

Introduction



Consequences of Epilepsy Through the Ages: When Is the Die Cast?

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Epilepsy is a common condition that spares no race, gender, ethnic group, or age. Using information obtained from the Rochester Epidemiology Project (1), Hesdorffer et al. (2) estimated that 1 of 26 individuals (3.8% of people born today) will develop epilepsy at some point in their lifetime. The incidence of epilepsy is greatly influenced by age. Children are at substantially higher risk for epilepsy than young and middle-aged adults (3, 4), with the incidence increasing again in older individuals (5, 6).

In addition to the incidence of epilepsy, the etiology of epilepsy differs across the life spans. Whereas seizures in children are often due to genetic causes, malformation of cerebral development, and hypoxic-ischemic encephalopathy, seizures in young adults are more likely due to head trauma and tumors; while in the older population, cerebrovascular events and dementing disorders become a common cause of seizures. Etiologic factors have major importance in determining outcome of epilepsy.

Age is critical in the clinical and electroencephalographic features of seizures. Disorders such as infantile spasms and Landau-Kleffner syndrome always begin in early childhood. EEG features such as hypsarrhythmia and electrical status epilepticus of sleep (ESES) are confined to childhood. Age is also a determinant for prognosis. Intellectual impairment (7–11), learning disabilities (12–14), social outcome (15, 16), and medical refractoriness (17, 18) all appear to be influenced by age of onset.

While many individuals with epilepsy do well in regards to seizure control and quality of life, epilepsy can have a devastating effect on all aspects of an individual's life (19, 20). Individuals with epilepsy are at high risk for death (21, 22) and comorbidities, including cognitive impairment (23) and depression (24–26). While the comorbidities of epilepsy extend across the life span of an individual, they are not uniform across the age groups. The time and extent of seizure-related sequelae of epilepsy are age related. While seizures can have profound consequences at any age, the outcome of epilepsy in a newborn differs considerably from that in the aged population.

The American Epilepsy Society Merritt-Putnam Symposium in 2010 explored critical issues regarding age and outcome. The articles herein represent summaries of key points from the lectures presented.

The relationship between age and the consequences of epilepsy and age is first reviewed by Tallie Z. Baram who provides the biological basis for age-related consequences of epilepsy across the life span. As elegantly outlined in her article, advances in our understanding of the mechanisms of seizure in the immature, mature, and aged brain provide the impetus for novel therapeutic interventions to prevent both the seizures and the consequences of such seizures.

The needs of patients with epilepsy vary as a function of age. The primary caretakers of children with epilepsy are the parents; whereas, in the adult, medical care is directed to the individual with the disorder. As individuals transition into older adulthood, epilepsy care is often managed by nursing home staffs. As emphasized by Peter R. Camfield, transitioning the patient from the child neurologist to the adult neurologist is typically not done well. Children with epilepsy have a considerable number of comorbidities, which unfortunately continue into adulthood (17, 27–29). Dr. Camfield provides essential information regarding the outcome of childhood epilepsy and provides valuable suggestions regarding the transition of neurologic care from the pediatric to adult setting. While the die may have been cast before the child transitions into adulthood, awareness of the long-term consequences of childhood epilepsy will allow health care professionals to intervene and positively influence outcome.

A major question in epilepsy is how epilepsy alters neurocognitive function. There is increasing evidence that neurocognitive and behavioral disorders may precede the onset of the epilepsy (30, 31) but be exacerbated by ongoing refractory seizures (11, 32). There is increasing evidence that the adverse neuropsychologic effects of seizures of epilepsy in childhood can be mitigated by interventional techniques. For example, children with epilepsy and cognitive impairment who have stable and supporting families are far more likely to improve in academic skills than children raised in dysfunctional households.

Epilepsy is increasing in the older population and represents a considerable comorbidity in patients with the neurologic condition causing the seizures. Older adults, often defined as those 65 years or older, are the most rapidly growing



segment of the population, and onset of epilepsy is higher in this age group than in any other (33). The incidence of epilepsy increases rapidly after age 65, and recent studies indicate that approximately 10% of nursing home residents are being treated with antiepileptic drugs (AEDs) (34). Making the diagnosis of epilepsy in the elderly can be challenging, since partial seizures are more common than generalized tonic-clonic seizures (34, 35). In addition, the partial seizures may be quite subtle, with momentary lapses of awareness. Seizures in the elderly are often either overdiagnosed or underdiagnosed, and either situation can have serious adverse consequences (36).

While it is clear that mechanisms and consequences of epilepsy are age related, the question is how this information is useful to clinicians in their management of patients. In preclinical testing, putative antiepileptic drugs are tested largely in adult rodents with acute seizures. In clinical studies, it is unusual for AEDs to be tested initially in children. Nevertheless, clinical trials have shown some AEDs to be particularly effective in children with specific epileptic syndromes. For example, vigabatrin is effective in the treatment of infantile spasms, particularly in children with tuberous sclerosis (37–39), and felbamate and lamotrigine demonstrate efficacy in Lennox-Gastaut syndrome (40, 41). As emphasized by Dr. Baram, the brain changes dramatically across the life spans. It is therefore not surprising that the adverse consequences of seizures may be age specific (42). Dr. Jacqueline A. French, in her chapter entitled “AED Treatment Through Different Ages: As Our Brains Change, Should Our Drug Choices Also?” addresses how age affects treatment decisions.

So when is the die cast? In many individuals, cognitive and psychiatric problems precede the onset of the epilepsy; where in others, adverse events occur after the onset of the epilepsy, owing to the seizures themselves, their treatment, or both. However, early recognition of the age-related consequences of epilepsy, whether they precede the epilepsy, occur at the onset of the epilepsy, or develop after the epilepsy provides the opportunity for intervention, which can improve the lives of the individual, regardless of age.

Disclosure

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