Epilepsia, 51(Suppl. 5):45, 2010
doi: 10.1111/j.1528-1167.2010.02831.x

Neurogenesis and epilepsy

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Summary

Persistent neural stem cells generate dentate granule cells (DGCs) throughout life. Evidence suggests that aberrant neurogenesis contributes to epileptic structural abnormalities, but that normally integrating adult-born DGCs may restore inhibition. Current research focuses on how epileptogenic insults alter neurogenesis, and whether restoring normal neurogenesis will attenuate epilepsy or its comorbidities. For an expanded treatment of this topic see *Jasper's Basic Mechanisms of the Epilepsies, Fourth Edition* (Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV, eds) published by Oxford University Press (available on the National Library of Medicine Bookshelf [NCBI] at www.ncbi.nlm.nih.gov/books).

KEY WORDS: Basal dendrites, Dentate granule cells, Dispersion, Medial temporal lobe epilepsy, Neural stem cells, Seizures, Sprouting, Valproic acid.

Persistent neural stem cells (NSCs) in the subgranular zone (SGZ) of the hippocampal dentate gyrus generate dentate granule cells (DGCs) throughout life (Altman & Das, 1965). Many adult-born DGCs integrate into the preexisting circuitry and acquire electrophysiologic characteristics of mature DGCs. Mounting evidence implicates DGC neurogenesis in certain forms of hippocampus-dependent learning and memory and in the modulation of emotional behavior or anxiety. Data from rodent models of medial temporal lobe epilepsy (mTLE) show that prolonged seizures acutely increase adult DGC neurogenesis, but the functional implications of altered neurogenesis in mTLE are poorly understood. Accumulating evidence suggests, however, that altered neurogenesis contributes to several well-characterized cellular abnormalities seen in human and experimental mTLE. These abnormalities include mossy fiber sprouting, DGC layer dispersion, and the appearance of DGCs in ectopic locations or with abnormal hilar basal dendrites (Kron et al., 2010). In contrast, other work suggests that adult-born DGCs that integrate normally during epileptogenesis may serve a compensatory role to restore inhibition (Jakubs et al., 2006).

Because adult hippocampal neurogenesis likely underlies specific hippocampus-dependent learning and memory functions, defective neurogenesis may also contribute to the progressive memory dysfunction seen in mTLE. This idea is supported by recent findings that cognitive impairment in an experimental mTLE model decreases when seizure-induced neurogenesis is inhibited with valproic acid, probably via its histone deacetylase inhibitory activity (Jessberger et al., 2007). In addition, DGC neurogenesis is suppressed in the chronic stage of experimental mTLE, raising the possibility that memory function may be impaired both by aberrant neurogenesis and a reduction of normal DGC neurogenesis. Current work aims to define the mechanisms by which epileptogenic insults alter adult neurogenesis, and whether restoring normal NSC behavior after such insults will attenuate the development of epilepsy or its comorbidities.

Disclosure

The authors declare no conflicts of interest.

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