Seizures & Epilepsy: Diagnosis and Treatment Options

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Objectives

• Understand the basic diagnosis of spells and seizures
• Learn basic medication treatment for epilepsy
• Review advanced treatment options for refractory epilepsy including epilepsy surgery and devices.

Evaluation of Spells

Seizures

Other (syncope, psychogenic, etc)

Acute Cause?

Yes

No

Acute symptomatic

Unprovoked

One Only

More than one

Single Seizure

Epilepsy

Evaluation of Spells

Seizures

Other (syncope, psychogenic, etc)

Acute Cause?

Yes

No

Acute symptomatic

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One Only

More than one

Single Seizure

Epilepsy
**Major Spell Categories**

- Seizures, epileptic
- Syncope
- Migraine
- Psychogenic
- Vestibular disorder
- Transient ischemia
- Transient global amnesia

**Evaluation of Seizures**

- **Acute Cause?**
  - Yes
  - No
  - Acute symptomatic: ETOH withdrawal, antibiotics
  - Buprion (Wellbutrin), low Na+
  - Unprovoked
    - One Only
    - More than one
      - Single Seizure
      - Epilepsy

**One seizure versus Epilepsy**

- **Unprovoked GTC (grand mal) seizures**
  - One Only
  - normal EEG & <60 years of age
    - Single Seizure
    - New onset epilepsy
  - More than one seizure
    - Or one + EEG finding suggesting recurrence risk or > 60 years of age

**Seizure and Spell Diagnosis**

A. History
   - patient
   - witness
B. Physical and Neurological Examination
C. Electroencephalogram (EEG)
D. Imaging-
   - CT
   - MRI
E. Video-EEG monitoring
Seizure and Spell Diagnosis

A. History
- patient &/or witness
- define terms—“black out”
- postictal amnesia?
- circumstance?
- staring spells, myoclonic

B. Physical and Neurological Examination
- orthostatic BP, neuro exam may be normal

C. Electroencephalogram (EEG)
- routine vs sleep deprived

Small (microvolt) electrical fields are generated by synaptic currents in excitatory cells

EEG measures this activity through the scalp but it can only detect it if thousands of neurons fire in synchrony

Identifying Seizure Types

Generalized

Partial

Absence
Myoclonic
Tonic-clonic (primary)
Tonic
Clonic
Atonic

Simple partial
Complex partial
Secondarily generalized

Adapted from Morrell.
International Classification: Generalized Seizures—primary generalized epilepsy

Non-focal, consciousness is impaired. No aura.
1. Generalized Tonic-Clonic (e.g., grand mal)
2. Generalized Clonic
3. Absence (e.g., Petit Mal)
4. Tonic (Stiffness, tone)
5. Atonic (loss of muscle tone)
6. Myoclonic (brief jerk)

Generalized refers to mechanism—cellular, synaptic, genetic

International Classification: partial seizures—partial or focal epilepsy

Focal/partial/localization related.
Associated with an aura.
1. Simple partial – consciousness not impaired
2. Complex partial – consciousness altered
3. Secondarily generalized seizures
   - grand mal seizure or GTC (generalized tonic clonic convulsion)
International Classification: partial seizures-partial or focal epilepsy

Seizure focus often not apparent on imaging

Secondary generalized refers to seizure spread and not basic mechanism

Diagnosis of Staring Spells

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Absence Seizures Generalized</th>
<th>Complex Partial Seizures</th>
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</thead>
<tbody>
<tr>
<td>Aura (warning)</td>
<td>None</td>
<td>Common</td>
</tr>
<tr>
<td>Postictal confusion</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Mean Duration</td>
<td>10 seconds</td>
<td>1-2 minutes</td>
</tr>
<tr>
<td>EEG</td>
<td>Generalized spike and wave</td>
<td>Focal spikes and sharp waves</td>
</tr>
<tr>
<td>Surgical treatment</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Temporal Lobe Seizures

- Motionless stare common
- Oral automatism - lip smacking, chewing
- Manual automatism - eg. repetitive picking at clothes; ipsilateral to focus
- Hand dystonic posturing - contralateral to focus
- Postictal aphasia common if dominant temp lobe focus
- Easiest to localize seizure focus
- Best outcome for epilepsy surgery

EEG in Spell Diagnosis

A. Electroencephalogram (EEG) - 30 min
B. Ambulatory EEG ± video
C. Video-EEG monitoring (epilepsy monitoring unit)
   1. 24 hours, inpatient
   2. Elective (spell diagnosis or presurgical) versus nonelective (emergency department for spell diagnosis, seizure management)
   3. Most patients elective

Misconception

Spells ➔ LOC + Normal interictal EEG = not epilepsy

Comments:

- Single routine EEGs often (50%) normal in partial epilepsy
- Multiple EEGs to ~3 increase the yield to 90% using routine and sleep-deprived recordings
- Only ictal (during seizure) recordings may be positive in some patients
Basic Spell Management

- Regardless of diagnosis, common trigger factors should be eliminated: stress, sleep deprivation, alcohol, caffeine, seizure triggering meds, recreational drugs
- Treat underlying medical problems
- Medication treatment may not be necessary
- Simple measures: e.g. hydration, elevating head of bed for orthostatic hypotension
- If epilepsy choose single medication at lowest therapeutic dose
- If no response to treatment, reconsider diagnosis

Medication for Epilepsy

- Become comfortable with 2-3 seizure medications
- New onset epilepsy
  - Levetiracetam (Keppra): broad spectrum, easy to titrate, no interactions but irritability (20%)
  - Oxcarbazepine (Trileptal): partial epilepsy, easy to titrate, avoid in elderly due to hyponatremia

Medication for Epilepsy

- Good add-on agents
  - Lamotrigine (Lamictal): broad spectrum, slow titration to prevent rash, mood disorder treatment
  - Zonisamide (Zonegran): broad spectrum, slow titration, weight loss
  - Lacosamide (Vimpat): partial epilepsy, slow titration to prevent side effects
Medication for Epilepsy

- Good agents, But Be Careful!
  - Valproate acid (Depakote)- broad spectrum, may treat mood disorder, avoid in women of child bearing age, tremor
  - Topiramate (Topamax)- broad spectrum, useful for migraine, cognitive & language side effects, weight loss.

Success Rate of Antiepileptic Drugs

- 63% remained seizure-free
- Seizure-free rates were similar between those treated with monotherapy with an older antiepileptic drug (67%) and those treated with monotherapy with a newer antiepileptic drug (69%)


Surgical Management of Epilepsy

- Devices (approved)
  - Vagal nerve stimulation (Cyberonics)
  - Responsive neurostimulation (Neupace)
- Surgical resection
  - Lesionectomy*
  - Temporal*
  - Extratemporal
  - Hemispherectomy
  - Disconnection procedures
- Best success rate

Surgical Resection in Epilepsy

- Concepts
  - Refractory epilepsy
  - Best results when single cortical focus
  - Benefits outweigh risks
- Evaluation
  - Phase I- scalp video-EEG monitoring, neuroimaging (MRI, SPECT, PET)
  - Phase II- invasive video-EEG monitoring: depth and grid electrodes
    - Allows cortical mapping
### Presurgical Evaluation
#### Phase I
- Interictal EEG data
- Video-EEG monitoring
- Ictal SPECT
- Neuropsychological testing
- MRI scanning
- PET scanning

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#### 32 year old RH male with refractory complex partial seizures
- Aura: sensation of abdominal bloating and interictal GI symptoms
- Episodes of staring, confusion and automatic movements of hand and mouth since age 10
- Rare secondarily generalized (grand mal) seizures
- Many different antiepileptic medications tried, but only able to go 2-4 weeks without seizures
- MRI brain scan was reported to be normal

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#### MRI

* 32 WM with right temporal lobe focus

* Smaller right hippocampus compared to left
Ictal SPECT (Single Photon Emission Computed Tomography)

Right temporal hyperperfusion

PET (Positron Emission Tomography)

Right temporal hypometabolism

32 year old RH male with refractory complex partial seizures

• On April 21, 2004, he had a right temporal lobectomy. Since surgery he initially had some rare auras, but otherwise has been seizure free.
• AED’s have been streamlined. He is driving and working.
• All GI symptoms ictal & interictal resolved.
Presurgical Evaluation
Phase II- invasive electrode implantation

Randomized, Controlled Trial of Surgery
For Temporal Lobe Epilepsy

<table>
<thead>
<tr>
<th></th>
<th>Surgical group</th>
<th>Medical group</th>
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<tbody>
<tr>
<td>Seizure-free for all seizures</td>
<td>58% All</td>
<td>8%</td>
</tr>
<tr>
<td>Seizure-free for all seizures</td>
<td>38% All</td>
<td>3%</td>
</tr>
<tr>
<td>Seizure-free for complex partial</td>
<td>64% Actual</td>
<td></td>
</tr>
<tr>
<td>partial seizure</td>
<td>surgery</td>
<td></td>
</tr>
<tr>
<td>Seizure-free for all seizures</td>
<td>42% Actual</td>
<td></td>
</tr>
<tr>
<td>including auras</td>
<td>surgery</td>
<td></td>
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Wiebe et al, 2001 (NEJM)

Vagal Nerve Stimulation
**Vagal Nerve Stimulation**

- Implanted on left side
- Change parameters with wand
- Generator battery changed every few years
- Early side effects and delayed efficacy
- Two modes of activation when first approved
  - Constant cycling
  - Magnet activated

**VNS Therapy Clinical Trial: E03**

Adverse events (occurring in ≥5% of patients)

- Hoarseness 37%
- Throat pain 11%
- Coughing 7%
- Dyspnea 6%
- Paresthesia 6%
- Muscle pain 6%


**VNS Long-Term Seizure Control**

**Response Rates Increase Over Time (E01-E05)**

<table>
<thead>
<tr>
<th>Last Visit Carried Forward (n = 440)</th>
<th>3 months</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients %</td>
<td>23.0%</td>
<td>36.8%</td>
<td>43.2%</td>
<td>42.7%</td>
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**AspireSR Device with 3rd Activation Mode**

*Graph showing heart rate changes and seizure detection timeline.*
RNS™ Neurostimulator with Leads

Implanted RNS™ System

RNS™ System Programming

- Detection sets
  - Detection algorithms selected by physician according to specific electrographic onset pattern
- Stimulation settings
  - Parameters modified by physician according to electrographic response
    - Frequency
    - Duration of stimulation
    - Pulse width
    - Current intensity