CHAPTER 8

EPILEPSY AND EPILEPTIC SYNDROME

Tomonori Ono and Aristea S. Galanopoulou*

1Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, New York, USA; 2Dominick P. Purpura Department of Neuroscience, Albert Einstein College of Medicine, Bronx, New York, USA

*Corresponding Author: Aristea S. Galanopoulou—Email: aristea.galanopoulou@einstein.yu.edu

Abstract: Epilepsy is one of the most common neurological disorders. In most patients with epilepsy, seizures respond to available medications. However, a significant number of patients, especially in the setting of medically-intractable epilepsies, may experience different degrees of memory or cognitive impairment, behavioral abnormalities or psychiatric symptoms, which may limit their daily functioning. As a result, in many patients, epilepsy may resemble a neurodegenerative disease. Epileptic seizures and their potential impact on brain development, the progressive nature of epileptogenesis that may functionally alter brain regions involved in cognitive processing, neurodegenerative processes that relate to the underlying etiology, comorbid conditions or epigenetic factors, such as stress, medications, social factors, may all contribute to the progressive nature of epilepsy. Clinical and experimental studies have addressed the pathogenetic mechanisms underlying epileptogenesis and neurodegeneration.

We will primarily focus on the findings derived from studies on one of the most common causes of focal onset epilepsy, the temporal lobe epilepsy, which indicate that both processes are progressive and utilize common or interacting pathways. In this chapter we will discuss some of these studies, the potential candidate targets for neuroprotective therapies as well as the attempts to identify early biomarkers of progression and epileptogenesis, so as to implement therapies with early-onset disease-modifying effects.

INTRODUCTION

Epilepsy is one of the most common neurological disorders affecting 50 million people worldwide. It is a chronic neurological disorder characterized by a predisposition to generate recurrent unprovoked epileptic seizures. An epileptic seizure is a transient...
abnormal synchronization of neurons in the brain that disrupts normal patterns of neuronal activity (electrographic seizure) and may manifest with a variety of signs and symptoms (electroclinical seizure). These may include focal or generalized convulsive or atonic behaviors (i.e., tonic-clonic, myoclonic, tonic, atonic), paroxysmal abnormal sensory or autonomic symptoms, impaired consciousness or alertness (absence seizures, complex partial seizures). Epileptic syndrome, on the other hand, is used to denote “a complex of signs and symptoms that define a unique epilepsy condition”.

Epilepsy is a general term encompassing a variety of “epilepsy diseases”, each of which is attributed to a single etiology. Epilepsy can be associated with a constellation of neurobiologic, cognitive, psychological and social sequelae, which may greatly impact on the quality of life, especially of patients who do not respond to available therapies. This has prompted the proposal to revisit the terminology of epilepsy and refer to it as a “disease” rather than a “disorder”, so as to raise the level of awareness and urgency to find better ways to address these issues and alleviate or cure epilepsy.

The progressive course of epilepsy (e.g., increase in frequency, duration and severity of seizures) and associated neurological dysfunction (e.g., physical, cognitive and behavioral impairment) can, in certain patients, mimic neurodegenerative diseases. The underlying pathogenetic mechanisms may relate to the progressive nature of epileptogenesis and its impact on the function and physiology of brain regions involved in cognition, the cumulative effect of the seizures and their therapies, epigenetic factors such as stress, changes in life style and environment.

Epileptogenesis is the process of forming a focus capable of generating spontaneous seizures. Epileptogenesis evolves and progresses over several years in humans or months in rodents and may disrupt normal neuronal development and differentiation. In combination with the ongoing effects of seizures or epileptic discharges, epileptogenesis may result in developmental disabilities and cognitive decline in epilepsy patients. Given the chronicity and progressive nature of these processes, a key question in epilepsy research is to identify neuroprotective therapies that halt or reverse epilepsy and its sequelae. In this chapter, we will review the clinical and experimental evidence for the neurodegenerative aspects of epilepsy addressing the following questions:

1. Is epilepsy a progressive disorder with neurodegenerative features?
2. Which mechanisms underlie neurodegeneration in epilepsy?
3. Is it possible to diagnose and prevent these neurodegenerative aspects of epilepsy?

CLINICAL FEATURES OF EPILEPSY: IS EPILEPSY A NEURODEGENERATIVE DISORDER/SYNDROME?

Overview of Epilepsy and Epileptic Syndrome

Seizures are usually described as having focal (or partial) or generalized onset; however in certain cases the onset cannot be readily determined. Focal-onset seizures are generated by abnormal activity stemming from one brain region. They are further classified as simple (with intact consciousness) and complex partial seizures (with altered level of consciousness). If seizures arise or engage bilaterally distributed networks they are described as generalized, such as generalized tonic-clonic, absence, atonic or myoclonic seizures.