# Patients with epileptic and functional seizures, a scoping review of underlying mechanisms

Rohan Kandasamy (1,2), Felix May (3,4), Mahinda Yogarajah (2,5)

1. National Hospital of Neurology and Neurosurgery Department of Clinical Neurophysiology, 2. UCL Queen Square Institute of Neurology, 3. North Bristol NHS Trust, 4. UWE Robotic Engineering and Computing for Healthcare, 5. National Hospital of Neurology and Neurosurgery Epilepsy Group

## Introduction

Functional seizures (FS) are  a common comorbidity of epilepsy [1]. Few studies compare people with dual diagnosis of epilepsy and functional seizures (PWDD), to those with functional seizures alone (PWFS).

Two previous systematic reviews have looked at the epidemiology [1] and associated psychiatric conditions [2]. Data suggests semiology, comorbidities and epidemiology differ between the two groups.

The overlap of epilepsy and functional seizures presents an opportunity to dissect mechanisms behind their genesis and evaluate proposed explanatory models.

Several models have been proposed to explain the emergence of functional seizures [3]. Some are psychologically framed, establishing roles of narrative and relationships to other psycho-pathologies, or frame functional seizures as learned behaviour or emerging fragments f re-experienced traumatic events.

A Bayesian model by Edwards et al focuses on neurobiological processes and makes specific predictions about generation of functional neurological symptoms [4].

Functional seizures remain difficult to treat, lacking a comprehensive path to relief. By clarifying the underlying processes, we can frame future research to better tackle these complex conditions, both in terms of investigation or diagnosis and of therapeutic interventions.

## Aim

Firstly, we aimed to capture and synthesise more relevant studies in our search, by using a more comprehensive search strategy, using more databases, and extending the number of years for the search. Secondly, we aimed to explore features that might serve to elucidate the underlying mechanistic differences between these two groups.

Previous reviews had focused on distinctive features or epidemiology. Our objective was to evaluate the fundamental aetiology of events in PWDD and PWFS to inform a model of functional seizures, with or without comorbid ES, that encompasses the nature of both patient groups. To do this, in the context of the neurobiological model discussed above, we focused on outcomes and associated symptoms and conditions, including a greater focus on intermittent somatic symptoms and conditions rather than examining the co-morbid psychiatric disorders of these groups.

## Method

We conducted a broad, high sensitivity search across 30 years in on the Google Scholar, Medline, Embase, APA PsycInfo and Cochrane databases. We also included studies from the references of included papers.

**Inclusion criteria**

- Video telemetry- (VT) or video-EEG confirmed dual diagnosis of epilepsy and functional seizures
- 18 - 75 years of age
- Primary research
- Published in the last 30 years

**Exclusion criteria**

- Ages <18 or >75
- Primary focus on learning difficulty patients
- Paediatric research
- Case studies or studies with only one patient in the target population
- Non-peer reviewed studies
- Abstract only

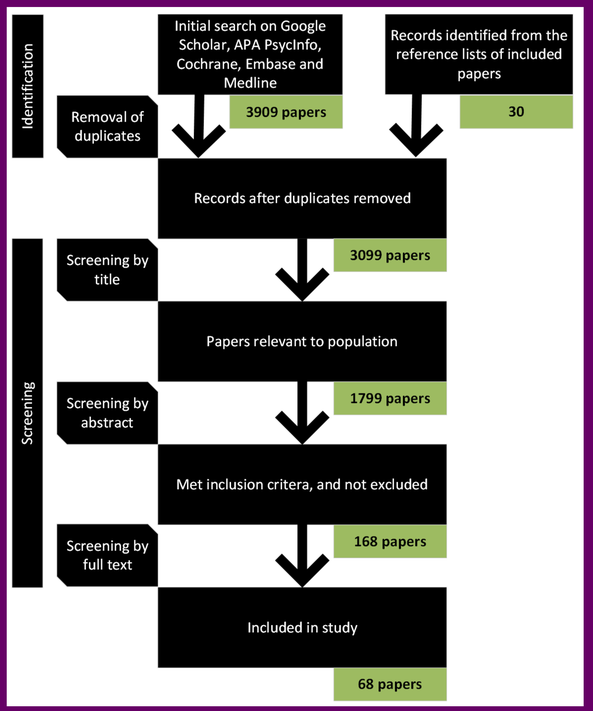


Figure 1: PRISMA diagram for the selection of relevant papers

## Results

After manual review of the suitable papers, 68 papers were identified as meeting the criteria, including a total of 2044 PWDD. The main differences and similarities pertinent to the study question are summarised in figure 2. While PWFS reported more general somatic functional conditions, PWDD responded to therapies that modified interoceptive inputs, and also reported ictal somatic/autonomic symptoms during their functional seizures. This suggested that they too had a roll for interoception in their functional seizures.

| Single diagnosis functional seizures | Dual diagnosis functional seizures and epilepsy |
|---|---|
| • More IBS, headache, fibromyalgia, chronic pain, GORD<br>• More PTSD<br>• More ictal somatic and autonomic features | • Poorer cognition<br>• Higher event frequency<br>• Poorer quality of life<br>• More “pseudostatus” |

**Both groups:**
- Suffer from affective disorders
- Have features of altered interoception
- Have features of trait dissociation
- Have some degree of impaired cognition

Figure 2: Summary of the main pertinent similarities and differences between PWDD and PWFS

## References

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## Discussion

The psychological models fail to explain why PWDD have fewer somatic symptoms/conditions than PWDD. The “hard-wired model” explains why PWFS might have these conditions (IBS, fibromyalgia etc.), but not why PWDD would not. The dissociative model fails to explain why epileptic seizures (ES) precede FS and why PWDD do not have as high a rate of PTSD as do PWFS. The model of FS as physical manifestation of emotional distress is concurrent with the finding of affective disorders in both populations, but does not explain the differences interictal symptomaticity in the patient groups. Finally, the model of FS as learned behaviour may explain why FS emerge after cessation of ES in pursuit of a lost secondary gain, but again fails to explain the interictal symptom differences. Most of these models consider trait dissociation as a component of the aetiology, but they fail to explain why it would be found in patients with epilepsy without FS.

Considering the differences and similarities between the patient groups in the context of the Bayesian model creates a hypothetical model for FS emerging in PWE due to altered mid-level priors, rather than the high-level hyper-precision seen in PWFS. A liability to interoceptive state change in response to noisy afferent inputs could be due to damaged interoceptive circuitry or due to conditioned responses to the interoceptive features experienced at the onset of ES.

## Conclusion

We found that PWDD are a patient group with poor quality of life, poor cognition, high event frequency and difficulty in reaching a diagnosis. Commonalities and differences between the patient groups are hard to explain within the psychological models of functional seizures. We found the Bayesian model was best able to encompass the differences in functional seizures experienced by those with and without comorbid epilepsy.

Prospective studies might measure interoception and interoceptive accuracy in PWFS and PWDD, as what we have found suggests that PWFS may have a general failure of interoceptive accuracy, rather than abnormal interoception specifically in the domain of their epilepsy.

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