Cellular and Molecular Mechanisms of Neuroinflammation in Epilepsy

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ABSTRACT

Epilepsy affects millions of people worldwide. Epilepsy is a chronic neurological disorder characterized by recurrent unprovoked seizures. Neuronal damage and inflammation are suggested to play a central role in the pathophysiology of epileptogenesis and chronic epilepsy. There is increasing evidence that excessive inflammatory actions of the neuroimmune system may contribute to the development of epilepsy following a variety of precipitating conditions, including brain injury, prolonged seizure events or status epilepticus, brain infections, stroke, and neurotoxicity. This review describes the current status of neuroinflammation in epilepsy and the therapeutic promise of targeting the brain immune system for chronic blockade of inflammation as an effective approach for preventing the onset of epilepsy and related hyperexcitability conditions.

KEYWORDS: Epileptogenesis, seizure, inflammation, microglia, astrocyte, cytokine, immune cells.

Introduction

Epilepsy is a chronic condition that is manifested with recurrent seizures and motor/sensory abnormalities. These events are the result of hypersynchronous neuronal activity propagating from a small brain region, termed as epileptic foci. In addition to seizures, common comorbidities include cognitive deficits and other mental disorders such as anxiety and depression. Epilepsy is in the top 3 most widespread neurological problems worldwide, and it is the fourth most common neurological disorder in the United States. Epilepsy affects more than 1% (>60 million) of people worldwide, with an estimated 2.4 million new people diagnosed with epilepsy every year, 150,000 in the US alone. Over a lifetime, 1 in 26 people will be diagnosed with epilepsy. Additionally, as many as 30 million epilepsy patients have limited or no access to treatment, compounding the disease’s impact on world health and productivity. Economic costs for epilepsy care are huge and run in billions of dollars. Although the focus of intense research for nearly half a century, current antiepileptic drug (AED) therapies are designed to merely control symptoms, not treat the underlying causes and at best are effective in ~70% of clinical cases (Perucca et al., 2007). There is a great need for drugs specifically designed to target the mechanisms behind the many forms of drug-resistant epilepsies. Furthermore, there is also an urgency to better understand the means by which normal brains are transformed into an epileptic state, a process termed epileptogenesis, as well as the mechanisms by which this state of unchecked excitation endures. In this article we have highlighted the current status of neuroinflammation in epilepsy and the therapeutic promise of targeting the brain immune system for chronic blockade of inflammation as an effective approach for preventing the onset of epilepsy and related hyperexcitability conditions.

Excessive Neuroinflammation in Epilepsy

Inflammation is the aggregate, and often double-edged homeostatic response elicited in tissue after exposure to infectious substances or injury. It consists of...