BIDIRECTIONAL RELATIONSHIP BETWEEN EPILEPSY AND PSYCHIATRIC DISORDERS

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Literature review

Abstract

Epilepsy is a common neurological condition with wide-ranging neuro psychiatric manifestations. The relationship between epilepsy and psychiatry has been recognised for centuries. However, the wide range of neuropsychiatric comorbidities and their extent is only now beginning to be appreciated. The impact of these comorbidities on patients' help-seeking behaviour, seizure control and quality of life suggests that early detection and treatment are of paramount importance. Clinical issues in relation to accurate recognition and appropriate management of neuropsychiatric conditions in epilepsy are discussed.

Keywords: epilepsy, psychiatry

The association between epilepsy and mental health problems is reported in ancient texts. Hercules is said to have suffered from epilepsy and 'madness'. For centuries, the care provisions for patients with both mental health problems and epilepsy reflected this overlap. However, despite long-standing recognition of this association and advancement in the care of patients with epilepsy, neuropsychiatric disorders in epilepsy are still often missed.

Patients with intellectual disability, particularly severe intellectual disability, may have different neuropsychiatric presentations from those without intellectual disability.

Available data suggest that psychiatric comorbidity occurs in 20–40% of patients with epilepsy, with an even higher incidence in people with treatment-resistant epilepsy and temporal lobe epilepsy. An additional 5–20% of patients attending epilepsy clinics show evidence of functional non-epileptic attacks. A range of psychiatric problems can occur in people with epilepsy, including affective disorders, psychotic illnesses and personality change. However, most studies have focused on the link between epilepsy and depression and consequently there is a lack of epidemiological data on the association between epilepsy and psychiatric disorders as a whole.

Early recognition and treatment of neuropsychiatric comorbidities in epilepsy is important. The effect of anti-epileptic medications and symptoms of epilepsy itself can either mask or mimic features of psychiatric problems. Patients with epilepsy may present with psychiatric symptoms which may not neatly fit in with commonly used diagnostic categories. Treating these conditions may also pose complexities and dilemmas. Hence, a good awareness of all of these issues will go a long way in improving the quality of care of patients with epilepsy and mental health problems.

Depression is the most common psychiatric disorder in patients with epilepsy and a significant cause of morbidity. Reported rates of depression in epilepsy are 20–55% for patients with recurrent seizures,

depending on the study (Kanner 2003). Precise data on incidence and prevalence are lacking; this could be due to differing methodologies and sample populations in studies, underreporting of depressive symptomatology by patients and underdiagnosis by clinicians. There is growing evidence of a biological link between depression and epilepsy, and depleted biogenic amines and gamma aminobutyric acid may be significant factors in the development of both disorders (Barry 2003).

Kanner *et al* (2000), reported that 60% of patients with depression and epilepsy had shown symptoms of depression for over a year before any treatment was recommended. The delay in recognising the need for treatment was not related to severity of depression.

Features of depression such as sleep disturbance, appetite change, lack of concentration and reduced energy levels are less useful clinically in diagnosing depression, owing to the intrinsic effect of epilepsy and the side-effects of anti-epileptic medications. More emphasis should be given to lack of interest, anhedonia and depressive cognitions in addition to subjective sustained sadness.

Preictal depression. This is considered to manifest as prodromal moods of depression or irritability that occur hours to days before a seizure and may last up to a few days. Symptoms typically resolve post-seizure. It is unclear whether the depressive symptoms are part of seizure manifestation or whether causative factors for depressive symptoms reduce the seizure threshold (Lambert 1999).

Ictal depression. Dysthymia or depressive symptoms (commonly, feelings of anhedonia, guilt and suicidal thoughts) may be manifestations of seizure activity. They are typically sudden in onset, brief, stereotypical and associated with other ictal phenomena (such as automatisms, fear and hallucinations).

Postictal depression. Kanner (2003) studied over 100 consecutive patients with poorly controlled partial seizure disorders and found that 43% had a median of five postictal symptoms of depression. The median duration for 66% of the symptoms was 24 h. Interestingly, postictal depression may also be associated with postictal psychoses.

Interictal depression. Prueter & Norra (2005) reported interictal depression as the most common presentation of depression in epilepsy. Although the exact prevalence is unknown, they estimated it to be between 20% and 70%, depending on the study.

Diagnosis can be made using either the ICD–10 (WHO) or DSM–IV (American Psychiatric Association 1994) criteria for depression, and patients often present with a clinical picture of major depression or dysthymia. Interictal depression often follows a chronic course, interspersed with short, symptom-free phases. Other notable symptoms include atypical pain, phases of euphoric/dysphoric affect, anxiety and phobic symptoms.

Blumer *et al* (2004) described interictal dysphoric disorder of epilepsy, which presents with recurrent brief episodes of mild depressive symptoms. This disorder was initially thought to be specific to patients with epilepsy but recent studies show the presence of similar episodes in other neurological conditions (Mula 2008).

Suicide. Studies have shown a two- to threefold increase in the standardised mortality ratio in patients with epilepsy (Ficker 2000). In a study by Hauser *et al* (1980), the cause of death in an epilepsy cohort by accidents and suicide was 6%.

A strong association has been reported between the risk of suicide and onset of epilepsy at an early age, particularly during adolescence (Nilsson 2002). Overall, the risk of suicide is 2.4 times higher in patients with epilepsy, 11–12 times higher in those with epilepsy and anxiety or psychosis, and 32 times higher in those with epilepsy and depression (Christensen 2007).

Anxiety. Very little attention has been given to distinguishing between the features of anxiety occurring in epilepsy or the subtypes of anxiety disorders in epilepsy populations. Consequently, the incidence and prevalence of these disorders are unclear. One large cross-sectional population-based study using primary care records showed an 11% rate of anxiety disorders in 5834 people who

had epilepsy compared with 5.6% in 831 163 people without epilepsy (Gaitatzis 2004).

Postictal anxiety, typically occurs shortly after a seizure and can be associated with postictal dysphoria or depression. Occasionally, anxiety is the only postictal symptom experienced; however, a combination of mood and anxiety symptoms is more common. This is usually related to seizure activity and is most likely to be self-limiting. No specific treatment other than reassurance is generally required.

Interictal anxiety is common and the fears (phobic anxiety) often relate to the perceived risk of personal injury and brain damage, and having seizures in unfamiliar situations. The phenomenology for interictal anxiety is not clearly defined, and this is possibly related to the difficulty in making a distinction between independent comorbid anxiety (i.e. anxiety is not a manifestation of underlying undetected seizure semiology) and interictal anxiety relating to underlying undetected seizure semiology.

Other risk factors

A community study has shown that female gender, younger chronological age, divorce or separation, low educational attainment and unemployment are associated with increased anxiety in patients with epilepsy (Mensah 2007).

Psychosis of epilepsy includes a range of psychotic disorders with variable phenomenology related to the seizure disorder. Psychosis of epilepsy was differentiated from schizophrenia in the 1950s, and it described paranoid delusions with visual and auditory hallucinations occurring in patients with epilepsy. Patients with psychosis of epilepsy rarely exhibit negative symptoms of schizophrenia, have a generally preserved personality and affect, and better premorbid functioning.

Psychotic experiences in the general epilepsy population are present in 0.6–7% (Krohn 1961), and these figures can increase to 19–27% (Devinsky 1993) in epilepsy centres. In a prospective study of psychosis and epilepsy, children with temporal lobe epilepsy had a 10% chance of developing interictal psychoses during a 30-year follow-up, whereas the risk in the general population was about 0.8% (Torta 1999).

Ictal psychosis of epilepsy

In ictal psychosis of epilepsy, psychotic symptoms are a manifestation of an underlying epileptic seizure. Commonly encountered symptoms are hallucinations (olfactory, gustatory, visual or auditory) or delusions (particularly grandiose or paranoid). The symptoms are usually self-limiting; however, rarely (in conjunction with partial status epilepticus) they may be mistaken for schizophrenia or mania. The presence of confusion, lack of systematised delusions and prominent non-auditory hallucinations can point to the presence of ictal psychosis of epilepsy rather than other schizophrenia-like psychotic disorders.

Ictal psychosis occurs with associated epileptic brain discharges and EEG changes will often be seen. The exception is patients with simple partial status, where an EEG may be normal. In the majority of cases, the focus is in the limbic and isocortical components of the temporal lobe. In about a third of patients, the focus is extratemporal, usually occurring in the frontal or cingulate cortex (Sachdev 1998).

Postictal psychosis of epilepsy

Postictal psychosis accounts for about 25% of epileptic psychoses. A common presentation is that of a patient with partial or generalised epilepsy who experiences a cluster of complex partial or tonic–clonic seizures. Within 72 h of postictal confusion, affective and psychotic symptoms develop. There is often a short period of clear consciousness before symptom onset. Affective symptoms with grandiose and religious delusions and simple auditory hallucinations are common.

The duration of postictal psychosis is generally short and up to 2 weeks is considered to be the maximum. The following neurological factors are associated with increased risk of developing postictal psychosis: bilateral seizure foci; processes associated with bilateral limbic lesions (e.g. encephalitis, head injury); and a relative

increase in seizure frequency preceding the psychotic symptoms (Devinsky 2003).

Interictal psychosis of epilepsy

The prevalence of interictal psychosis of epilepsy in populations with epilepsy is between 3 and 7% (Toone 2000). It is characterised by the presence of psychotic symptoms not temporally related to seizure activity and a mental state characterised by delusions and hallucinations in clear consciousness. Bizarre or disorganised behaviour, thought disorder, personality change, negative symptoms of schizophrenia or affective changes are not commonly seen. Before a diagnosis of interictal psychosis can be made, the following conditions need to be ruled out: anti-epileptic drug toxicity, non-convulsive status epilepticus, recent head trauma, and alcohol or drug intoxication or withdrawal.

Alternative psychosis of epilepsy or forced normalisation

This disorder, described by Landolt (1953) as forced normalisation and by Tellenbach (1965) as alternative psychosis, is characterised by an inverse relationship between seizure control and the occurrence of psychotic symptoms. The concept of forced normalisation also requires an EEG becoming more normal or entirely normal over time. It was thought to occur after years of treatment. It is more frequently recognised by European clinicians, and most commonly presents with paranoid psychosis without clouding of consciousness and with associated affective symptoms. Several anti-epileptic drugs are associated with this presentation (e.g. ethosuximide, vigabatrin, topiramate, zonisamide) and suppression of seizures is considered a possible aetiological factor. It is now recognised that although this phenomenon may be seen in a small subgroup of patients, this is not the main explanation for comorbid psychotic illness in epilepsy (Krishnamoorthy 2002).

Comorbid personality disorders and epilepsy

The extent of personality disorders in association with epilepsy is 0.7–2.0% of general practice populations (Edeh 1987; Forsgren 1992). In those with partial epilepsy (particularly temporal lobe epilepsy), rates of personality disorder range from 13 to 35%. A study reviewing personality disorders among individuals with treatment-refractory epilepsy found dependent and avoidant personality disorders to be the most common (Lopez-Rodriguez 1999).

Organic personality disorder

Some people with epilepsy (particularly those with temporal lobe epilepsy) develop behavioural changes. The most common of these are:

viscosity – a tendency for prolonged interpersonal contact, with pedantry and lack of socially appropriate ending of conversations

hyposexuality – decresed libido and impotence (about 50% of male patients with temporal lobe epilepsy)

· religiosity – very strong preoccupation with religion and philosophy

· hypergraphia – compulsive writing

· aggression – increased incidence of interictal violence and hostility.

The combination of these traits is sometimes referred to as Gastaut–Geschwind syndrome.

An inevitable decline in personality associated with epilepsy, often referred to as epileptic personality, has been rejected. It is recognised that past reports of such a decline may have been describing the effects of psychosocial factors such as institutionalisation and biological factors such as sedative medication or brain damage.

Functional non-epileptic attacks

These are a diverse group of disorders in which paroxysmal events (fits or 'funny turns') may be mistaken for epilepsy, but are not caused by epilepsy (no seizures or epileptiform activity in the brain). They are either physiological (about 10–20%) or psychogenic (about 80–90%) in origin. Diagnosis can be particularly difficult and requires specialist assessment.

Causes of functional non-epileptic attacks

Psychogenic causes	Physiological causes
• Depersonalisation disorder	• Syncope
• Hypochondriasis	• Transient ischaemic attacks
• Somatisation disorder	• Paroxysmal movement disorders
• Dissociative disorders	• Narcolepsy
• Conversion disorders	• Non-epileptic myoclonus
• Panic disorders	
• Factitious disorders	

A variety of terms are used to describe non-epileptic seizures: hystero-epilepsy, hysterical seizures, pseudoseizures, pseudo-epileptic seizures, non-epileptic pseudoseizures, hysterical epilepsy and non-epileptic attack disorder (Gates 2002).

any of these terms are disparaging and also are not representative of underlying pathophysiology. Szaflarski *et al* (2000) estimated the annual incidence of psychogenic non-epileptic seizures in the general population to be about 3 per 100 000, with an estimated prevalence of 33 per 100 000 (Benbadis 2000). Approximately 5–20% of patients in epilepsy clinics have been considered to have only non-epileptic fits.

About 80% of patients with psychogenic non-epileptic seizures are women and are aged between 15 and 35 years, although elderly and paediatric patients may also develop them (Shen 1990). It is important to note that non-epileptic seizures may occur in people with epilepsy (about 33%).

The underlying mental processes leading to non-epileptic fits and their exact pathogenesis remain unclear, but a number of psychological factors/disorders are often aetiologically relevant. These include affective/anxiety disorders, somatoform and/or dissociative disorders, abnormalities of personality (borderline personality disorder being the most common), and a history of sexual or physical abuse.

Neuropsychiatric aspects of epilepsy surgery

Post-epilepsy surgery neuropsychiatric problems mirror the overlap of psychiatric problems with epilepsy. Overall rates of neuropsychiatric problems following epilepsy surgery can be very similar to rates in people with epilepsy in general. However, some patients can show improvement in pre-existing neuropsychiatric problems, whereas others can develop new problems. *De novo* psychosis is rarely seen post-epilepsy surgery (0.5–1%). More commonly, about a third of patients can present with anxiety and depression 6–12 weeks after the surgery irrespective of surgery outcome. Foong&Flugel (2007) summarise the neuropsychiatric issues in relation to epilepsy surgery.

Both epileptic disorders and their treatment can affect the mental state of patients and produce a wide variety of symptoms. A range of mental health problems can be seen in patients with epilepsy that can lead on to significant distress, dysfunction and impair their quality of life. Neuropsychiatric problems in epilepsy are difficult to diagnose and they are frequently missed or overlooked. Successful treatment can have a profound effect on a patient's quality of life and may contribute towards better seizure control.

Conclusions

Both epileptic disorders and their treatment can affect the mental state of patients and produce a wide variety of symptoms. A range of mental health problems can be seen in patients with epilepsy that can lead on to significant distress, dysfunction and impair their quality of life.

Neuropsychiatric problems in epilepsy are difficult to diagnose and they are frequently missed or overlooked. Successful treatment can have a profound effect on a patient's quality of life and may contribute towards better seizure control.

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