Dentate granule cell neurogenesis after seizures induced by pentylenetrazol in rats

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Persistent neurogenesis occurs in the adult mammalian brain throughout life including humans, providing a new clue for investigating the plasticity of brain structure and function after pathological insults. Using systemic bromodeoxyuridine to label dividing cells, we studied the proliferation rate of neural precursor cells in the rat dentate gyrus at various time points after pentylenetrazol-induced seizures. We observed a significant increase in the proliferation rate of neural precursor cells in the dentate gyrus 3, 7, and 14 days after seizures. The number of bromodeoxyuridine labeled cells returned to baseline levels by 28 days after seizures. Most of newborn cells migrated into the granule cell layer from the subgranular zone, displayed the neuronal phenotype, and developed morphological characteristics of differentiated dentate granule cells. Using c-fos expression as an indicator of neuronal activation, we found that seizure-induced newborn neurons in freely moving adult rats are able to respond to pathophysiological stimuli in the same way as neighboring neurons do. Administration of either the N-methyl-D-aspartate (NMDA) receptor blocker MK-801 (1 mg/kg, i.p.) or the 2-(aminomethyl) phenylacetic acid/ kainate (AMPA/KA) receptor antagonist DNQX (15 mg/kg, i.p.) significantly reduced the number of bromodeoxyuridine labeled cells in the dentate gyrus after seizures ($P < 0.05$). Double immunohistochemical staining showed that both the mature granule cells and the majority of bromodeoxyuridine -labeled, mitotically active cells expressed the NMDA receptor subunit NR1 and the AMPA/KA receptor subunit GluR2. These results indicate that epileptic seizures lead to increased neurogenesis in the adult rat dentate gyrus through glutamatergic mechanisms acting on NMDA and AMPA/KA receptors.