Neurosurgery

Our History is our Prison……
Progress is made by escaping the past........
THINK OUTSIDE THE BOX!!
Temporal Lobe Epilepsy
Cause or Effect?

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What Happens in TLE?

- Neurochemical
- Structural
- Unknown
What Causes TLE?

- Febrile Seizures?
- Trauma?
- Genetic?
- Hypoxia?
Structural Changes

- Hippocampal Sclerosis
  - Dentate hilar neurons, pyramidal cell loss
  - Aberrant mossy fibers
  - Granule cell migration
Neurochemical

- Glutamate Toxicity
- Negative feedback
Pathology

- Granule cell dispersion with abnormal mossy fiber sprouting
- Hyperexcitable state through aberrant synapses
Studies

- Most on animal models “kindling”
- Few human studies
- NO ANATOMICAL STUDIES AT THE ULTRASTRUCTURAL LEVEL
- Same studies looking at variations of the same theme ie) No one thinking Outside the Box
Methods

• Human Hippocampi obtained from fresh Temporal lobectomies (n=6)
  – Ages 24-50
  – 1 febrile seizure, 1 trauma
Methods

- Tissue collected in 3.75% Acrolein/2% paraformaldehyde
- Thin sections 40 microns
- 1/2 processed light 1/2 processed for EM
- NO IMMUNOHISTOCHEMISTRY
Anatomy
Methods

- Immuno for Collagen types I-IV
So What?

- Collagen does not exist in the human brain outside of dura and blood vessels
- Collagen causes cell migration
- Collagen is epileptogenic
- Penfield describes Cicatrix causing seizure activity
Scar = Seizure

- Hoeppner et al
  - Collagen content in scar directly related to seizure activity
Proposed Paradigm

Initial Event → Hypoxia → Reactive Astrocytosis
Astrocytosis = Sprouting

• Oliviero et al
  – Astrocytosis has chemoattractant effects to “guide” Mossy fibers
Astocytosis alone not sufficient

- Mitchell et al
  - Astrocytic cell death via Kainic acid does not itself cause Mossy fiber sprouting
Findings

- First reported case of collagen in the human brain outside the dura or vasculature
- Migrating granule cells in the molecular layer consistently surrounded by glia/collagen scaffolding
- Sprouted mossy fibers around collagen deposits
Conclusion

- You CAN DO meaningful research/experiments during research and residency
- Take advantage of 80hr work week