

# The neurology–psychiatry interface in epilepsy

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Epilepsy and mental illness have a bidirectional association. Psychiatrists are likely to encounter epilepsy as comorbidity. Seizures may present as mental illness. Equally, the management of psychiatric conditions has the potential to destabilise epilepsy. There is a need for structured epilepsy awareness and training amongst psychiatrists. This paper outlines key considerations around diagnosis, treatment and risk while suggesting practical recommendations.

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## Introduction

Epilepsy is a common neurological disorder with a prevalence in Ireland of approximately 1% (Linehan *et al.*, 2009). The definition of epilepsy has evolved over the last two decades and an internationally accepted clinical definition (Fisher *et al.*, 2014) as adopted by the international league against epilepsy reflects clinical considerations, risk of further seizures as well as the issue of disease resolution. While epilepsy is a complex neurological condition and managed primarily by neurologists, in this paper we outline diagnostic, therapeutic and risk-related aspects that highlight the relevance of this neurological illness to the practising psychiatrist.

## Epilepsy and mental health

Psychiatrists encounter epilepsy as both a comorbidity and a differential diagnosis. Olfactory hallucinations in a patient with psychosis may raise the possibility of temporal lobe epilepsy (TLE) (Flor-Henry, 1969) or seizure activity may have a role in challenging behaviour in a person with an intellectual disability (Blickwedel *et al.*, 2017).

Encountering epilepsy in psychiatric patients is not uncommon as psychiatric morbidity is over-represented in individuals with epilepsy with increased rates of affective disorders (25–74%), anxiety disorders (10–25%) and psychosis (2–7%) (Jones *et al.*, 2010). A recent Irish

study (Murphy *et al.*, 2018) noted the prevalence of epilepsy in general psychiatric inpatient settings to be over 3%; three times that of general population estimates. This is perhaps unsurprising as some of these illnesses, particularly psychotic illness are thought to have a neurodevelopmental origin (Murray & Lewis, 1987). Additionally, there is evidence of genetic overlap between psychosis and epilepsy (Clarke *et al.*, 2012).

Epilepsy and psychiatric disorders are individually related to higher mortality rates. In epilepsy this is particularly true of those with uncontrolled seizures (Robertson *et al.*, 2015). The two conditions are also associated with a higher risk of suicide and other physical comorbidities.

## Epilepsy and people with intellectual disabilities

The prevalence of epilepsy in people with intellectual disabilities is significantly higher. A recent systematic review and meta-analysis (Robertson *et al.*, 2015) showed a pooled epilepsy prevalence of 22.2% (95% confidence interval 19.6–25.1) in those with intellectual disabilities with prevalence increasing as the severity of disability increased. The Royal College of Psychiatrists has published recent guidance for the management of epilepsy in those with intellectual disabilities which recommends epilepsy training as part of higher specialist training (HST) for those psychiatrists who specialise in intellectual disabilities in the United Kingdom (Royal College of Psychiatrists, 2017b). In Ireland, people with intellectual disabilities often receive care in general adult psychiatric settings, particularly where individuals have

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a mild-to-moderate intellectual disability or additionally if individuals require involuntary treatment. Thus reasonable knowledge of epilepsy concerns in people with intellectual disability is important across the psychiatric specialism in Ireland.

## Diagnostic issues

### *Seizures can present as symptoms of mental illness*

Complex partial seizures can present as poor impulse control, 'rage attacks', suicide attempts, rapid mood swings, depression, psychotic episodes, bulimia, panic attacks, obsessive-compulsive symptoms and somatic complaints (Stern & Murray, 1984). A patient may be treated with psychotropic medication for years before an organic cause is suspected. Herein lies the value of being alert to epilepsy as a differential diagnosis where there are atypical presentations, diagnostic overshadowing, treatment resistant illness, neurological signs, history of central nervous system illness such as encephalitis, a concerning medical history such as one involving unexplained loss of consciousness or a family history of seizures.

A particularly important type of seizure that may present as mental illness is TLE which can present as psychosis. Psychosis in TLE (Belletsky & Mirsattari, 2012) may have either a relapsing-remitting (concurrent with seizures) or chronic course (involving interictal phase) and preictal states may present with an altered sensorium, including a range of perceptual abnormalities including visual, auditory, olfactory or gustatory illusions or hallucinations.

Frontal lobe epilepsy can present with behavioural disturbance, psychiatric symptoms including depression or psychosis and cognitive changes (Braakman *et al.*, 2011; Gold *et al.*, 2016); it can be associated with attention deficit hyperactivity disorder (ADHD) in children (Braakman *et al.*, 2011).

There may be a relationship between seizure control and psychotic symptoms in some patients. The term 'forced normalisation' is used to describe psychotic episodes associated with the remission of seizures and disappearance of epileptiform activity on electroencephalogram in individuals with epilepsy (Loganathan *et al.*, 2015). Further there could be psychotic activity associated with seizures during the pre-ictal, ictal or post-ictal stages. There could be identified changes in affect and mood associated with seizures (Kanner & Rivas-Grajales, 2016). The management of such psychoses require a careful balance between anti-epileptic medications, antipsychotic or other psychotropic drugs, with close clinical monitoring and communication between the patient, their family, and involved specialities.

In people with intellectual disability presenting with challenging behaviour, it is important for the treating clinician to rule out seizure activity given the high rate of seizure disorder as a comorbidity in this group (Blickwedel *et al.*, 2017; Roberston *et al.*, 2015). The assessing clinician may need to consider the role of factors such as seizure frequency, peri-ictal events and the role of anti-epileptic drugs (AEDs) additionally in their formulation (Kerr *et al.*, 2016).

### *The value of an Electro-Encephalogram (EEG)*

An electro-encephalogram (EEG) may be helpful in the investigation of possible seizure disorder. However, caution is required in interpretation as either no abnormal activity or only minimal changes such as focal slowing or brief patterns of spikes and waves may be evident even in individuals with diagnosed epilepsy. The sensitivity of interictal EEG varies from 29–55% (Pillai & Sperling, 2006) with higher estimates for repeat examinations and activation techniques whilst specificity is variable with estimates in excess of 90% for some epilepsy syndromes (Oliviera & Rosado, 2004). Video-EEGs have significantly greater diagnostic yield (Pillai & Sperling, 2006). There needs to be specific caution in interpreting EEGs in people with intellectual disability as they may have abnormal brain wave patterns linked to a congenital brain defect or damage.

EEG departments helpfully use photic stimulation, hyperventilation or sleep deprivation (all of which lower the seizure threshold) to help evaluate cases where a referral clearly queries the diagnosis of epilepsy. Video-EEG is the only definite way to diagnose functional seizures and behavioural disturbance linked with epileptic activity. This is sometimes limited to tertiary centres but as an investigation this can be invaluable in providing diagnostic certainty.

### *Indications for Magnetic Resonance Imaging (MRI) of the Brain*

Where an organic cause is suspected in individuals presenting with either behavioural disturbance or symptoms suggesting a mental illness and particularly where focal deficits are noted on neurological examination, magnetic resonance imaging (MRI) of the brain should be obtained. Brain MRIs are often superior to Computerised Tomography due to their higher resolution allowing them to identify smaller space occupying lesions and separate more clearly grey and white matter. Despite this, a normal MRI of the brain does not exclude a diagnosis of epilepsy. MRI abnormalities may be seen in 80% of patients with refractory focal epilepsy but estimates are four times lower in patients with a single unprovoked seizure or epilepsy in remission (Roy & Pandit, 2011).

## Therapeutic issues

### *Psychotropics and seizure threshold*

Seizure thresholds may be affected by the majority of psychotropic agents, although there is a large variance between psychotropic agents in relation to such an effect. As a basic tenet, psychotropic agents that have sedative effects have an increased likelihood to be associated with inducing seizures (Taylor *et al.*, 2015). This is important as even when prescribing antidepressants or antipsychotics in a patient with well controlled epilepsy, there is a potential for destabilisation which should be highlighted to the patient, his/her carer and clinical correspondence copied to the concerned neurologist or general practitioner. An effect on seizure threshold may have implications for driving and safety in other social situations.

Guidelines are constantly evolving in this area but the Maudsley Prescribing Guidelines 13<sup>th</sup> edition (Taylor *et al.*, 2018) currently state that selective serotonin reuptake inhibitors (SSRIs) (except citalopram), the antidepressant mirtazapine and the antipsychotic agents risperidone, aripiprazole, haloperidol, amisulpiride and sulpiride are associated with a minimal impact on seizure thresholds and thus should be considered for the management of mood or psychotic disorders in individuals with epilepsy. Caution must also be exercised in discontinuing benzodiazepines, lamotrigine or sodium valproate (when used as mood stabilisers) as these may be masking latent seizures in a patient who has well controlled epilepsy.

ADHD is overrepresented in individuals with epilepsy (Williams *et al.*, 2016). Stimulant medication and potentially atomoxetine used in the treatment of ADHD have the potential to reduce seizure threshold (Harpin *et al.*, 2008).

### *Anti-Epileptic Drugs (AEDs) and psychiatric/behavioural manifestations*

There is increasing evidence of psychiatric disorders or behavioural disturbance arising due to treatment with AEDs. AEDs may be neutral, have positive effects on the management of mental illness or negative effects (Nadkarni & Devinsky, 2005; Royal College of Psychiatrists, 2017a). Positive effects of AEDs include, for example, the antidepressant effect of lamotrigine or mood stabilising effects of sodium valproate. Negative effects of AEDs include cognitive problems and dependence risk with barbiturates and the risk of psychosis and affective disorders with phenytoin and vigabatrin. Levetiracetam in particular has been associated with behavioural disturbance and affective adverse effects (Abou-Khalil, 2008). Such adverse effects have

been associated with significant AED discontinuation rates (Stephen *et al.*, 2017).

### *AED/Psychotropic interactions*

Another area of caution when prescribing psychotropics is the potential for pharmacokinetic interactions through cytochrome P450 enzymes (Taylor *et al.*, 2018). Some commonly prescribed antidepressants such as fluoxetine and sertraline at higher doses can increase anticonvulsant plasma levels. Some anticonvulsants such as phenytoin and carbamazepine can reduce plasma levels of psychotropics. Of note, recent guidance for AED prescribing (Royal College of Psychiatrists, 2017a) advocate against the first line use of older AEDs such as phenytoin and phenobarbitone in epilepsy.

### *Teratogenicity*

Sodium valproate can be prescribed both for affective disorders and seizure control. The use of this medication is best avoided in women of child bearing age given its significant teratogenic potential (Ornoy, 2009). Particular care must be taken with additional safeguards such as a clear discussion of risks and benefits as well as the use of contraception should its use be necessary, in keeping with recent regulations (Sisodiya, 2018).

### *Medication adherence*

In patients with comorbid mental illness and epilepsy, non-adherence with prescribed medication has the potential to precipitate relapse in mental illness and destabilise seizure control. Both conditions are separately known to have limited adherence rates with one study citing that a third of those with epilepsy may not be adherent to prescribed medication (Getnet *et al.*, 2016). Up to 60% of those with psychosis may be non-adherent at some point over a 4 year follow up period (Valenstein *et al.*, 2006). Patients may therefore need suitable education, oversight and support for continuity with medication.

### *Specific considerations in people with intellectual disabilities*

The prescription of psychotropic medication in people with intellectual disabilities requires care due to a lower threshold for side effects and an increased prevalence of physical comorbidities. Medication, when clearly indicated, should be used cautiously at lower doses with specific monitoring for outcomes and emergence of side effects. The prescription of antiepileptic medication in people with intellectual disabilities and epilepsy requires particular care in respect of issues around

consent, capacity to consent, the involvement of carers, monitoring of outcomes and specific choice of medication (Royal College of Psychiatrists, 2017).

### Areas of Risk

Given that psychiatric treatment can potentially destabilise seizure control, a clinician may need to be mindful of the social risk profile that this may create. Alcohol misuse, for example, is a significant comorbidity with mental illness (Regier *et al.*, 1990) and carries the risk of destabilising seizure control (Hillbom *et al.*, 2003).

### Driving

Experiencing a seizure whilst driving can risk injury to the person or other road users. In Ireland, regulations governing driving for those with epilepsy are published by the Road Safety Authority (RSA, 2016) and this makes an essential reference document for practitioners. They make different recommendations for those with daytime and nocturnal seizures as well as some specific aetiologies. The RSA recommends a 12-month seizure free period prior to recommencing driving for those with daytime seizures, alongside other stipulations such as compliance with treatment.

### Activities of daily living

Guidance from the National Institute for Health and Care Excellence (NICE) (2018) highlights the need to be mindful of risks in those with seizures in activities of daily living. Such may extend to psychiatric inpatient settings. Examples would include situations such as operating electrical equipment and swimming if undertaken as part of occupational therapy. Bathing arrangements require special care and showers are safer than baths in those with seizures. Where the person wishes to bathe, continuous observation during that time would be the only measure that mitigates risk. Risks associated with activities of daily living require particular care and specialist care planning in people with intellectual disabilities who are more likely to have other physical comorbidities, a greater sensitivity to changes in medication and require assistance with communication (Royal College of Psychiatrists, 2017b).

### SUDEP

The risk of sudden unexpected death in epilepsy (SUDEP) is 1 in 1000 person years but can be as high as 1 in 100 person years in those with treatment resistant epilepsy and uncontrolled seizures (Shankar *et al.*, 2017). There are potentially modifiable risk factors that mitigate this risk such as nocturnal monitoring, compliance and advice on sleeping position (Shankar *et al.*,

2016). For the psychiatrist an awareness of the impact of treatment adherence and co-morbid alcohol or psychoactive substance (ab)use are important due to them being modifiable risk factors for individuals with epilepsy. Some studies suggest that intellectual disabilities are a risk factor for SUDEP (Young *et al.*, 2015). Specialist advice from a neurologist may be helpful when considering the prescription of new psychotropic in those with poorly controlled seizures and this is particularly important in those with comorbid intellectual disabilities. A good tool to inform patients of their risk of SUDEP is the SUDEP and Seizure Safety Checklist (SUDEP Action, 2017).

### Management of prolonged seizures

Doctors working in psychiatry may find themselves responding to a prolonged seizure for an inpatient or working with patients who have a history of past status epilepticus. The management of such can often be foreseen and a history at the time of admission is often the best time to prescribe a 'rescue medication' on an 'as required' basis. Buccal midazolam may be safer and more acceptable to patients than other modalities of benzodiazepine use (Scott *et al.*, 1999). Training in administering midazolam and the other aspects of emergency care in status is invaluable for first responders.

### Discussion

Epilepsy is a prevalent neurological disorder that is over-represented in patients in psychiatric services (Murphy *et al.*, 2018). Patients with epilepsy report uncertainty for their future and describe the fear of having a seizure as the 'worst thing about having epilepsy' and as important as the limitations in lifestyle, school, driving and employment that may occur with this diagnosis (Fisher *et al.*, 2000). Carers for those with epilepsy have a high level of knowledge (McEwan *et al.*, 2007) around epilepsy and can be an invaluable source of information when assessing a patient and this is particularly true for patients with an intellectual disability (Espie *et al.*, 2003) where there may be special needs around communication. A diagnosis of epilepsy has been demonstrated to not alone reduce the quality of life of the patient but also adversely impact on the quality of life of the care-givers (Guti-Errez *et al.*, 2018).

A psychiatrist should be alert to the bi-directional impact of mental illness and physical illness on each other. The spectrum of physical illness that a psychiatrist particularly needs to be aware of includes endocrine, metabolic, cardiac and neurological disorders. Epilepsy is one such neurological disorder at the interface of medical specialities that requires particular care in view of its higher mortality and complex risk profile.

**Table 1.** Information to be recorded in psychiatric inpatient notes

## Aspects of epilepsy to be recorded in psychiatric inpatient notes

1. What are the types of seizure?
2. What are the triggers for a seizure?
3. What does a seizure look like (before, during and after a fit)?
4. What is the regular epilepsy medication?
5. Is there a predetermined plan for rescue medication advised by neurology?
6. Do the following risks need consideration in the inpatient setting?
  - a) Safety during activities of daily living, particularly bathing
  - b) Occupational activities e.g. therapy groups particularly swimming, operating tools when on leave from the inpatient setting
  - c) Will the current treatment plan affect risk of sudden unexpected death in epilepsy (SUDEP)?
  - d) Are staff aware of a plan to manage a prolonged seizure?

Simple interventions and effective communication has the potential to offer incremental benefit for patients in diagnosis, therapeutics and risk management.

A useful aid for key aspects of history and management considerations for patients with epilepsy in psychiatric inpatient settings is presented as Table 1. This has been formalised into a diagnosis triggered tool which has been piloted in Irish settings (Murphy *et al.*, 2017; Moloney *et al.*, 2017) and is attached as supplementary online material to this article. Additional sources of advice for psychiatrists when managing a patient with comorbid epilepsy are included as an online appendix.

There is substantial training for neurologists in relation to epilepsy both in basic and HST schemes and this is a disorder managed primarily by consultant neurologists, often in tertiary centres. There is a need for increased awareness of this disorder as a comorbidity in the psychiatric setting (Murphy *et al.*, 2018). With awareness and a systematic approach to assessment, this may be an area where psychiatric expertise can contribute to safer and better lives for people with epilepsy.

### Supplementary materials

To view supplementary material for this article, please visit <https://doi.org/10.1017/ipm.2018.49>

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### Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committee on human experimentation with the Helsinki Declaration of 1975, as revised in 2008. The authors assert that ethical approval for publication of this paper was not required by their local REC.

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