EDITORIAL

Epilepsy—burning questions and emerging therapies

Epilepsy imposes a major burden at both global and individual levels. Worldwide, about 1% of people have epilepsy, and nearly 4% will experience epilepsy at some point during their lifetime.

In almost 30% of patients with epilepsy, antiseizure medications do not provide sufficient seizure control. Treatment-resistant epilepsy is a disabling disorder that can dramatically impair quality of life, and is linked with severe morbidities and increased mortality. Surgery is an option only for a minority of patients with refractory epilepsy, and even in disorders amenable to surgical intervention, such as temporal lobe epilepsy, there is a risk of cognitive impairment. Novel therapies for medication-resistant epilepsy are, thus, in high demand.

2013 saw major breakthroughs in epilepsy research: novel genes involved in epilepsy syndromes were discovered, the patterns underlying sudden unexpected death in epilepsy (SUDEP) were elucidated, and translational research paved the way to gene therapy for epilepsy.

Nature Reviews Neurology is excited to publish this special Focus on Epilepsy issue, which brings together an ensemble of cutting-edge investigators from leading research institutes around the world to highlight the important challenges and progress in epilepsy research and clinical practice.

In the News & Views section, Michael Duchowny and Sanjiv Bhatia discuss the prospects of optimizing surgical intervention in temporal lobe epilepsy to minimize adverse effects on verbal memory, and Elinor Ben-Menachem and Gregory Krauss comment on a new follow-up study that assessed the safety and efficacy of an implantable, responsive neurostimulation device—a treatment approved by the FDA in 2013—in patients with medically intractable epilepsy.

Efficient management of epilepsy is particularly important in paediatric patients because of the possible detrimental effects of the uncontrolled seizures on the developing brain. In the Reviews section of this issue, Jo Wilmshurst and colleagues outline the most important challenges in treating infants and children with epilepsy. The scarcity of Class I evidence in paediatric epilepsies remains a problem, and many standard practices are not based on clinical evidence.

In 2013, the American Academy of Neurology published an evidence-based guideline update for chronic vagus nerve stimulation. Although vagus nerve stimulation can reduce seizure frequency in many patients with medically retractable epilepsy, electrical brain stimulation has the potential to provide targeted and more-robust seizure control without adverse effects on the vocal apparatus. Robert Fisher and Ana Luisa Velasco review the use of deep brain stimulation in epilepsy, highlighting the most important knowledge gaps.

SUDEP remains the leading cause of mortality in patients with refractory epilepsy, with an estimated lifetime risk of 35%, but the awareness of the increased risk of sudden death remains poor among both patients and physicians. Cory Massey and co-authors review the current knowledge of the mechanisms of SUDEP, along with potential interventions and preventive treatments.

Over the past few years, an increasing number of epilepsies have been found to have a genetic contribution. Rhys Thomas and Samuel Berkovic review the recent discoveries and urge clinicians to adopt a new paradigm: the proportion of idiopathic epilepsies is much smaller than previously thought, so the possibility of finding a genetic diagnosis should not be overlooked.

The bounty of newly discovered epilepsy-related genes, along with decreasing cost of whole-exome sequencing, means that genetic testing and personalized medicine are entering clinical practice. In the Perspectives section, Annapurna Poduri and colleagues discuss the ethical dilemmas related to genetic testing in the epilepsies.

Increasing our understanding of the genetic background of epilepsy is just a starting point in finding a cure for this condition. In their Perspectives article, Dimitri Kullmann and colleagues expand the horizon of epilepsy therapies by outlining a roadmap towards clinical trials.

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Competing interests
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