Stress, depression and seizures

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The prevalence of depression in individuals with temporal lobe epilepsy (TLE) is much higher than that of other chronic disorders with apparent similar severity. The basis for this high prevalence of depression, as well as of cognitive defects including memory problems, is unclear. One obvious element is anatomical: The limbic structures, including the hippocampus, amygdala and related cortices, underlie memory and emotional functions; these are the brain regions impacted by the epileptic seizures. While this scenario infers that depression is a result of epilepsy, an alternative possibility is that both TLE and depression might arise independently from a common insult that affects the common anatomy of depression and TLE. Mechanistically, glutamate-mediated excitotoxicity, loss of neurons and appearance of abnormal networks have been proposed to account for TLE-related depression. In addition, a role for stress mediators in both the emotional and the cognitive correlates of epilepsy is emerging. Neurosteroids, glucocorticoids and the excitatory stress hormone corticotropin releasing hormone are all strong candidates for mediating epilepsy-related depression and cognitive deficits. Neurosteroids enhance GABA-A receptors, with implication to cognition and depression. CRH is an excitant and, when released during severe stress such as during seizures, destroys dendritic spines and synapses, impacting memory in the hippocampus and emotional function in the amygdala. This presentation will discuss established and emerging information on stress-related mechanisms involved in epilepsy-related depressive and cognitive outcomes, with profound implication for prevention and therapy.

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