

DEPRESSION AND ANXIETY IN EPILEPSY

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Epilepsy, anxiety, and depression are all common disorders. It is therefore not surprising that the conditions coexist in a significant number of patients. Indeed, some authors estimate the lifetime prevalence of depression in association with epilepsy to be as high as 55%. Despite this there has been remarkably little research into the mechanism of depression and anxiety in epilepsy, and even less of its treatment. Most epilepsy clinics are overloaded with referrals and the consultation naturally tends to focus on the patient's seizures and treatment thereof; but it is vitally important that doctors treating people with epilepsy are able to recognise the symptoms of anxiety and, in particular, those of depression. Depression lowers quality of life significantly yet it is an eminently treatable condition. Depression can directly increase seizure frequency through the mechanism of sleep deprivation; failure to recognise depression or inadequate treatment can lead to suicide. Depression also often worsens concordance with antiepileptic medication. Doctors in epilepsy clinics often fail to diagnose depression in their patients and, even when they do, many remain inadequately treated. In primary care, many general practitioners (GPs) are reluctant to give antidepressants to people with depression and epilepsy, fearing that they may exacerbate seizures. As will be seen from the discussion below, this fear is largely unjustified. The mental health of people with epilepsy is often ignored. If this article does nothing else it should encourage readers to examine their practice and ask if they address this important aspect of epilepsy care.

DEPRESSION

Depression in epilepsy may be linked temporally to seizures, but the most common disorder is that of inter-ictal depression. In addition to the recognised symptoms of anhedonia (lack of enjoyment), reduced appetite, poor energy, and sleep disturbance, inter-ictal depression or dysphoria is more likely to be associated with agitation and psychotic features or impulsive self-harm than is depression in people without epilepsy; a fact worth remembering when faced with a restless or truculent patient in the clinic.

Pre-ictal depression may appear hours before a seizure; if this pattern can be recognised a short acting benzodiazepine such as clobazam may be used to abort seizures. Ictal depression is rare, much less common than ictal fear or anxiety, but can be profound.¹

Epidemiology

Estimates of the prevalence of depression in epilepsy vary. A point prevalence of depression of 50–55% is quoted in patients attending hospital epilepsy clinics or videotelemetry units. These figures are based on populations including those with more severe epilepsy, but the few community studies that do exist suggest that prevalence in the community is not insignificant: 20–30% in those with recurrent seizures and 6–9% in those in remission are found to be depressed. However, depression is probably no more common in epilepsy than in other chronic neurological conditions.

There are conflicting data on factors which increase the risk of depression. Most studies show that uncontrolled seizures are associated with a higher prevalence than seizure freedom, but people with temporal lobe epilepsy appear to be at greater risk than those with idiopathic generalised epilepsy, suggesting that it is not just the presence of seizures or social consequences of a diagnosis of epilepsy which are to blame. Depression in a first degree relative has also been identified as an independent risk factor pointing to a genetic predisposition. Paradoxically, depression can follow remission of epilepsy either after epilepsy surgery or the initiation of an effective antiepileptic drug, as part of the phenomenon of forced normalisation first described by Landolt. Indeed, the first few months after epilepsy surgery, successful or otherwise, have been identified as being a period of increased risk for psychiatric disorders; because of this, it is essential that patients being worked up for surgery undergo assessment by a psychiatrist linked to the programme.

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Suicide

In people with epilepsy, death by suicide is more common than in the population as a whole (5% compared to 1.4%). Factors associated with increased risk have been reported to include: younger (25–49 years) male patients, co-existing psychopathology including personality disorders, temporal lobe epilepsy, personal difficulties including social or work-related problems, prolonged duration of epilepsy, and inadequate control of seizures. People with epilepsy often have access to large quantities of antiepileptic drugs and 80–90% of suicide attempts (which outnumber successful suicides by a factor of 10) are overdoses.

Antiepileptic drugs and depression

The schism between psychiatry and neurology in the 20th century impoverished both specialties. Thankfully this separation seems to be less evident now and the treatment of both epilepsy and depression exemplify the need for close collaboration. Patients taking antiepileptic medication may become depressed as a result of their treatment. Sadly, data from drug trials are often unhelpful since the symptoms reported—for example, nervousness, abnormal thinking—are non-specific. The antiepileptic drugs most closely associated with acute depression on initiation of treatment are vigabatrin, phenobarbitone, and topiramate. Depression with topiramate may be linked to abrupt cessation of seizures or drug toxicity. Patients starting tiagabine may develop symptoms of agitation, withdrawal, and mood disturbance suggestive of depression; depression is reported with tiagabine but it is essential that such patients undergo an electroencephalogram (EEG) to exclude tiagabine associated non-convulsive status epilepticus.

Positive psychotropic effects of antiepileptic drugs are seen in many psychiatric disorders: carbamazepine and lamotrigine are used for bipolar disorders and valproate for acute mania. Unfortunately there is no good evidence to show that these drugs lift mood in epilepsy patients.

Recognition of depression

Not all patients who are depressed appear weepy and withdrawn. Complaints such as lack of energy, weight loss, poor concentration, or other physical problems may be symptoms of depression which the physician in the epilepsy clinic may dismiss or ascribe to antiepileptic medication. Open ended questions such as “how are you feeling today?” or “are you still interested in things?” and giving the patient adequate time to reply will often uncover negative feelings. A useful screen for mood disorder which can be completed reasonably quickly is the PRIME-MD patient questionnaire or the Centre for Epidemiologic Studies depression scale, especially if this is given to the patient to complete in the waiting room before they are seen.² More detailed assessment can be done by a number of other questionnaires of which the Beck and hospital anxiety and depression (HAD) scale are often quoted.

Management

Even if a diagnosis of depression is made in people with epilepsy, many do not receive adequate treatment. Information in the *British National Formulary* (BNF) and in patient leaflets for all classes of antidepressant state that they are contraindicated or should be used with caution in people with epilepsy; as a result general practitioners are reluctant to prescribe antidepressants and patients often fail to take them

when they do. Evidence that antidepressants are associated with seizures comes largely from patients who have taken overdoses. That tricyclic overdose carries a high risk of provoked seizures is unquestionable, but the risk with low dose is probably minimal. Nevertheless, because of the risk of overdose in patients with depression tricyclic agents are best avoided and use of the selective serotonin reuptake inhibitors (SSRIs) or serotonin–norepinephrine reuptake inhibitors (SNRIs) are to be preferred.³ Evidence to support this is hard to find, but there has been one open label study of sertraline in epilepsy that showed worsening of seizures in only 6% of patients.⁴ Given the morbidity and mortality associated with untreated depression, this risk is low. Pharmacokinetic drug interactions between SSRIs and antiepileptic drugs are rare, with the exception of inhibition of carbamazepine and phenytoin metabolism by fluvoxamine. Care needs to be taken with the combination of either carbamazepine or oxcarbazepine and SSRIs because of the tendency for both to cause hyponatraemia.

If antidepressants are indicated, who should prescribe them? Choice of antidepressant will depend upon a number of factors including whether one with sedating (mirtazepine), arousing (fluoxetine), or anxiolytic (venlafaxine) properties is required; familiarity with common side effects of antidepressants is also essential since the patients need to be warned about these. In situations such as this close cooperation with primary care and liaison psychiatry services is most helpful.

Epilepsy specialists are often asked if electroconvulsive therapy (ECT) is contraindicated in epilepsy. ECT can be lifesaving, particularly for those patients with psychotic depression, and epilepsy is no contraindication.

Outcome

Treatment outcome depends on the cause. Acute antiepileptic drug related depression beginning shortly after initiation of treatment resolves promptly in the majority of cases. Warning patients, their carers, and GPs of this potential side effect is important as is discontinuation of the offending drug. There is a dearth of evidence on the outcome of treatment of inter-ictal depression in epilepsy, but the sertraline study referred to above showed that 54% of 100 patients had total remission of their psychiatric symptoms. Since patients with depression attending neurology out-patients as a whole appear to have persistent depression,^{5,6} this result is encouraging and should prompt us actively to seek out and treat symptoms of depression in our patients.

ANXIETY Diagnosis

As with depression, anxiety can be seizure related or inter-ictal. Fear is a common manifestation of partial seizures originating in the temporal lobe and it can sometimes be difficult to distinguish between these and panic attacks. Panic disorder consists not only of discrete panic attacks but also an anticipatory fear of them and their consequences which in itself can be disabling; this, together with the short duration and lack of situational triggers in seizures, usually provides the diagnosis, but occasionally panic attacks can co-exist with epilepsy. The symptoms of generalised anxiety disorder are excessive worry and anxiety in association with the somatic symptoms of restlessness, poor concentration, sleep disturbance, fatigue, irritability, and muscle tension. As with depression, asking open ended questions about a

patient's wellbeing may elicit these symptoms or they can be sought more actively by the use of screening questionnaires such as the PRIME-MD. Phobic disorders are common in epilepsy and are often the result of poor seizure control leading to agoraphobia and social phobia. Anxiety is often a dominant symptom of the adjustment disorder which most patients go through when first diagnosed with epilepsy. States of heightened anxiety can come to be self reinforcing with an increase in seizure frequency. The HAD scale is very helpful in diagnosis. It takes the patient 10 minutes to complete and can be scored very quickly. There are clear cut off points indicating the need for treatment.

Epidemiology

Both hospital based and community studies of epilepsy have found the prevalence of an inter-ictal anxiety disorder to be between 10–25% and, in the majority, this is a generalised anxiety disorder.

The aetiology of anxiety in epilepsy is unknown though people have speculated that it is the result of the unpredictable nature of seizures and a perceived "loss of control".⁷

Patients with a previous history of anxiety and depression are at higher risk post-surgically, again emphasising the importance of psychiatric assessment before epilepsy surgery.

Treatment

No studies have addressed the treatment of anxiety in epilepsy specifically, but the SSRIs are usually used, with citalopram and sertraline appearing to be particularly effective when anxiety and depression coexist. Patients need to be warned that initiation of treatment can be associated with increased anxiety in some people and this can require 2–3 weeks of benzodiazepine cover. Cognitive behavioural

therapy is a structured psychological treatment which is of proven efficacy for depression and anxiety. The approach depends upon clear descriptions of symptom onset and maintenance with homework between sessions to reduce symptom severity. This can be done by challenging distorted thoughts and using behavioural techniques.

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