

Sex Differences in Epilepsy Development in the Mouse Pilocarpine Model

B. Clossen, S. Reddy

Texas A and M Health Science Center

Purpose

Sex differences are well known in epilepsy. Seizure susceptibility and the incidence of epilepsy are generally higher in men than women. Changes in seizure sensitivity are also evident at puberty, pregnancy and menopause. Although sex differences in acute seizure susceptibility are widely investigated, there is little information on sex differences in the development of chronic epilepsy in experimental models of epileptogenesis. Chronic epilepsy models with spontaneous seizures are less frequently used because they are tedious and require extensive EEG monitoring. Such models provide many outcomes that mimic a human epileptic condition. In acquired epilepsies, spontaneous seizures begin after injury to a normal brain as a consequence of trauma, stroke, infection or status epilepticus (SE). In this study, we utilized the pilocarpine model of epileptogenesis in mice to investigate the potential sex differences in the development of epilepsy with spontaneous recurrent seizures (SRS).

Methods

We used the pilocarpine model of chronic epilepsy. Epileptogenesis was triggered in male and female mice with SE induced by a single-dose pilocarpine administration. Mice were treated diazepam 2 h after the beginning of SE. They were implanted with telemetric or wireless EEG electrodes. All animals underwent continuous, 24/7 video-EEG monitoring for 3 months to detect the occurrence and severity of spontaneous seizures. As another outcome measure, the severity of hippocampal damage was assessed in histologic sections at 3-months after SE.

Results

Kaplan-Meyer's analysis of 3-months post-SE data indicated that the overall incidence of epilepsy development in males was higher than in females despite similar progression of epileptogenesis. In the male group, 67% of animals developed epilepsy within 1 month post-SE. In the female group, 80% of animals exhibited epileptic seizures within 1 month post-SE. The mean latency for SRS and average seizure severity & duration were similar between groups. The mean frequency of spontaneous seizures was significantly greater in females than in males. Consequently, female mice with epilepsy spent significantly more time with seizure activity than males with epilepsy. Pronounced hippocampal neurodegeneration of principal cells and interneurons were observed in epilepsy mice, confirming the hallmark neuropathology of epileptogenesis.

Conclusion

These preliminary data indicate likely sex differences in epileptogenesis in the pilocarpine model of epilepsy in mice. Further studies are in progress to investigate whether neurosteroid treatment started after SE is antiepileptogenic or disease-modifying. ** Supported by NIH grant NS051398 **