Advances in the Diagnosis & Treatment of Epilepsy

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Epilepsy is common medical condition!

- Around 50 million people in the world have epilepsy
- The majority can live normal lives with proper treatment
- Diagnosis and Therapy continues to advance

What is a Seizure? What is Epilepsy?

A **seizure** is an episode of abnormally synchronized and high frequency firing of neurons in the brain, that results in abnormal behavior or experience of the individual.

- **Provoked Seizure:** Due to systemic illness, i.e., hypoglycemia

**Epilepsy** is a disorder in which there is a tendency to have recurrent **unprovoked** seizures.

- Epilepsy is defined by 2 or more unprovoked seizures
- ~1% of general population
Usually seizures are:

- Look the same each time
- Brief (~10 seconds to 2 minutes)
- Involve repetitive behaviors
- Have clear beginning, middle, and end
- Occur randomly and unexpectedly
Epilepsy Peaks Early and Late

Hauser, Annegers, and Kurtland
Epilepsia 1981:489-501
Causes of Epilepsy Differ by Age

- Perinatal Injury
- Metabolic Defect
- Congenital Malformation
- Infection
- Genetic Epilepsy
- Postnatal Trauma
- Brain Tumor
- Vascular Disease

Age (yrs.)

Birth 2 3 5 10 20 30 50 70
Unfortunately….

- Epilepsy is more than just seizures
- Has other important impacts on the lives of children and adults
Impact on Children

- Self-esteem and behavior issues
- Decline in school performance
- On average, children with epilepsy tend to be 1 year behind the expected reading level
Impact all Ages

- Depression and anxiety disorders
- Restrictions in activities of daily living
- Difficulties in concentration and memory
- Concern over having children
- Driving
- Difficulties in relationships
- Sexual difficulties
- Discrimination at work
So, How do we Diagnose Epilepsy?

- Clinical
- +
- “Electrical”
- =
- Electroclinical Diagnosis
Evaluation

**Establish Diagnosis:**

- **Goal:**
  - Epilepsy versus Non-Epileptic
  - Type of seizures and epilepsy

- **Tools:**
  - EEG
  - VEEG monitoring

**Search of Cause:**

- History
- Exam
- Imaging
Electroencephalogram
EEG

- Represents a record of the minute shifting brain voltage potentials from the surface of the brain recorded over the scalp.
EEG
Spikes and Sharp Waves: Focal
Video-EEG Monitoring

- Continuous synchronized EEG and Video recording
- Monitors patient’s behavior and EEG
- **Scalp**: Electrodes Similar to EEG
- **Invasive**: Electrodes within or on the surface of the brain.
Video-EEG Monitoring

- Long term inpatient monitoring allows for recording of seizure events.
- Clinical and electroencephalographic features can be reviewed aiding in seizure characterization and localization.
Reasons for Video-EEG

1. Sudden events of unclear nature
2. Sudden increase in seizure frequency
3. Seizure-free: wanting to come off seizure medication
4. Presurgical evaluation to localize seizure onset
MRI scan: Mesial Temporal Sclerosis
Ictal-Interictal SPECT

www.mayo.edu/pediatrics-rst/ brain-epilepsy.html
Interictal PET Imaging

pet.radiology.uiowa.edu/epilepsy-interictal.htm
So How do we Treat Epilepsy?

- The Treatment has to be right for the seizure type
- The Treatment has to be right for the individual
## What Do mean by Right for the Individual?

<table>
<thead>
<tr>
<th>Help</th>
<th>Not Hinder</th>
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<tbody>
<tr>
<td>Reach goals</td>
<td>Not cause side effects worse than the seizures!</td>
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<tr>
<td>• Eg., driving</td>
<td>• Not worsen other medical problems</td>
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<td>Other medical problems</td>
<td>• Not interact with other life-saving treatments</td>
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<tr>
<td>• Migraines</td>
<td>• Cosmetic Effects</td>
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<tr>
<td>• Depression</td>
<td></td>
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<td>• Anxiety</td>
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What do mean by right for the Seizure Type?
Seizure Types

- **Generalized (Generalized-Onset) Seizures** involve widespread bilateral regions simultaneously.

- **Focal (Partial-Onset seizures)** start in one location and spread locally, but may generalize secondarily.

http://www.ilae-epilepsy.org/Visitors/Centre/ctf/seizure_types.cfm
Seizure Types

Generalized

Focal
Classification of Seizures

Partial - Onset
- Simple partial
- Complex partial
- Secondarily generalized

Generalized - Onset
- Absence
- Myoclonic
- Generalized tonic-clonic
- Tonic
- Clonic
- Atonic
# Treatment options by Seizure Type

## Partial - Onset
- Medications
- Resective Surgery
- Vagus Nerve Stimulator
- Diet Therapies
- Research Meds
- Neurostimulation

## Generalized - Onset
- Medications
- Diet Therapies
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- Corpus Callosotomy
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Overview of Medical Therapy
Partial List

Partial Seizures
- **First Generation**
  - Phenytoin (Dilantin)
  - Carbamazepine (Tegretol)
  - Phenobarbital/Mysoline

- **Second Generation**
  - Leviteracetam (Keppra)
  - Topiramate (Topamax)
  - Lamotrigine (Lamictal)
  - Lacosamide (Vimpat)

Generalized Seizures
- **First Generation**
  - Valproate (Depakote)
  - Zarontin (Ethosuximide)

- **Second Generation**
  - Lamotrigine (Lamictal)
  - Topiramate (Topamax)
  - Zonisamide (Zonegran)
  - Rufinamide (Banzel)
PRO’s and Con’s of First vs. Second Generation Medications

- **Pro’s**
  - Known efficacy
  - Broad familiarity
  - Lower cost
  - Coverage by third party payer
  - Long term experience

- **Con’s**
  - More side effects
  - Effects on other medication
  - Effects on bone health and other hormonal effects
Rational Use of AEDs

- Newly diagnosed epilepsy, n=470
  - Seizure-free 47%
  - Uncontrolled seizures 53%

- Monotherapy 1st AED
  - Seizure-free 13%
  - Uncontrolled seizures 40%

- Monotherapy 2nd AED
  - Seizure-free 1%
  - Uncontrolled seizures 39%

- Monotherapy 3rd AED
  - Seizure-free 3%
  - Uncontrolled seizures 36%

- Adjunctive Therapy
  - Seizure-free 3%
  - Uncontrolled seizures 36%

PharMetrics, April 2002 to June 2003
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Diet Therapy for Epilepsy

- **All Diets**
  - High fat
  - Moderate protein
  - Low carbohydrates

- **Ketogenic Diet**
  - Very restrictive
  - All food needs to be weighed

- **Modified Atkins Diet**
  - Less restrictive
  - Only limits the amount of carbohydrates

- **Low Glycemic Index Diet**
  - Less restrictive
  - Allow for more carbohydrates
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When Do We Consider Resective Epilepsy Surgery?

- Partial Epilepsy

- Treatment Resistant Epilepsy
  - Failure to become seizure free after $\geq 2$ adequate trials of 2 AEDs used appropriately

- Intolerable adverse effects of AEDs?
Why?

- Rate of Seizure Freedom with continued trials of Szt med is low (5%)
- Potential for injury with uncontrolled epilepsy over a lifetime is high!
- Rate of Seizure Control with Resective Epilepsy Surgery is in comparison is high (30-80%) with a low complication rate
- Reduction or Elimination of Szt med is frequently possible
Evaluation for Surgery

Scalp EEG

Neuroimaging:
- MRI
- PET
- SPECT
- MEG
Evaluation for Surgery

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Neuropsychological evaluation
Evaluation for Surgery

Scalp EEG

Neuroimaging:
- MRI
- PET
- SPECT
- MEG

Is there a “lesion” which is clearly the seizure focus?

Lesion:
- Tumor
- Vascular
- Development
- MTS

Neuropsychological evaluation
Evaluation for Surgery

And can it be removed without mapping the function of the brain outside of the operating room?

If yes to both questions....
Proceed to Surgery


http://www.fleni.org.ar/files/servicio_193_8
Evaluation for Surgery

Scalp EEG

Neuroimaging:
MRI
PET
SPECT
MEG

And can it be removed without mapping the function of the brain outside of the operating room?

If no to either question....
Intracranial Electrodes

www.bcm.tmc.edu/neurol/struct/epilep/epilepsy_grid.html
Summary of Evaluation

- If non-invasive tests show a clear area where the seizures are coming from, the patient can proceed to resective surgery (taking the seizure focus out)

- If not, an initial operation to record the seizures with electrodes on the brain may be needed (intracranial operation)
Rates of Surgical Success*

- Temporal Lobectomy 70-80%
- “Lesion” Resection 70-80%
- “Non-Lesional” Resection 30-50%
- Medical Management 5%

* Absence of Disabling Seizures
Surgery for Generalized or Partial Epilepsy with onset in multiple locations

- Corpus Callosotomy

- Separation of the communication between the 2 hemispheres of the brain

- Rarely a cure but reduces severity of seizures, eg. falls
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Vagal Nerve Stimulator

www.cyberonics.com
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What’s the Horizon

Devices

- Neuropace
- Deep Brain Stimulation

New Medications

- Retagabine
- Many new and potentially exciting medications are in development!
Clinical Trials

- What is a clinical trial?

- Key terms
  - Randomization and Control
  - Blinding
  - Placebo
What Should I Know?

• Previous safety record of study medication or device

• Chance of getting it vs. placebo?

• How long? What to expect at each visit?

• Access to study agent after the trial?
How do Clinical Trials Work?

- Informed Consent
- Screening
- Enrollment and Study Period
- Withdrawal
- Extension Studies
Where can I find clinical trials?

- www.epilepsygroup.com
- www.clinicaltrials.gov
- Facebook: Epilepsy LifelinksNewtherapyNews
- See an epilepsy specialist
Conclusion

- In most cases, seizures can be well controlled with medications with minimal side effects
- The correct diagnosis to guide treatment is essential
- Epilepsy is more than just seizures, and the treatment may require a team approach
Some cases are more difficult to control, and treatment with diet therapy or surgery may be used, or clinical trials may be an option.
Thank You