

Epilepsy in the new century

Treatment has advanced, but a stigma still surrounds this disorder

Epilepsy affects some 120 000 to 200 000 Australians. It is defined as a disorder with recurrent unprovoked seizures, but 4%–5% of the population may experience at least one seizure at some point in their lives.¹ About half the people who develop epilepsy present in the first two decades of life. A second peak occurs in people older than 60 years.

Pathophysiology and clinical genetics

For 25 years, the classification of epilepsy syndromes has been embedded in the seizure type (partial or generalised onset) and the presence or absence of an underlying brain disorder (symptomatic or idiopathic),² along with acceptance that there is a genetic basis with complex patterns of inheritance for idiopathic epilepsy. Indeed, in the past decade or so, examination of large pedigrees with multiple affected members has led to the discovery of several epilepsy genes. These gene defects most commonly disrupt the function of voltage-gated or neurotransmitter-gated ion channels, producing alterations in neuronal excitation within brain networks.³

These discoveries have enhanced our understanding of seizure pathophysiology, but they have also begun to cast doubt on the current classification of the epilepsies. The distinctions between partial and generalised and between idiopathic and symptomatic are difficult to support when individuals sharing gene defects present with very different epilepsies.⁴ Despite this, the known epilepsy genes do not yet explain the most common epilepsies, where gene combinations interacting with environmental or epigenetic factors are expected to provide the answers.

Neuroimaging

There have been tremendous advances in neuroimaging technology. Magnetic resonance imaging (MRI) can demonstrate a variety of cerebral pathologies not reliably found with computed tomography (CT). These include hippocampal atrophy in mesial temporal lobe epilepsy, focal and diffuse malformations of cortical development, and vascular malformations and focal encephalomalacia. A CT brain scan is no longer an adequate investigation for epilepsy.

The ability to measure volumes of specific brain structures and quantify signal change has opened new areas of neuroscience research in humans with epilepsy. Cross-sectional and, more recently, longitudinal studies of regional brain volumes have provided evidence of progressive brain damage with intractable focal seizures.⁵

Functional neuroimaging with positron emission tomography (PET) and single photon emission computed tomography (SPECT) are valuable in assessment for epilepsy surgery, but have contributed little to our understanding of the aetiology of epilepsy. The development of new PET and SPECT ligands and MRI spectroscopy holds the promise of advances using in vivo neurochemistry.

Treatment and prognosis

With therapy, 60%–70% of people with epilepsy will have a good prognosis with complete control of seizures on the first medication tried. In the past 10–15 years we have seen the introduction of lamotrigine, vigabatrin, gabapentin, tiagabine, topiramate ocar-

bamazepine and levetiracetam to the therapeutic armoury. These new antiepileptic drugs (AEDs) provide a greater range of options and differing side-effect profiles than existed with the older array of AEDs (barbiturates, phenytoin, carbamazepine and valproate).⁶ However, 20%–30% of patients will not respond completely to medication and there has been no major change in the proportion of children and adults whose seizures remain refractory to medication — even with the release of these new AEDs.

There has been a growing awareness of the futility of years of different AED trials in individuals and AED polytherapy.⁷ The failure of two well-supervised medication trials in partial epilepsy should alert the physician of the need to consider options such as epilepsy surgery. A randomised, controlled trial of surgery for temporal-lobe epilepsy has shown 58% of the surgical candidates were seizure-free at one year, compared with 8% of medically treated patients.⁸ Surgery should not be seen as the last resort, but as a complement to medical treatment in refractory cases.

Comorbidity of epilepsy

Doctors have become very adept at counting seizures to determine the success of interventions. In the past decade, attempts have been made to assess the impact of epilepsy and its treatment upon a person's quality of life. We are becoming more aware of the effects of the older AEDs on endocrine function and their teratogenic potential.⁹ Long-term AED use is associated with osteopenia, and vitamin D and calcium supplements are appropriate.

More than 30% of patients with epilepsy may suffer depression. The depression is not simply the result of a chronic medical illness; it seems that the two disorders may share a common pathological substrate. Recognition and treatment of depression is important to the success of the treatment of the epilepsy itself.¹⁰

The future

In the next decade or so, we can expect that genetic testing for particular epilepsies will complement and perhaps lessen our current dependence on clinical profiles and electroencephalography. It is conceivable such testing may aid us in selecting the most appropriate AED and predicting hypersensitivity side effects of AEDs. Currently, AEDs are administered to control seizures or the clinical expression of epilepsy, but we have no means to intervene to prevent epileptogenesis. Advances in our knowledge will certainly occur in the next decade. But without a greater understanding of epilepsy and seizures in the community, we will not lessen the stigma that still surrounds the disorder in schools and the work place. Epilepsy is a common disorder and deserves attention in public education programs.

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