Imitators of Epilepsy
December 2, 2011

Ronald P. Lesser, M.D.
Professor of Neurology and Neurosurgery
Department of Neurology
The Johns Hopkins Medical Institutions
Baltimore, MD
Disclosure

- I in the past, but no longer, have been on Speaker's Bureaus and have given lectures supported by, or have been a consultant for the following companies, all of which have had or are developing products that could be used to treat epilepsy: Abbott Laboratories, Bertek Pharmaceuticals, Burroughs Wellcome (now GlaxoSmithKline), Cyberonics, Medtronic, Novartis, Ortho-McNeil, Wallace Laboratories, Warner-Lambert/Parke-Davis, Wyeth. I or my spouse have stock in the following companies, each of which has at least one product that can be used to treat epilepsy: Abbott, Johnson & Johnson, Pfizer. I have been a site investigator for studies funded by Lorex Pharmaceuticals, Wallace Laboratories, Warner-Lambert Company and have received funding from Medtronic; none of these have occurred for the past several years. For several years, until 2004/6, I organized a periodic dinner meeting for the Maryland Epilepsy Group. These meetings included meals purchased by Parke-Davis/Pfizer or UCB. They primarily dealt with surgical or imaging topics, but one dealt with mechanisms underlying the effects of anticonvulsants.
Disclosure

• Since 1999, I have been, or am, a sub-investigator for a number of drug studies for which I receive no compensation. These have been funded by the following: Eisei (rufinamide, perampanel), Johnson & Johnson (JNJ-26489112), National Institutes of Health (progesterone), Novartis (oxcarbazepine, rufinamide, BGG492), Parke-Davis (pregabalin), Schwarz Biosciences (lacosamide), Sepracor (eslicarbazepine), SK Bio-Pharmaceuticals (YKP3089), UCB (brivaracetam, lacosamide, levetiracetam), Neuronex (intranasal diazepam), Upsher-Smith (intranasal midazolam). I have received funding from and I am entitled to sales royalty from Bio-logic Systems, Inc (now owned by Natus Medical Incorporated), which has developed products related to my research involving a computerized method for analyzing physiologic data. I also receive royalties from Persyst Development Corporation for sales of software I developed for reporting results of EEG evaluations. The terms of my arrangement with Bio-logic Systems and with Persyst have been reviewed and approved by the Johns Hopkins University in accordance with its conflict of interest policies.
Learning Objectives

• understand characteristics of the most common imitator of epilepsy
• consider etiologies
• consider other disorders that can be confused with epilepsy
• consider treatment
Psychogenic Non-Epileptic Seizures (PNES)

a physical way of expressing
an emotional conflict or concern

The patient may or may not
be aware of the conflict or concern

It may or not be possible
to determine the conflict or concern
Incidence of PNES

- **Iceland**
  - 35/100,000 - epilepsy\(^1\)
  - 1.4/100,000 - PNES\(^1\)

- **United States**
  - 29-53/100,000 - epilepsy\(^2\)
  - 1-2/100,000 - PNES\(^3\)

---

1 Sigurdardottir and Olafsson, 1998
2 Hauser and Hesdorffer 1990
3 estimate
Prevalence of PNES

- point prevalence of epilepsy = 0.6%
- 1/3 of all seizures are intractable
- patients with these often go to epilepsy centers
- PNES: 10-20% of patients at epilepsy centers
- therefore 50,000-100,000 patients in U.S.?
  - “sampling error”
  - delayed diagnosis

This slide is unavailable.
Prevalence of PNES

Reported cases – 21 articles

- 4-77 years old
- 734 women
  250 men

- Lesser, 1996
This slide is unavailable.
Diagnostic delay

• Some patients are*
  dependent
  angry or hostile
  manipulative
  isolated
  resistant to psychiatric diagnosis
• This can impede diagnosis

*Groves, 1978
This slide is unavailable.
<table>
<thead>
<tr>
<th>Condition</th>
<th>AED Status</th>
<th># Patients</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNES + Sz</td>
<td>AED +</td>
<td>260</td>
<td>7.8y (9.8)</td>
</tr>
<tr>
<td></td>
<td>AED -</td>
<td>53</td>
<td>4.9y (6.6)</td>
</tr>
<tr>
<td>PNES only</td>
<td>AED +</td>
<td>161</td>
<td>8.4y (10.2)</td>
</tr>
<tr>
<td></td>
<td>AED -</td>
<td>53</td>
<td>4.9y (6.6)</td>
</tr>
<tr>
<td>“spikes” +</td>
<td></td>
<td>17</td>
<td>12.5y (15.6)</td>
</tr>
<tr>
<td>“spikes” -</td>
<td></td>
<td>195</td>
<td>7.1y (8.7)</td>
</tr>
</tbody>
</table>
Co-occurrence with Epilepsy

- 20-60%
  - Özkara and Dreifuss 1993
- 9-30%
- may vary with clinical situation
- any given person may have two diagnoses
- consider each diagnosis by itself
# Delayed Diagnosis of PNES

<table>
<thead>
<tr>
<th>Group</th>
<th># patients</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNES + Sz</td>
<td>260</td>
<td>7.8y (9.8)</td>
</tr>
<tr>
<td>AED -</td>
<td>53</td>
<td>4.9y (6.6)</td>
</tr>
<tr>
<td>PNES only</td>
<td>161</td>
<td>8.4y (10.2)</td>
</tr>
<tr>
<td>AED +</td>
<td>161</td>
<td>8.4y (10.2)</td>
</tr>
<tr>
<td>AED -</td>
<td>53</td>
<td>4.9y (6.6)</td>
</tr>
<tr>
<td>“spikes” +</td>
<td>17</td>
<td>12.5y (15.6)</td>
</tr>
<tr>
<td>“spikes” -</td>
<td>195</td>
<td>7.1y (8.7)</td>
</tr>
</tbody>
</table>

- Reuber et al., 2002
Delayed Diagnosis of PNES

See Krauss et al. 2005
38 patients treated for somatization disorders

53% decrease in subsequent costs

Smith et al. 1995
Accuracy of clinical diagnosis

You’d better ask the doctors here about my illness, sir. Ask them whether my fit was real or not.

-Smerdyakov to Ivan in *The Brothers Karamazov*

- King et al. 1982
Accuracy of clinical diagnosis

- King et al. 1982

- Hospital

- Later

- Wrong

- Right

- Epilepsy

- PNES

- Admission

- Hospital

- Later

- # pts

- 0

- 10

- 20

- 30

- 40

- 50

- 60

- 70

- 80

- 90

- P
Pseudo-PNES

- epilepsy
- syncope
  - Hyperventilation syndrome
- movement disorders, migraine, parasomnias, g-e reflux

Syncope
medical student volunteers

- Dieter Schmidt
Accuracy of clinical diagnosis

- visual diagnoses/reports can be unreliable
- EEG often needed to verify visual impressions
- patients with frequent seizures
  outpatient EEGs may record seizures
- others, admission to EMU needed
  withdraw medication
  wait for seizures
What about Sandy and Nicole?

• Does Sandy have epilepsy? PNES? both?
• Does Nicole have epilepsy? syncope? PNES? 2/3? 3/3?
EMU Monitoring

- added (10% system) electrodes often useful
- withdraw anticonvulsants
- interictal spikes can occur in persons with no history of epilepsy
- epileptiform vs. nonspecific EEG changes
- beware of normal variants and artifacts
EMU Monitoring

- EEG normal with PNES
- scalp EEG often normal in persons with simple partial seizures
Onset

PNES
- often gradual onset, can be short
- apparent sleep but actually awake (EEG)
- symptoms at onset palpitations, malaise, choking, numbness, peripheral sensory changes, pain, odors, tastes, hallucinations

Epilepsy
- usually short
  - longer duration in some
- awake or asleep
- symptoms at onset altered mood, experience, autonomic changes, peripheral/GI sensory changes, odors, tastes, hallucinations

Onset

PNES

- behavior changes
- hyperventilation syndrome
- may resemble epilepsy
- emotional etiology

Epilepsy

- behavior changes
- epigastric
- special senses
- unilateral sensory or motor
- may have emotional etiology
Sensory

PNES

• may or may not follow anatomic pathways

Epilepsy

• follows anatomic pathways
• 59 y/o priest
• history of alcoholism and depression
• episodes for 13 months
• bilateral weakness, numbness
  affecting extremities, rectum
• notes occasional odor
• no loss of consciousness
• meds: phenytoin 300mg
• normal EEGs
Towards the left rectal
On the side
Hip I should say...
  Left hip?
Yes

Now right elbow
Right knee, very very light
The left side is still having a little grumble to it
All right doctor
Now my right just above the right rectal, that part of the body
Part of the sensation

Left side is all finished
Everything is finished.
• Second sensory area
• Glioblastoma multiforme
• Died within one year
<table>
<thead>
<tr>
<th>Motor</th>
<th>PNES</th>
<th>Epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• rigidity, pelvic thrusting*</td>
<td>• rigidity alone rare</td>
<td></td>
</tr>
<tr>
<td>• quasi-clonic, flailing, thrashing, trembling</td>
<td>• thrashing, kicking may occur (frontal lobe)</td>
<td></td>
</tr>
</tbody>
</table>
| • side-to-side movements** of head/body | • bilateral movements  
  – *but* focal motor seizures (frontal lobe) | |
| • asynchronous*** | • usually synchronous, may be asynchronous (frontal lobe) | |
| • eyes closed | • eyes open | |

*4%  **15%  ***9%  Leis et al. 1992*
• 40 y/o woman
• episodes for 11 months
• tingling, rt scalp
• → speech & movement arrest
  loss of consciousness  GTC sz
  2 / week – 3 / 6 weeks
• chest pressure – “cat on chest” & feels “drained”
• → speech/movement arrest
  → nausea, dizziness  → tired, headache
  6 / 9 months
• pacemaker placed after tilt table test
  → continued episodes, 1 lasting 2 hours
  appears distressed, eyes closed
This slide is unavailable.
Vocalization

PNES
• crying, yelling, screaming, stuttering
• Sobbing
• complex dramatic, tragic, obscene, mystical

Epilepsy
• cry at onset of generalized tonic or tonic-clonic seizures
• grunting during clonic movements
• various vocalizations during complex partial seizures
Injury

PNES
• bite tongue (tip/side) / lips
• bruises, lacerations
• may not respond during avoidance testing or to painful stimulation
  – may allow intubation
  – complications of treatment: respiratory arrest, septicemia, pneumonia, urinary tract infection, cellulitis, foot drop

Epilepsy
• bite tongue (side)
• bruises/lacerations
• no response to avoidance testing during generalized tonic-clonic seizure
• may respond during complex partial seizure or postictally

-Howell et al 1989
Urination / Defecation

PNES  Epilepsy

• both are reported  • both are reported
Autonomic Changes

PNES

• salivation, hyperventilation, choking, coughing, cyanosis, pallor, flushing, headache, chest pain, laryngeal spasm, pharyngeal spasm

• hyperventilation syndrome

Epilepsy

• similar
Duration

PNES

• usually longer more than 2 minutes

Epilepsy

• usually shorter less than 2 minutes
Prolactin

- 15-30 minutes after attack
- several fold increase
- most accurate: generalized tonic-clonic temporal lobe seizures
- less accurate: simple partial seizures frontal lobe seizures
- false positives and negatives can occur
## Ictal heart rate - staring spells

<table>
<thead>
<tr>
<th></th>
<th>CPS</th>
<th>PNES</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR ≥ 130% of baseline</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>HR &lt; 130% of baseline</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>29</td>
</tr>
</tbody>
</table>

- Sensitivity (Sens) 30/36 = 83%
- Specificity (Spec) 28/29 = 97%
- Positive predictive value (Pos pred) 30/31 = 97%
- Negative predictive value (Neg pred) 28/34 = 82%

Oipherk and Hirsch, 2002
Seizure induction

- iv’s, moistened patches, photic stimulation, tuning fork, suggestion
- allow vs. coerce
- 70% inducible
- be sensitive to emotional needs and sense of dignity of the patient

Diagnosis of PNES ≠
Etiology of PNES

• often do not easily fit into standard classifications
• Some patients found to be psychologically normal
• some but not all studies find relative increase in cognitive difficulties
Diagnosis of PNES ≠ Etiology of PNES

- External interactions
- Internal / internalized conflicts
- Psychoses, Schizophrenia
- Personality disorders
- Other

- External interactions
  - inadequate personality, reinforced behaviors, adjustment reaction, family conflict, sexual or physical abuse, anger, hostility
- Internal / internalized conflicts
  - affective disorders, panic attacks, anxiety, ocd, misinterpretation, highlighting, conversion/somatization/dissociative/depersonalization disorders, post-traumatic stress disorders,
- Psychoses, Schizophrenia
- Personality disorders
  - borderline, malingering, factitious disorder, histrionic, narcissistic, antisocial, passive-aggressive, avoidant, passive-dependent, substance abuse
- Other
  - head trauma, cognitive difficulties, a.d.d., tic, genetic influences
Initiation of treatment is an important part of the diagnostic process

• tactfully present the diagnosis
• explore possible reasons for disorder
• recommend therapy
  – some do well after this single session
  but most need more

Initiation of treatment is an important part of the diagnostic process

- little data on usefulness of psychiatric drugs
- useful for some etiologies:
  - affective disorders
  - ocd
  - schizophrenia
- less useful for others:
  - personality disorders
Initiation of treatment is an important part of the diagnostic process

- In most cases see the patient at least once more
  - symptoms improved? exam findings?
  - emotional counseling?
- If appropriate, continue following the patient.
Initiation of treatment is an important part of the diagnostic process

- often only rudimentary data link seizures, personality, and treatment

- we need to evaluate effectiveness of specific strategies in specific types of patients
References