Psychogenic Non-epileptic Seizures, and Veterans

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

The Brothers Karamazov; F. Dostoevsky, 1881
What elephant?
Psychogenic Non-epileptic Seizures (PNES), and Veterans

- Defining the problem
- Traumatic Brain Injury and PNES
- Psychiatric factors; therapy
Epilepsy

◆ The most common problem faced by neurologists worldwide*

◆ ~1% of the world burden of disease (WHO)

*excluding headache, back pain

Singhai; Arch Neurol 1998
Medina; J Neurol Sci 2007
Murray et al; WHO, 1994
Kobau; MMR, August 2008

US prevalence ~0.85%

Prevalence (per 100 persons)

0 0.2 0.4 0.6 0.8 1 1.2 1.4
Cases per 100 persons

Epilepsy  Neuropathy  Cerebrovascular  Dementia
Non-Epileptic Seizures (NES)

- A transient alteration in behavior resembling an epileptic seizure but *not due to paroxysmal neuronal discharges*;
Disorders that may mimic epilepsy (adults)

- Cardiovascular events (syncope)
  - Vasovagal attacks (vasodepressor syncope)
  - Arrhythmias (Stokes-Adams attacks)

- Movement disorders
  - Paroxysmal choreoathetosis
  - Myoclonus, tics, habit spasms

- Migraine - confusional, basilar

- Sleep disorders (parasomnias)

- Metabolic disorders (hypoglycemia)

- Psychological disorders
  - Psychogenic seizures
Non-Epileptic Seizures (NES)

- A transient alteration in behavior resembling an epileptic seizure but not due to paroxysmal neuronal discharges;

- Psychogenic Non-epileptic Seizures (PNES)
  - without other physiologic abnormalities
  - with probable psychological origin
Non-Epileptic Seizures (NES)

- Epileptic
- Non-epileptic

Seizures

10% - Physiologic
- Syncope
- Movement Disorders
- Hypoglycemia
- Parasomnias...

90% - Psychogenic
- Conversion
- Somatization
- Dissociative
- Malingering...

Many have ‘medically refractory’ seizures
Hystero-epilepsy

Charcot
‘Arc de cercle’ in patient with ‘hystero-epilepsy’

From Iconographie Photographique de la Salpetriere; Bourneville and Regnard, 1876 (patients of Charcot)
AN ACCOUNT
OF A
DEMONSTRATION ON THE PHENOMENA
OF Hystero-epilepsy:
AND ON THE MODIFICATION WHICH THEY UNDERGO UNDER THE
INFLUENCE OF MAGNETS AND SOLENOIDS;
Given by Professor Charcot at the Salpêtrière.

BY ARTHUR GAMGEE, M.D., F.R.S.,
Brackenbury Professor of Physiology in Owens College, Manchester.

On the mornings of Friday and Saturday, August 23rd and 24th, several physicians and scientific men, amongst whom were Professors Virchow, Grainger Stewart, Turner, Oscar Liebreich, Ray Lankester, ovarian region. (By perusing the account afterwards given of the convulsive attacks of hystero-epilepsy, the reader will understand the grounds for the diagnosis of the ovarian irritation in these cases.) Professor Charcot brought this patient before us to demonstrate that usually it is possible in patients affected with hystero-epilepsy to induce the mesmeric condition. The patient being seated opposite to him, at the distance of about two feet, he steadily maintained the index finger of his right hand at a short distance from the centre of her forehead; she was directed to look steadily at the finger, and did so. Several minutes elapsed (the time was not actually noted), and the patient did not seem sensibly affected. She declared that "to day she had no desire to sleep".—At 10.4 A.M., the previous attempts, which may have lasted ten minutes, having failed, Professor Charcot, placing his head on a level with that of the patient, commenced to stare fixedly into both her eyes.—At 10.5, the eyelids drooped, and, at the same time, began to wink in a rapid tumultuous manner; this phenomenon continuing throughout the whole duration of the induced sleep, and being, Professor Charcot remarked, constant; at the same time, a tonic contraction of the flexors of both forearms occurred, the fists becoming temporarily clenched. At 10.7, the patient, being asleep, Pro-

“Hystero-epilepsy is a nervous disease of women of great rarity, affecting them especially during the child bearing period of life... associated with hyperesthesia of one or both ovarian regions...."
Joseph Babinski

AKA Joseph Jules François Félix Babinski

Born: 17-Nov-1857
Birthplace: Paris, France
Died: 29-Oct-1932
Location of death: Paris, France
Cause of death: Illness
Remains: Buried, Cimetière des Champeaux, Montmorency, France

Gender: Male
Religion: Christian
Race or Ethnicity: White
Occupation: Doctor, Scientist

Nationality: France
Executive summary: The Babinski sign

Military service: French Military Health Service (1916-20)

Neurologist Joseph Babinski is best known for his 1896 discovery of what is now called the Babinski sign, a reflexive extension of the big toe and fanning of the other toes when the foot is stroked in a particular manner,
“…You’d better ask the doctors here about my illness, sir. Ask them whether my fit was real or not.”

The Brothers Karamazov; F. Dostoevsky, 1881
PNES
Impact on the Patient

» Antiepileptic Drug therapy (>70%)
  » Side effects; often multiple AEDs

» Disability
  » Restrictions on driving
  » Restrictions on work

» Psychological/Social effects

» Costs of assessment and treatment
  » Estimated VA total cost: >$55 million / year
**Psychogenic Seizures (PNES)**

**-Frequency (civilians)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>King et al</td>
<td>1982</td>
<td>20%</td>
</tr>
<tr>
<td>Bowman et al</td>
<td>1996</td>
<td>33%</td>
</tr>
<tr>
<td>Martin et al</td>
<td>2003</td>
<td>32%</td>
</tr>
<tr>
<td>Benbadis et al</td>
<td>2004</td>
<td>30%</td>
</tr>
<tr>
<td>Salinsky et al</td>
<td>2011</td>
<td>26%</td>
</tr>
</tbody>
</table>

King DW et al; Neurology; 1982
Bowman ES, Markand ON Am J Psychiatry; 1996
Martin R et al, Neurology; 2003
Benbadis SR et al, Epilepsia; 2004
Salinsky MC, Neurology; 2011
Psychogenic Seizures
Increased Risk in Veterans

- Relatively high rates of TBI
  - 19% of OEF/OIF
  - Increased seizure risk
  - Most common putative cause for PNES\textsuperscript{1,2}

- Relatively high rates of PTSD
  - Estimates of 20%
  - Established risk factor for PNES\textsuperscript{3,4}

- Compensation
  - Illness behavior

\textsuperscript{1} Barry et al; Epilepsia 1998
\textsuperscript{2} Westbrook et al; Epilepsia 1998
\textsuperscript{3} Bowman and Markand, Am J Psychiatry 1996
\textsuperscript{4} Rosenberg et al, Epilepsia 2000
Psychogenic Seizures (PNES)
U.S. Veterans

- Are PNES more common in veterans than civilians?
  - Referred for inpatient epilepsy monitoring
- Is there a longer delay to diagnosis of PNES in veterans as compared to civilians?
- Do veterans with PNES have greater exposure to anti-epileptic drugs as compared to civilians?
Psychogenic Seizures in Veterans
Subjects

- Portland VAMC Epilepsy Monitoring Unit
  - Shared by veterans and civilians (from Oregon Health & Science University)
  - All patients evaluated by same care team, with same equipment, protocols
Epilepsy Monitoring Unit Discharge Diagnoses

Veterans
(N=203)

- Epilepsy: 18%
- PNES: 25%
- Mixed: 4%
- NES Other: 12%
- Nondiagnostic: 41%

Civilians
(N=726)

- Epilepsy: 40%
- PNES: 26%
- Mixed: 3%
- NES Other: 27%
- Nondiagnostic: 4%

PNES – Psychogenic Non-epileptic Seizures
ES – Epileptic Seizures

Salinsky et al, Neurology; 2011
## Psychogenic Seizures
### Veterans Compared to Civilians

<table>
<thead>
<tr>
<th></th>
<th>Veterans</th>
<th>Civilians</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of PNES patients</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Age at EMU admission</td>
<td>49.0 (24-66)</td>
<td>34.5 (19-74)</td>
<td>&lt;0.001 (W)</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>80</td>
<td>26</td>
<td>&lt;0.001 (F)</td>
</tr>
<tr>
<td>% using AEDs at admission</td>
<td>72%</td>
<td>80%</td>
<td>ns</td>
</tr>
<tr>
<td>Cumulative AED-years (median)</td>
<td>4.0 (0-50)</td>
<td>1.0 (0-30)</td>
<td>&lt;0.01 (W)</td>
</tr>
<tr>
<td>Interval from onset of spells to diagnostic admission (months)</td>
<td>60.5 (3-408)</td>
<td>12.5 (2-144)</td>
<td>&lt;0.001 (W)</td>
</tr>
</tbody>
</table>

F – Fishers Exact test    W – Wilcoxon test
Number of Patients

Interval From Onset of PNES to Diagnostic Admission (years)

Veterans

Civilians
Delay in diagnosis of PNES - Why it matters

- Continued treatment with AEDs
  - Often multiple AEDs

- Delay in appropriate treatment
  - Continued disability; cost

- Potential worsening of long-term outcome
PNES in U.S. Veterans

Why the delay in diagnosis?

» Availability of Epilepsy Monitoring Units (EMUs) within VAMC?
  – 50% from states with no VA EMUs
    – Epilepsy Centers of Excellence

» Acceptance of seizures related to TBI?
  – Primary provider?
TBI as Proposed Cause of PNES

Civilians vs. Veterans

For veterans - 50% of TBIs were military TBIs
Veterans with PNES
TBI Severity

Mild TBI = Concussions or brief LOC (<30 min.)
Post-traumatic Epilepsy (civilians)

TBI Severity

Percent of patients

- Mild TBI: 29%
- Moderate-Severe TBI: 71%

Post-traumatic Epilepsy (population based)

Source: Annegars et al; NEJM, 1998
Veterans with PNES vs. Epilepsy
TBI Severity

<table>
<thead>
<tr>
<th>TBI Severity</th>
<th>Psychogenic</th>
<th>Epileptic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild TBI</td>
<td>87%</td>
<td>37%</td>
</tr>
<tr>
<td>Moderate-Severe TBI</td>
<td>14%</td>
<td>63%</td>
</tr>
</tbody>
</table>

p < 0.001
TBI Severity and Seizures
U.S. Veterans

- Hx of mild TBI as cause of seizures
  » 82% with PNES

- HX of severe TBI as cause of seizures
  » 90% with epilepsy
TBI OEF/OIF veterans

- Unclassified: N=1,438 (3.8%)
- History of TBI: N=1,985 (5.3%)
- Penetrating: N=117 (0.03%)
- Severe: N=309 (0.08%)
- Moderate: N=12,250 (32.5%)
- Mild: N=21,619 (57.3%)

Pugh, MJ; with permission
Psychogenic Non-epileptic Seizures (PNES), and Veterans

- Defining the problem
- Traumatic Brain Injury and PNES
- Psychiatric factors; therapy
What psychiatric disorders are associated with PNES?

What therapeutic approaches can be used?
PNES in Veterans

- What psychiatric disorders are associated with PNES?
  - PTSD?
    - Associated with PNES in civilian studies\(^1,2\)
    - 33-65% in **mild** military TBI \(^3,4\)
      (Less in moderate-severe TBI)\(^5\)

- What therapeutic approaches can be used?

2. Rosenberg et al, Epilepsia 2000
3. Hoge et al, NEJM 2008
5. Zatzick et al, Arch Gen Psychiatry 2010
## Veterans with PNES vs. ES Mental Health Evaluations

<table>
<thead>
<tr>
<th></th>
<th>Psychogenic</th>
<th>Epileptic</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>68</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Age at Admission</td>
<td>48.4</td>
<td>49.9</td>
<td>NS</td>
</tr>
<tr>
<td>Any Axis 1 Diagnosis (%)</td>
<td>77.9</td>
<td>66.7</td>
<td>NS</td>
</tr>
<tr>
<td>Number of Axis 1 Diagnoses</td>
<td>3 (0-8)</td>
<td>2(0-6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any Axis 2 Diagnosis (%)</td>
<td>27.9</td>
<td>16.7</td>
<td>NS</td>
</tr>
</tbody>
</table>
Axis I Diagnoses by Seizure Type

Percent of patients

- PTSD: 55.9% (*** p<0.001)
- Major Depression: 18.5%
- Alcohol abuse: 20%
- Substance abuse: 40%
- Other Depression: 60%
- Adjustment d/o: 80%

Salinsky et al, Epilepsy and Behavior; 2012
Veterans with PNES vs. Epilepsy
Multivariate Analysis

<table>
<thead>
<tr>
<th>Psychiatric</th>
<th>Historical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Axis I diagnoses</td>
<td>Age at admission</td>
</tr>
<tr>
<td>Any Axis II diagnosis</td>
<td>Sex</td>
</tr>
<tr>
<td>PTSD</td>
<td>Duration of seizures</td>
</tr>
<tr>
<td>Major depression</td>
<td></td>
</tr>
<tr>
<td>Other depression</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td></td>
</tr>
<tr>
<td>Substance abuse</td>
<td></td>
</tr>
<tr>
<td>Adjustment d/o</td>
<td></td>
</tr>
<tr>
<td>Bipolar d/o</td>
<td></td>
</tr>
<tr>
<td>Any Psychiatric Admit</td>
<td></td>
</tr>
<tr>
<td>Number of Psychiatric Admits</td>
<td></td>
</tr>
</tbody>
</table>

**PTSD**

- **Odds Ratio**: 5.7
- **p**: <0.001
TBI (mild) → PTSD → PNES

*Mediation analysis

*p<0.05
PTSD

\*p<0.05

TBI (mild)

Health Problems

Mediation analysis

Hoge et al, NEJM; 2008
Pietrzak et al, J Nerv Ment Dis; 2009
WILL NOT FAKE SEIZURES
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Psychogenic Seizures - Treatment

- Psychotherapy
- Cognitive-Behavioral Therapy*
- Medication
- Meditation
- Biofeedback
- EMDR
- Relaxation therapy

-Cochrane Review 2005
-NES Treatment Workshop 2006
-Goldstein et al, Neurology, 2010*
-LaFrance et al, Epilepsy and Behavior, 2009*
Mean predicted seizure frequency (adjusted for pre-randomization seizure frequency)

Seizure frequency

Start of Treatment  End of Treatment  Follow-up

Cognitive-behavioral therapy
Standard medical care (counseling)

3 month treatment; 6 month follow-up

Goldstein et al, Neurology, 2010
Psychogenic Seizures
Outcome *(diagnosis matters!)*

<table>
<thead>
<tr>
<th>Author</th>
<th>N/ % f/u</th>
<th>f/u interval; months (SD)</th>
<th>Seizure free (interval)</th>
<th>AED free</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selwa, 2000</td>
<td>85/67</td>
<td>19-48</td>
<td>40% (?)#</td>
<td>68%</td>
</tr>
<tr>
<td>Kanner, 1999</td>
<td>45/100</td>
<td>6-26</td>
<td>29% (6 months)</td>
<td>?</td>
</tr>
<tr>
<td>Walczak, 1995</td>
<td>72/71</td>
<td>12-27</td>
<td>35% (6 months)#</td>
<td>53%</td>
</tr>
<tr>
<td>Ettinger, 1999</td>
<td>76/74</td>
<td>18 (10)</td>
<td>52% (?)</td>
<td>59%</td>
</tr>
<tr>
<td>Reuber, 2003</td>
<td>210/47</td>
<td>49 (3)</td>
<td>56% (?)#</td>
<td>48%</td>
</tr>
<tr>
<td>McKenzie, 2010</td>
<td>260/72</td>
<td>6-12</td>
<td>38% (2 mo.)</td>
<td>75%</td>
</tr>
</tbody>
</table>

*Shorter duration of illness at diagnosis correlated with better outcome*
Psychogenic Seizures in Veterans

Key Points

- **PNES are common in veterans**
  - ~25% of EMU admissions (similar to civilians)
  - ? rate in outpatients

- **Delayed diagnosis in veterans vs. civilians**
  - Increased AED usage
  - Prolonged disability; cost
  - Worse prognosis (?)

- **Risk factors**
  - Mild TBI as etiology
  - History of PTSD
Portland VAMC
Epilepsy Center of Excellence

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Eilis Boudreau MD, PhD
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Paul Motika MD
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