Epileptogenesis

In a mechanistic context, epileptogenesis is the process by which a brain network that was previously normal is functionally altered toward increased seizure susceptibility, thus having an enhanced probability to generate spontaneous recurrent seizures (SRSs).

Photosensitive epilepsy.

A variety of neuropeptides play important roles as neurotransmitters or neurotransmitter modifiers in the brain, and may be involved in the incidence and development of epilepsy. In recent years, the following neuropeptides: galanin (GAL), neuropeptide Y (NPY), neuropeptide substance P (SP), cholecystokinin (CCK), as well as wake-promoting neuropeptide (ORE) have been discovered to be closely associated with epilepsy [1)].

Maladaptive epigenetic changes, which include methylation of DNA and acetylation of histones - among other mechanisms, are now well recognized to play a functional role in the development of epilepsy and its progression. The methylation hypothesis of epileptogenesis suggests that changes in DNA methylation are implicated in the progression of the disease. In this context, global DNA hypermethylation is particularly associated with chronic epilepsy. Likewise, acetylation changes of histones have been linked to epilepsy development. Clinical as well as experimental evidence demonstrates that epilepsy and its progression can be prevented by metabolic and biochemical manipulations that target previously unrecognized epigenetic functions contributing to epilepsy development and maintenance of the epileptic state. A review of Boison discusses epigenetic mechanisms implicated in epilepsy development as well as metabolic and biochemical interactions thought to drive epileptogenesis. Therefore, metabolic and biochemical mechanisms are identified as novel targets for epilepsy prevention. They specifically discussed adenosine biochemistry as a novel therapeutic strategy to reconstruct the DNA methylome as an antiepileptogenic strategy as well as metabolic mediators, such as beta-hydroxybutyrate, which affect histone acetylation. Finally, metabolic dietary interventions (such as the ketogenic diet) which have the unique potential to prevent epileptogenesis through recently identified epigenetic mechanisms will be reviewed [2)].

Studies have shown that microRNAs play a role in the development of epilepsy by regulating downstream target Messenger RNA.

Traumatic brain injury (TBI) and status epilepticus (SE) have both been linked to the development of human epilepsy. Although distinct etiologies, research has suggested the convergence of molecular mechanisms underlying epileptogenesis following these insults. One such mechanism involves the neurotrophin brain-derived neurotrophic factor (BDNF) and its high-affinity receptor, tropomyosin receptor kinase B (TrkB). In a review, Lin et al. focus on available data regarding the pathophysiologic role of BDNF/TrkB signaling in epilepsy development. They specifically examine the axonal injury and SE epilepsy models, two animal models that recapitulate many aspects of TBI- and SE-induced

epilepsy in humans respectively. Thereafter, they discussed aspiring strategies for targeting BDNF/TrkB signaling so as to prevent epilepsy following an insult or suppress its expression once developed [3].

1)
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3)
Lin TW, Harward SC, Huang YZ, McNamara JO. Targeting BDNF/TrkB Pathways for Preventing or Suppressing Epilepsy. Neuropharmacology. 2019 Aug 1:107734. doi: 10.1016/j.neuropharm.2019.107734. [Epub ahead of print] Review. PubMed PMID: 31377199.