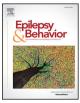
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Review Panic and epilepsy in adults: A systematic review

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ABSTRACT

The purpose of the current paper was to review the empirical literature on the cooccurrence of panic and epilepsy, in order to determine whether there is an increased risk of panic attacks and panic disorder among adults with epilepsy and an increased risk of epilepsy among adults with panic disorder. Given the overlap between panic and ictal fear, a preliminary aim of the current review was to critically evaluate the methodology used to differentiate between diagnoses of panic disorder and epilepsy in existing research. A literature search was conducted in relevant electronic databases, and articles that directly focused on panic and epilepsy are elevated among individuals with panic disorder and that panic attacks are elevated among individuals with epilepsy, but rates of panic disorder among people with epilepsy are inconsistent. However, most studies did not use sufficiently rigorous methods to differentiate between panic disorder and epilepsy. Therefore, a critical next step in this area of research is to develop a standard procedure for differentiating ictal fear from panic attacks and panic disorder.

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1. Introduction

It has been well-established that rates of anxiety disorders are disproportionately higher among individuals with epilepsy compared with that among the general population (50% vs. 18%) [1–3]. Moreover, greater anxiety is associated with greater epilepsy severity and levels of psychosocial impairment [4]. Additionally, anxiety symptoms are stronger predictors of quality-of-life concerns among individuals with epilepsy than seizure frequency and depression symptoms [5,6]. Despite these high prevalence rates and the corresponding negative impact of anxiety more broadly, there is a dearth of research examining the association between epilepsy and specific anxiety disorders.

One specific anxiety disorder that warrants further investigation among individuals with epilepsy is panic disorder. A panic attack is an abrupt increase in fear and physiological arousal that peaks within minutes and involves four or more of the following symptoms: increased heart rate, sweating, trembling, shortness of breath, choking, chest pain, nausea, dizziness, hot or cold flashes, paresthesia, derealization or depersonalization, fear of losing control or going crazy, and fear of dying [7]. Panic disorder is characterized by recurrent, unexpected panic attacks combined with persistent worry about future panic attacks and/or behavioral changes (e.g., avoidance) [7]. This debilitating disorder affects approximately 2.7% of the general population in a

* Corresponding author. E-mail address: lidgarae@mail.uc.edu (A.L. Johnson). given year and is associated with increased rates of substance use, healthcare utilization, and role impairment [8,9]. Panic attacks are particularly important to examine in the context of epilepsy due to their conceptual and symptomatic overlap with ictal fear, which is the most frequently reported emotional aura and is particularly prominent in patients with epileptiform discharges from the temporal lobe [10,11].

When ictal fear occurs as part of a seizure, there are multiple physiological and psychological symptoms present that are indistinguishable from symptoms of a panic attack (e.g., nausea, tachycardia, hot flashes, trembling, paresthesia, shortness of breath, sweating, depersonalization, loss of control) [1,12,13]. In fact, there are several published case studies in which panic attacks were initially misdiagnosed as treatment-resistant seizures or in which epilepsy was misdiagnosed as panic attacks or panic disorder [12,14–19]. One potential barrier to the accurate diagnosis of panic and epilepsy is the limited ability of some patients to report history of symptoms accurately due to the known cognitive deficits common in people with epilepsy [20] and the similarity of panic symptoms to certain epilepsy symptoms (i.e., ictal fear; [1,12,13]). Additionally, the two conditions often cooccur [15,18], making differential diagnosis even more difficult, and there are even some case reports suggesting that epilepsy surgery may be a risk factor for developing panic disorder [21,22]. Notably, multiple evidence-based treatments (i.e., cognitive-behavioral psychotherapy, selective-serotonin reuptake inhibitor, selective-norepinephrine reuptake inhibitor) exist for the treatment of panic disorder [23]. Therefore, it is critically important to be able to accurately differentiate between epilepsy and panic, in



order to understand their cooccurrence and to appropriately and effectively treat both conditions.

Given the overlap between panic and ictal fear, the preliminary aim of the current review was to critically evaluate the assessment methodology used in these studies to differentiate between diagnoses of panic disorder and epilepsy. Following this initial aim, the primary aim of the present paper was to review the empirical literature documenting the cooccurrence of panic and epilepsy in order to determine whether there is an increased risk of panic attacks and panic disorder among adults with epilepsy and of epilepsy among adults with panic disorder.

2. Methods

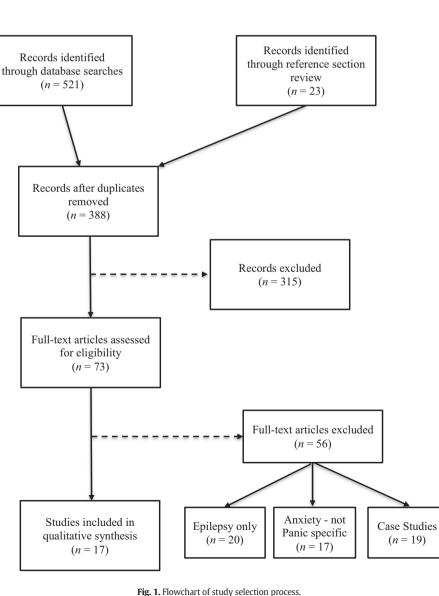
2.1. Search strategy and selection criteria

The literature search followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (see Fig. 1). Specifically, a literature search was conducted using electronic search engines (i.e., PsycINFO and PubMed) using the following keyword algorithms: (epilepsy OR seizure) AND (panic OR "anxiety disorder"). After removing duplicates, the reference sections of these articles were reviewed to identify any other possibly relevant studies. The resulting 388 articles were then screened for relevance. The majority of these studies were not directly relevant to the present review, because they examined ictal fear rather than panic attacks or panic disorder, focused primarily on children or adolescents, were case studies, or were not published in English. The full texts of the resulting 73 articles were then reviewed, and an additional 56 articles were excluded because of the following: (1) they focused on anxiety, but not specifically panic (n = 17); (2) they focused on epilepsy only (n = 19); and (3) they were not empirical studies (i.e., case studies; n = 19). We focused on the remaining 17 articles in the present review.

3. Results

3.1. Differentiating between ictal fear and panic

Seven studies reported utilizing comprehensive methods to obtain an accurate epilepsy diagnosis (i.e., electroencephalogram (EEG) evidence of epilepsy and diagnosis by a neurologist) [24–30]. Of the remaining studies, five used self-report assessment methods [31–35], one used neurological examination only [36], one used only medical record review of International Classification of Disease (ICD) codes [37], one used current prescription of antiepileptic medicines [38], and two did not report diagnostic methods but recruited from patients at well-established epilepsy surgery programs [39,40]. Panic attacks and



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