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Review article

Epilepsy coexisting with depression

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ABSTRACT

Depression episodes in epilepsy is the most common commorbidity, affecting between 11% and 62% of patients with epilepsy. Although researchers have documented a strong association between epilepsy and psychiatric comorbidities, the nature of this relationship is poorly understood.

The manifestation of depression in epilepsy is a complex issue having many interacting neurobiological and psychosocial determinants, including clinical features of epilepsy (seizure frequency, type, foci, or lateralization of foci) and neurochemical or iatrogenic mechanisms. Other risk factors are a family history of psychiatric illness, particularly depression, a lack of control over the seizures and iatrogenic causes (pharmacologic and surgical). In addition, treatment with antiepileptic drugs (AEDs) as well as social coping and adaptation skills have also been recognised as risk factors of depression associated with epilepsy.

Epilepsy may foster the development of depression through being exposed to chronic stress. The uncertainty and unpredictability of seizures may instigate sadness, loneliness, despair, low self-esteem, and self-reproach in patients with epilepsy and lead to social isolation, stigmatization, or disability. Often, depression is viewed as a reaction to epilepsy's stigma and the associated poor quality of life. Moreover, patients with epilepsy display a 4–5 higher rate of depression and suicide compared with healthy population.

Contents

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Introduction

Epilepsy is the most common, chronic, serious neurological disease, which affects 65 million people in the world [1], and psychiatric disorders, especially depression, seem to be more frequent in patients with epilepsy than in the general population. Comorbid depression has a profound impact upon the quality of life of patients with epilepsy [2]. The population-based studies reveal that it affects more than a third of patients with epilepsy [3].

The relationship between depression and epilepsy was reported even in ancient times [4]. Modern investigations began in the 1970s when Trimble and Reynolds [5] identified the behavioral and cognitive complications of antiepileptic drugs (AEDs), especially phenytoin and the barbiturates. These observations led on to more systematic studies of the effects of AEDs on cognition and mood in patients with epilepsy and volunteers [6], and to studies of the clinical phenomenology of the affective disorders [7]. The first, and thus far, the only published controlled trial of an antidepressant for the treatment of depression in epilepsy was published in 1985 [8].

Epidemiology of depression

Depressive symptoms are not the same as major depressive disorder although overlap does occur in 32% over a 15-year period [9]. Additionally, among adults, between 4.6% and 19.9% of depression becomes bipolar disorder over a 10-year period, and among children, 7.7–36.8% of depression converts to bipolar disorder [10].

Adverse effects of AEDs also overlap with symptoms of depression, such as fatigue, sleep disturbance, weight gain and memory problems, although some AEDs possess a positive psychotropic profile. These include carbamazepine, gabapentin, lacosamide, lamotrigine, pregabalin or valproate [11,12]. Initiation of treatment with phenobarbital, tiagabine, topiramate or vigabatrin may be associated with acute depression [11]. Also, levetiracetam or zonisamide have been associated with adverse psychotropic effects [12]. Thus, it is important to specify what type of depression is being studied and how it is measured in epilepsy [13]. Psychogenic non-epileptic seizures are a concern as they occur in 11–16% of outpatients with intractable epilepsy. To the extent that psychogenic non-epileptic seizures are mixed in with epilepsy in studies of the epilepsy–depression comorbidity, the extent of this comorbidity may be overestimated [13].

The lifetime prevalence for major depressive disorder (MDD) is around 10% in the general adult population but is estimated at over 17% in patients with epilepsy and even higher (30% and above) in those with drug-refractory focal epilepsy [11,14,15]. The prevalence of depression may be even in the range of 50–55% in hospitalized patients with epilepsy whilst in the paients with remission, depression is less frequent (6–9%) [12].

One of the factors that contributed to the interest in comorbidity of epilepsy and disorders of affect was the introduction of several AEDs in the decades between 1990 and 2010. These agents, often with quite strong chemical profiles enabling seizure control to be achieved in some previously treatment-intractable cases, revealed a spectrum of side effects, which included psychiatric disorders, including depression [3].

Some recent attempts to distinguish psychopathology of depression that could be linked with the pathology have revealed that the majority of comorbid depression in prevalent epilepsy is atypical. Some investigators have even designated a specific form of depression referred to as interictal dysphoric disorder (IDD) [16–19]. The fact that some AEDs are used in the management of bipolar disorders in psychiatric practice provides an interesting link between epilepsy, psychopathology and neurochemistry, which is being actively investigated [3]. Other investigations of depression in epilepsy have specifically examined electrophysiological, biochemical, and neuroimaging variables. These studies find some consistency between depression and frontal and temporal dysfunction [20], notably hypofrontality and amygdala enlargement [21], polytherapy, especially with barbiturate-related drugs, and AEDs that are GABAergic [22].

In addition to the studies of people with existing epilepsy, depression has been examined as a risk factor for developing epilepsy. Such studies find that depression increases the risk for epilepsy raising the possibility that depression and epilepsy may actually share a common pathophysiology [23–25]. There are now considerable data on the association between epilepsy and depression, suggesting that a history of depression is associated with an increased risk for developing epilepsy [26] and for experiencing continued seizures after epilepsy onset [27] and after anterior temporal lobectomy where the presumed seizure focus has been excised [28]. Findings of an increased risk for continued seizures in people with a history of major depression are consistent with the increased prevalence of depression in prevalent epilepsy [29].