepsy made by a neurology/epileptology specialist.
Population exclusion criteria:
- Samples including only patients with comorbid epilepsy and FDS.
Intervention inclusion criteria:
- Studies focused on assessing subjective and/or objective stress markers in patients with epilepsy and/or patients with FDS.
Intervention exclusion criteria:
- Studies focused on clinical features only (e.g., seizure frequency, clinical signs).
- Studies focused on the diagnostic process, management and prognosis.
- Single case studies, Book reviews, Journal notes, Journal Letters, Conference abstracts.
Comparison:
- Two populations (epilepsy and FDS patients) will be compared. Studies with just one of these groups will also be included, the comparison will be made at the level of the synthesis.
Outcomes:
- Stressful events, subjective stress and objective stress markers as potential seizure triggers (i.e., reported and/or observed to occur prior to the onset of a seizure). Studies measuring stress markers up to 24 hours prior to seizure occurrence will be included and findings on timeframes between stress markers and seizure occurrence will be presented.

Source of evidence screening and selection Following the search, all identified citations will be collated and uploaded into a scoping review software and duplicates removed. Following a pilot test, titles and abstracts will then be screened by two or more independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant sources will be retrieved in full. The full text of selected citations will be assessed in detail against the inclusion criteria by two or more independent reviewers. Reasons for exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with an additional reviewer/s.

All selected studies will undergo a quality assessment. Whilst it is not essential for a scoping review, it is important to highlight the key strengths and weaknesses in the existing literature. The quality assessment will include use of relevant CASP appraisal tools (e.g., cross-section, cohort, case-control checklists), with possible adaptations, depending on the nature of the studies identified.

Data management Data will be extracted from papers included in the scoping review by two or more independent reviewers using a data extraction tool. The data extracted will include specific details about the participants, concept, context, study methods and key findings relevant to the review question.

A draft data extraction list is provided below. The draft data extraction list will be modified and revised as necessary during the process of extracting data from each included evidence source. Modifications will be detailed in the scoping review. Any disagreements that arise between the reviewers will be resolved through discussion, or with an additional reviewer/s.

Draft data extraction list:
Author
Year
Study type
Sample size
Age distribution
Ethnic categories
Control group details
Functional seizures group: diagnostic procedures (e.g., video-electroencephalography, ictal/interictal EEG; seizure provocation; clinical assessment)
Epilepsy group: epilepsy subtype (temporal/frontal/parietal/occipital lobe epilepsy, focal aware seizures, focal unaware seizures, generalized tonic-clonic seizures)
Background and baseline clinical data
Seizure triggers in both populations (FDS, epilepsy)

Stressful events, subjective stress ratings and objective stress markers (i.e., autonomic and neuroendocrine/HPA-axis markers)
Psychological symptom scores on validated measure (FDS, epilepsy)
Descriptive and inferential statistical values for both groups and between-groups comparisons, where available.

Reporting results / Analysis of the evidence To address the anticipated heterogeneity in the evidence base, we will employ a structured three-phase data synthesis framework. Phase 1 will involve initial mapping and classification of data based on study design, population characteristics, and temporal scope of pre-ictal assessment. Phase 2 will organize findings by stress marker type, creating distinct analytical categories for objective physiological markers (e.g., cortisol, EEG patterns, heart rate variability, electrodermal activity, and other autonomic indices), and subjective self-report measures (anxiety scales, perceived stress inventories). Phase 3 will involve cross-cutting synthesis across both study types and stress marker categories, examining patterns in methodology and findings, identifying convergent and divergent results within and between epilepsy and FDS populations, and mapping methodological strengths and gaps across different study designs.

Presentation of the results The results of the search and the study inclusion process will be reported in full in the final scoping review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping review (PRISMA-ScR) flow diagram.

The data will be presented graphically or in diagrammatic or tabular form. A narrative summary will accompany the tabulated and/or charted results and will describe how the results relate to the reviews objective.

Language restriction Publications in English language.

Country(ies) involved Czech Republic, United Kingdom.

Keywords Epilepsy, functional seizure, dissociative seizure, stress, seizure trigger.

Dissemination plans Results will be disseminated through conference presentations, publication in a peer-reviewed academic journal, and through social media posts and/or press releases.

Contributions of each author

Author 1 - Karin Revajová - Author 1 will draft the manuscript, prepared the scoping review protocol and will be one of the reviewers.
Email: karin.revajova@kcl.ac.uk
Author 2 - Viktória Pytelová - The author will read and provide feedback on the manuscript and will be one of the reviewers.
Author 3 - Patrícia Všianská - The author will read and provide feedback on the manuscript and will be one of the reviewers.
Author 4 - Markus Reuber - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy. The author will read, provide feedback and approve the final manuscript.
Author 5 - Richard Brown - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy. The author will read, provide feedback and approve the final manuscript.
Author 6 - Susannah Pick - The author provided overall direction of the research strategy and leads the research. The author will read, edit, provide feedback and approve the final manuscript.
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