Epilepsy

Therapeutic Approaches to epileptogenesis

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According to the World Health Organization, approximately 50 million people worldwide have epilepsy. Despite significant progress in the management of epilepsy and increasing number of antiepileptic drugs, 30-40% of patients remain refractory to available medications. The current treatment of epilepsy is based on the suppression of symptoms by antiepileptic drugs. It is an urgent need to modify the progress of epilepsy, i.e. epileptogenesis, in patients with a known increase risk of epilepsy, such as a history of brain injury.

Epileptogenesis

Epileptogenesis is a process by which a normal brain develops epilepsy, a chronic condition in which seizures occur. It is a series of events that occur between the event that causes epilepsy and the first spontaneous seizure.

Cause of epileptogenesis:

A variety of brain insults can result in epileptogenesis, including neurodegenerative diseases, traumatic brain injury, stroke, brain tumour, infections of the central nervous system, and genetic predisposition. These conditions can lead to spontaneous seizures and progress further to the development of epilepsy.

Mechanisms of epileptogenesis:

Epileptogenesis refers as a dynamic process that progressively alters neuronal excitability, establishes critical interconnection, and changes the brain structure**.** In epileptogenesis, an array of events occur on molecular and cellular levels, including neurodegeneration, neurogenesis, gliosis, axonal damage, recruitment of inflammatory cells into brain tissue, reorganisation of the extracellular matrix, and reorganisation of the molecular architecture in individual neuronal cells.

Identification of epileptogenesis biomarkers

The development of epileptic seizures is unpredictable following an initial precipitating insult, or given a genetic risk factor, both in animals and humans, therefore the identify potential antiepileptogenic compounds and to test their efficacy, particularly in a clinical setting, rely on reliable biomarkers of epileptogenesis. A biomarker of epileptogenesis may also be used to predict a progressive epilepsy condition, and, perhaps, pharmacoresistance. If so, patients could be immediately referred for more aggressive treatments, such as surgery. Epileptogenesis-related alterations in gene expression profiles in the brain might be imaged

by selective PET tracers. Such changes might also be identified in peripheral blood, for instance in white blood cells, providing a diagnostic fingerprint that could serve as a noninvasive biomarker of epileptogenesis. Inflammatory changes appear to be a constant factor of epileptogenesis in virtually every animal model studied and should provide insights into the development of new biomarkers.

Development of potential antiepileptogenic drugs

Because the traditional approaches of using antiepileptic drugs have shown their ineffective in preventing epileptogenesis, novel approaches a needed. Accumulative data indicate that interventions in the processes of epileptogenesis might prevent the development of seizures and ameliorate epilepsy severity. Currently, the large scale molecular profiling studies are providing potential targets for antiepileptogenic strategies. These studies has highlight gene groups that link to identified epileptogenic mechanisms, including inflammation, immune response, reaction to wounding, synaptic transmission and plasticity, ion transport, channel and receptor function and neurotransmitter metabolism. These findings contribute to the understanding of epileptogenesis and the development of antiepileptogenic strategies. . Emerging evidences show that gene regulation mechanisms, such as epigenetic modification and miRNAs, may be crucial in the pathogenesis of epileptogenesis, which may offer new therapeutic targets for the treatment of epilepsy.

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