

WHAT IS CLAIMED IS:

1. A model for the analysis of events associated with brain seizures, the model comprising:

a kindled animal brain that, upon stimulation, provides for neural events reflecting functional and neural circuit changes; and allows analysis of the neural events resulting from a single seizure.

2. The model of claim 1 wherein the analysis of the neural events comprises one or both of electrophysiology and magnetic resonance imaging (MRI).

3. The model of claim 1 or claim 2, wherein the analysis of the neural events is performed with simultaneous measurement of electrophysiology and functional magnetic resonance imaging (fMRI).

4. The model of any of claims 1-3, wherein the stimulation is electrical and targeted to a region of interest.

5. The model of claim 5, wherein the region of interest is the hippocampus.

6. The method of any of claims 1-5, wherein the neural events reflecting functional and neural circuit changes comprise one or more of focal to bilateral tonic-clonic (FBTC) seizures, changes in excitatory ventral hippocampal (VH) networks, changes triggered by sub-threshold stimulus, and induction of a migrating seizure core.

7. The method of claim 6, wherein the stimulation that provides for neural events reflecting functional and neural circuit changes is electrical stimulation.

8. The method of claim 7, wherein the electrical stimulation is delivered by optogenetics.

9. The method of claim 8, wherein the animal brain comprises neurons genetically engineered to comprise a light activatable polypeptide.

10. The model of claim 9, wherein the light-activatable polypeptide is a channelrhodopsin.

11. The model of claim 10, wherein the channelrhodopsin is operably linked to a promoter expressed in excitatory hippocampal neurons.

12. The model of claim 11, wherein the promoter is calmodulin-dependent kinase II alpha (CaMKII α) promoter.

13. The method of any of claims 8-12, wherein the stimulation that provides for neural events is below the threshold to trigger seizures.

14. The model of claim 13, wherein the stimulation is from about 5 Hz to about 15 Hz.

15. The method of claim 13, wherein the stimulus is applied to evaluate underlying functional circuit changes.

16. The method of any of claims 8-12, wherein the stimulus is sufficient to trigger a seizure.

17. The model of claim 16, wherein the stimulation is from about 35 Hz to about 45 Hz.

18. The model of claim 16, wherein the stimulus is applied to evaluate seizure circuit dynamics.

19. The model of any of claims 1-18, wherein a migrating seizure core is identified.

20. The model of claim 19, wherein the migrating seizure core is used in localization of a seizure onset zone.

21. The model of claim 20, wherein the SOZ is imaged by single-photon emission computed tomography (SPECT).

22. The model of any of claims 1-21, wherein kindling is achieved using electrostimulation, optogenetics or chemical treatment.

23. The model of claim 22, wherein optogenetic kindling is performed by:

a. delivering a polynucleotide that encodes a light-activatable protein to a target neuron to a first region of the brain,

b. illuminating the first region of the brain repeatedly with a frequency and a pulse width sufficient to induce kindling; and

c. repeating step b. over the course of multiple days.

24. The model of any of claims 1-23, wherein the animal is sedated and treated with a short-acting neuromuscular blocker to abolish motion during imaging of seizures.

25. The model of claim 24, wherein the animal is sedated with dexmedetomidine and blocked with vecuronium.

26. A method for developing a therapeutic intervention for epilepsy, the method comprising:

treating the model of any of claims 1-25 with a therapeutic intervention, and determining the effect on neural events reflecting functional and neural circuit changes.

27. The method of claim 26, wherein the therapeutic intervention is surgical.

28. The method of claim 26, wherein the therapeutic intervention is electrical.

29. The method of claim 28, wherein the therapeutic intervention comprises deep brain stimulation.

30. The method of claim 28, wherein the therapeutic intervention is pharmacologic.

31. The method of any of claims 26-30, wherein the neural event comprises a seizure.

32. The method of any of claims 26-30, wherein the neural event comprises a migrating seizure core.

33. The method of any of claims 26-30, wherein the neural event comprises an epileptic comorbidity.

34. The method of any of claims 26-30, wherein the neural event comprises a focal to bilateral tonic-clonic (FBTC) seizure.

35. The method of any of claims 26-30, wherein the neural event comprises alterations in a excitatory ventral hippocampal (VH) network.