Plain English Title

EPILEPSY STUDIED IN A TEST TUBE

Scientific Title

IN VITRO NEUROPHYSIOLOGY OF EPILEPSY
EPILEPSY      ABNORMAL EEG

Epilepsy patient undergoing EEG

Typical epileptic EEG wave: **spike-and-slow-waves**
Typical epileptic EEG wave: **spike-and-slow-wave.**

Cells composing the brain

Neuronal cells

*Neurons*

Neurons isolated and alive

Epileptic electric waves of isolated neurons

Electrodes
STUDYING EPILEPSY IN SINGLE CELLS
AGENDA

1) The generation of brain electricity
   Neurons as batteries
2) What happens in single neurons in epilepsy?
3) How do neurons synchronize? The role of MAP-kinase CREB pathway.
6) Recording micro-EEGs. The gradual coupling of microscopic discharges
7) Can **chronic** epilepsy be studied in a test tube? Yes!
AGENDA

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PHYSICAL AND BIOLOGICAL BATTERIES

Physical systems
Volta battery

+ + + +

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Flow of current through wire

Biological systems
Ionic transporters

Flow of current through ion channels

Intracellular electrode

Extracellular Field electrode
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ELECTRICAL WAVEFORM
OF AN EPILEPTIC SINGLE NEURON

From Ayala et al.
Brain Research, 1973
Going into recordings on brain slices and isolated neurons
EPILEPSY IN A TEST TUBE (*IN VITRO*)
STUDIES IN THE 1970s (Traub, Miles and Wong)

EPILEPTIC DISCHARGES IN BRAIN SLICES

- Single cell (intracellular)
  - Field (extracellular)

EPILEPTIC DISCHARGES IN ISOLATED NEURONS

2A, 2B, 2C
Studying interconnections between neurons
Spontaneous bursting
Pacemaker (like in the heart)

Propagation

Synchronized bursting

Microscopic discharges

Large discharges detected by scalp EEG
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KEY MECHANISM OF NEURONAL SYNCHRONY
The MAP-kinase CREB pathway

CREB  CAMP responsive element binding protein
Layer-Specific CREB Target Gene Induction in Human Neocortical Epilepsy

Thomas L. Beaumont,2 Bin Yao,1 Aashit Shah,1 Gregory Kapatos,2 and Jeffrey A. Loeb1,2
1Department of Neurology and 2The Center for Molecular Medicine and Genetics, Wayne State University School of Medicine, Detroit, Michigan 48201
MAP kinase-CREB activation in brain of epileptic rats

A

Spiking

Control

500μV
5 seconds

B

pCREB

MAP kinase-CREB block cures epileptic rats

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PREPARING VIALABLE BRAIN SLICES

1. Placing brain in a glass container

2. Cool up the brain on ice bucket

3. Cut slices

Brain slices
Brain slices generate epileptic discharges

A

B

C

D

E

0.3 mM 4-AP
1 mM 4-AP

0.5 mM Kynurenic

Discharges/min

Time (min)

Discharges/min

Time (min)

Discharges/min

Time (min)
Common types of brain waveform patterns in people with epilepsy recorded also in the test tube
PERSISTENT SEIZURES IN THE TEST TUBE
Microscopic epileptic waveforms gradually synchronize
Spontaneous bursting
Pacemaker (like in the heart)

Propagation

Synchronized bursting

Microscopic discharges

Large discharges
detected by scalp EEG
AGENDA

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   Yes!!
Brain slice from a normal rat:

- Smaller and shorter seizures

Brain slice from an epileptic rat:

- Larger and longer seizures
NORMAL RAT

EPILEPTIC RAT

Slice 1
Slice 2
Slice 3
Slice 4
Slice 5
Slice 6
Slice 7
Slice 8
Slice 9
Slice 10
Slice 11
SUMMARY AND CONCLUSIONS

1. Single cell seizures
   Synchronization of neurons

2. MAPkinase activated
   In chronic foci

3. MAPkinase inhibitor
   Cures seizures

4. Acute seizures: coupling of microfoci

5. Chronic epilepsy
   in test tube

Phase I
Independent microfoci

Phase II
Synchronous microfoci
Flip-flop

Larger and longer seizures