Neuropsychiatry of epilepsy

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Introduction

Neuropsychiatry is defined as "a field of scientific medicine that concerns itself with the complex relationship between human behaviour and brain function, and endeavours to understand abnormal behaviour and behavioural disorders on the basis of an interaction of neurobiological and psychosocial factors".[1] There is a great deal of overlap and clinical interaction with specialties such as neurology, neurosurgery, neuropsychology, psychiatry of old age, liaison psychiatry and psychiatry of learning disability. Epilepsy is one of the most prevalent neurological disorders and is probably the most important cause of neuropsychiatric referral. We discuss below the main clinical management issues pertaining to the psychiatric co-morbidity in epilepsy.

Epilepsy and psychiatric disorder

Epilepsy, affecting 5-10 per 1000 population,[2] is characterised by the occurrence of at least two unprovoked seizures brought about by abnormal discharge of cortical neurons. The lifetime risk of developing psychiatric disorder with epilepsy is extremely high with such individuals having greater psychiatric co-morbidity when compared to the general population, neurological controls and individuals with a chronic non-neurological condition.[3] Psychiatric co-morbidity is estimated to be between 20%-30%[4] within a community setting, however in specialised treatment settings, these rates are even more pronounced, eg. neurology/neuropsychiatry clinics where rates up to 50% are not uncommon.[5]

These high rates may be accounted for by the chronic and debilitating nature of epilepsy that leaves individuals with feelings of helplessness and loss of control. Psychiatric disorders can arise due to the underlying seizure discharges too. Disorders manifesting in the peri-ictal period are associated with abnormal seizure discharge whereas such discharges are thought to be absent with disorders arising during the inter-ictal period. When recurrent and unabated, seizure discharges damage brain areas implicated in emotional regulation and can subsequently lead to long-lasting psychiatric deficits. The psychiatric effects of anti-epileptic medication are significant and can worsen pre-existing psychiatric disorder directly. An indirect mechanism is through the reduction of drug levels of antidepressants/antipsychotics through liver enzyme induction. Moreover there are nutritional deficiencies that can arise with anti-epileptics, eg. folate deficiency with valproate.

Amongst the psychiatric illnesses encountered, depression and anxiety disorders are by far the commonest. Depression affects up to 30%,[6] while anxiety disorders affect roughly 25% of individuals with epilepsy. Psychoses (2%-7%) and personality disorders (1%-2%) are less common but also encountered.[7] A large population based cohort study published recently observed that people with epilepsy have a 2.5 fold increase in risk of developing schizophrenia or schizophrenia-like psychoses – particularly in the absence of a family history of psychosis.[8] This implies that epilepsy is indeed a risk factor for the future development of schizophrenia. Historically, it has been reported that, compared with schizophrenia, the psychoses of epilepsy are associated with better preservation of affect and personality, an increased incidence of visual hallucinations, and purely delusional states and response to treatment with anti-epileptic medication.[9] Realistically, even the most astute of clinicians would have difficulty differentiating the two disorders. However, ascribing the right diagnosis to individuals with the psychoses associated with epilepsy as opposed to schizophrenia has its merits; including the prevention of potential stigma of a psychiatric label and providing more appropriate treatment.

Amongst the ICD-10 classified personality disorders, avoidant and dependent sub-types have been found to predominate among individuals with epilepsy. This possibly relates to the environment of uncertainty regarding seizure experiences and also the ensuing overprotection such individuals may experience from their families.[10] An inter-ictal behaviour syndrome/personality disorder has been described in Temporal Lobe Epilepsy (TLE) whose features include preoccupation with philosophical and religious concerns, anger, excessive emotionality, viscosity, circumstantiality, altered sexuality and hypergraphia.[11] It has been assigned an eponym, the Gastaut-Geschwind syndrome. However a recent review on the issue of an 'epileptic personality' suggests that personality traits rather than a personality disorder per se seems more likely and these tend to resemble the cluster C categorisation of disorders in DSM-IV.[12] The review concludes by stating that these personality changes are not specific to TLE but also seen in other neurological and non-neurological conditions.

The number of individuals who suffer with 'pseudoseizures'

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or non-epileptic attack disorder (NEAD) is harder to quantify and rates between 10-50% have been observed, dependent on the treatment setting.[13] NEAD is considered a dissociative disorder in the European setting (ICD-10); however it is a somatoform disorder in the USA (DSM-IV). Despite the international classification differences, these individuals possess common traits: they tend to have higher levels of psychopathology, a history of sexual abuse, are female and up to 30% do possess an underlying seizure disorder.[14] Moreover NEAD tends to manifest before the age of 40 years and is commoner in individuals who have observed a friend or family member with an epileptic illness.

Temporal lobe epilepsy (TLE)

TLE is a sub-type of epilepsy renowned for higher rates of psychiatric illness and rates between 50%-70% are not uncommon.[15,16] It is postulated that these higher rates arise due to deficits in the temporal lobe structures that comprise the limbic system and impact on emotional processing and regulation.[17-19] Depression affects a significant proportion of individuals with TLE, up to 30%.[7] Anxiety disorders are a close second with rates up to 25%.[7]

Psychosis is another entity that is more common in TLE with the association between the temporal lobe and psychosis only being made in the last century. This was initially reported by Slater & Beard[22] in 1963 while Flor-Henry[23] subsequently noted the similar clinical phenotypes of TLE with psychosis and schizophrenia in 1969. The prevalence of psychoses in TLE is estimated to be between 5%-10% which is ten times higher than that seen in the general population and in certain settings this figure is more substantial.[24] Psychoses generally tend to manifest approximately 11-15 years after an epileptic disorder is diagnosed[25] with the post-ictal psychoses being by far the most common.[26]

The psychoses associated with TLE are generally regarded not to improve with epilepsy surgery and thus such candidates are generally excluded from surgical intervention. However patients with co-morbid schizophrenia need not necessarily be deprived of surgical treatment as they benefit from such therapy.[27]

Past researchers have been interested in the neuropathology of psychosis associated with TLE as a 'mock-up' of schizophrenia.[28] However in the surgically resected tissue of such subjects, hamartomas, gangliogliomas and dysembryoblastic neuroepithelial tumours were found in excess,[29,30] and we now see that this neuropathology is quite distinct from that of schizophrenia.[31] It is worth noting that, while epilepsy surgery is a treatment for epilepsy, it is a recognised risk factor for the development of psychosis *de novo*. In a recent TLE case series, 11 developed psychosis post-operatively among a prospective cohort of 320 individuals within the first post-operative year.[32]

Psychiatric disorder and epilepsy treatment

The mainstay of treatment of epilepsy involves medication. These medications all have the potential to precipitate psychiatric side-effects including cognitive, psychomotor, affective and psychotic changes. Amongst these, phenobarbitone, phenytoin, primidone, vigabatrin, topiramate, tiagabine and benzodiazepines are associated with higher rates of depression. Primidone, vigabatrin, topiramate and tiagabine are associated with psychosis at a rate of between 1%-5%. Interestingly, some of the newer anti-epileptic drugs such as vigabatrin, tiagabine and topiramate while possessing cleaner 'neurological' side-effect profiles, can have significant psychiatric consequences as described above. Certain anti-epileptic medications reduce the efficacy of tricyclic antidepressants or antipsychotics due to the induction of hepatic metabolism especially through the cytochrome P_{450} system: chief culprits are phenytoin, phenobarbitone and carbamazepine.

Vagal nerve stimulation is a novel therapy that is used in the prophylaxis of seizures after unsuccessful drug therapy especially in the setting of refractory partial-onset seizures. It has demonstrated favourable long-term results and seizure frequency can be reduced by up to 50%.[33] It is postulated that such intervention may also be beneficial in treatment resistant depression; however the results of long-term clinical trials are currently awaited.[34]

Treatment of psychiatric disorder in epilepsy

Antidepressants

The antidepressants that are considered safe to use in epilepsy are the selective serotonin re-uptake inhibitors (SSRI's) and the serotonin-noradrenaline re-uptake inhibitors (SNRI's).[33] They have a much lower seizure induction potential relative to the other antidepressants and appear to be well tolerated. However, when taken in overdose, the seizure threshold is reduced and as a result, seizures are more likely to occur. Tricyclic antidepressants (TCAs) are a recognised treatment for depression in epilepsy, however they have the potential to reduce the seizure threshold. Among the TCAs-clomipramine is the most likely to cause this undesirable side-effect.

Among the other antidepressants, trazodone, nefazodone and the monoamine-oxidase inhibitors are relatively safe for use in patients with comorbid epilepsy. Although there is currently limited data regarding mirtazapine, its use in individuals with a history of seizures has been documented. However phenytoin and carbamazepine have been associated with lower mirtazapine plasma levels. Moreover since instances of neutropenia and agranulocytosis have been described with mirtazapine use; the practice of combining mirtazapine with another bone-marrow suppressing agent such as carbamazepine, is best avoided.

Antipsychotics

The safest agents for the treatment of psychosis associated with epilepsy appear to be the atypical agents such as olanzapine, risperidone and quetiapine.[33] They lack significant seizure-threshold lowering potential and have a favourable side-effect profile. Typical antipsychotics such as haloperidol may also be used. Clozapine and chlorpromazine have consistently been shown to have a high propensity to induce seizures and as such their prescription should be precluded.

Conclusion

Epilepsy is associated with significant psychiatric co-morbidity and psychiatrists need to possess a good understanding of the particular presentations, treatment and drug interactions relevant to this association. Epilepsy requires a holistic approach in order to promote both good neurological and psychiatric outcomes. The expansion of

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neuropsychiatry services in Ireland is thus an important goal.[35]

Declaration of interest : None

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Cover series 2006

The artwork for the cover series 2006 has been taken from an exhibition that ran last summer at The Courthouse, Tinahely, Co Wicklow, called 'Stepping outside'. The artists are all from the art therapy group at the Central Mental Hospital in Dundrum, Co Dublin, Ireland.

Art, as a therapeutic activity for patients, commenced in the late 1970s and became part of the vocational education programme in 1985. Patients' work has been exhibited in a number of initiatives including the Lundbeck Art Initiative. In January 2004 the Central Mental Hospital art programme scooped Lundbeck's major prize – the Center of Excellence Award – for providing "the best environment, materials and art space for its artists".

During 2005 exhibitions have been held in various venues throughout the country, including: Cork, Kilkenny, Dublin and Wicklow.

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