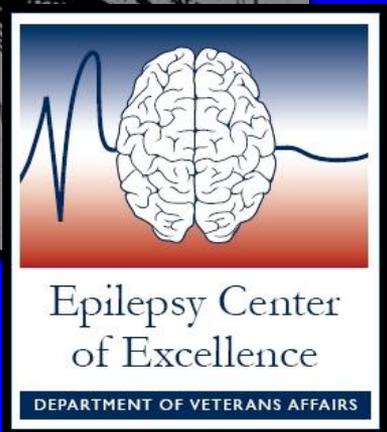


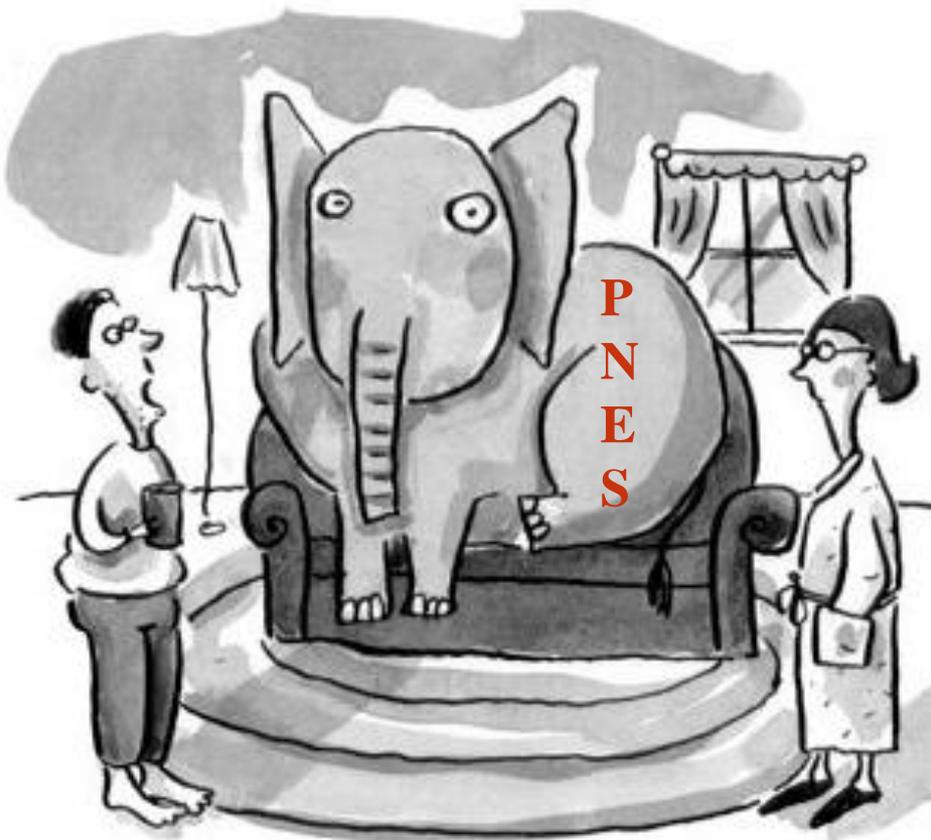
Psychogenic Non-epileptic Seizures, and Veterans

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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?

Tomassi

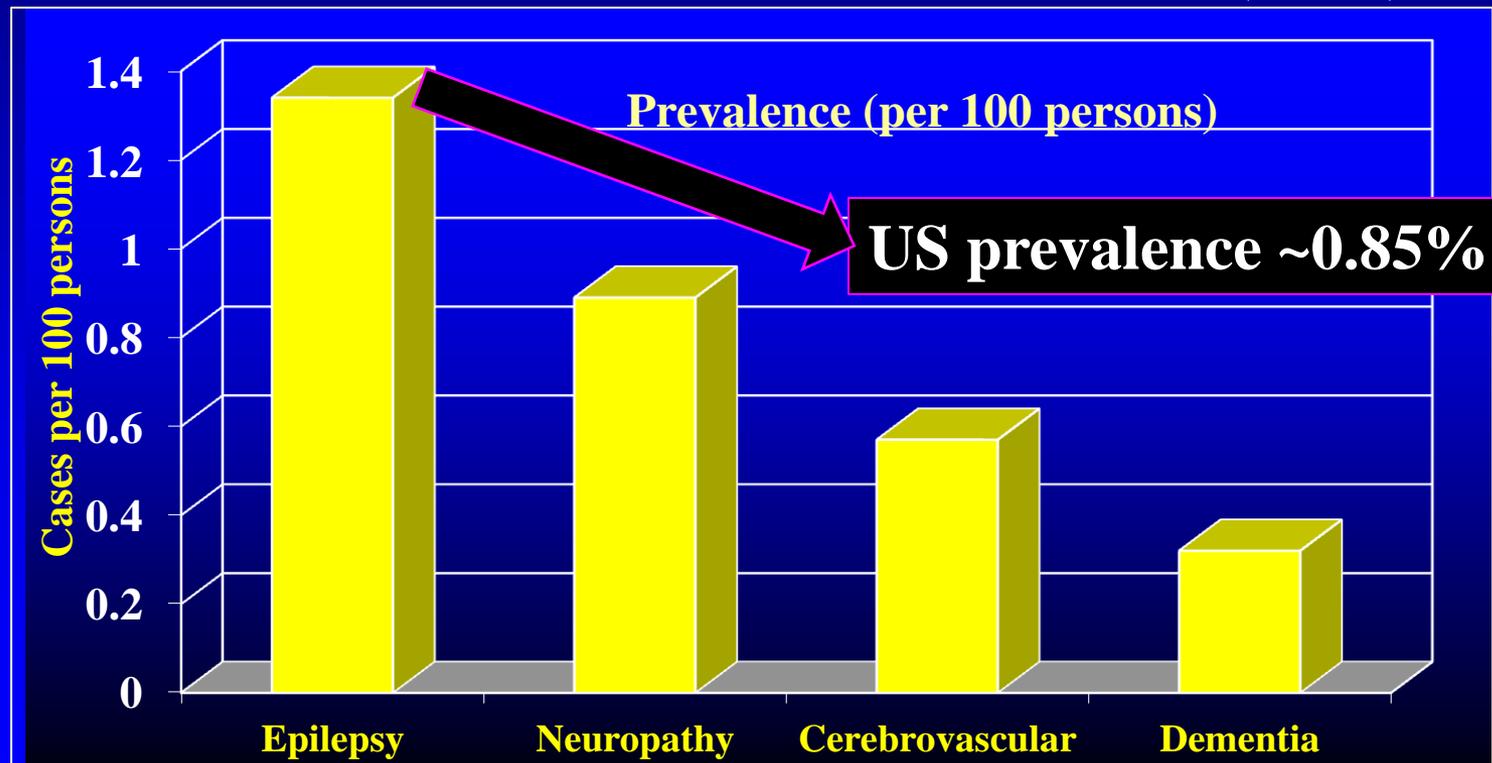
Psychogenic Non-epileptic Seizures (PNES), and Veterans

- ◆ **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
Murray et al; WHO, 1994

Medina; J Neurol Sci 2007
Kobau; MMR, August 2008

Non-Epileptic Seizures (NES)

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

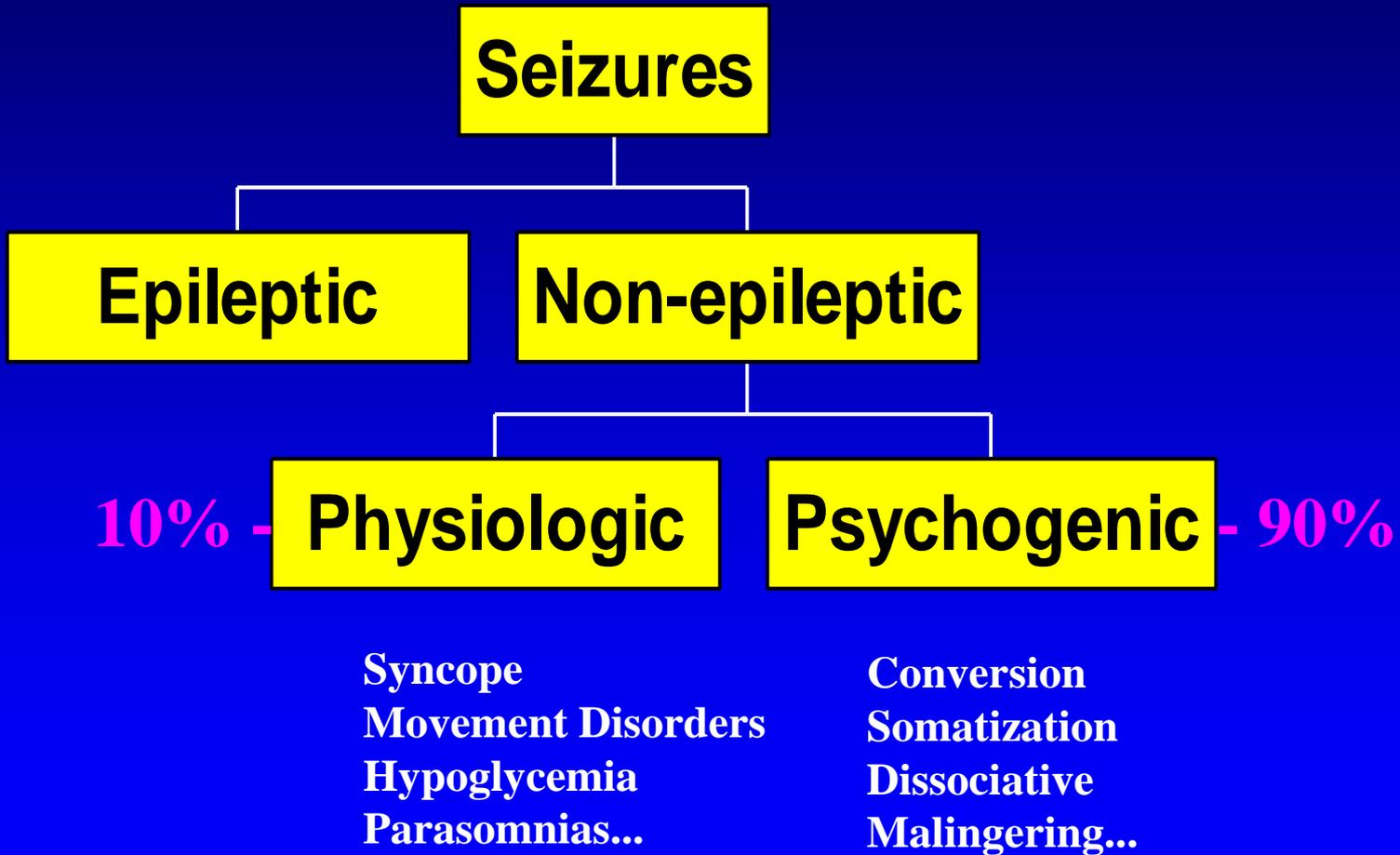
Disorders that may mimic epilepsy (adults)

- ◆ **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)



Many have 'medically refractory' seizures



Hystero-epilepsy

Charcot

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



**From *Iconographie Photographique de la Salpêtrière*;
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 10.6, the eyelids drooped, and, at the same time, began to wink in a rapid tremulous 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,



The International Journal of Psychoanalysis

(1945). International Journal of Psycho-Analysis, 26:1-8

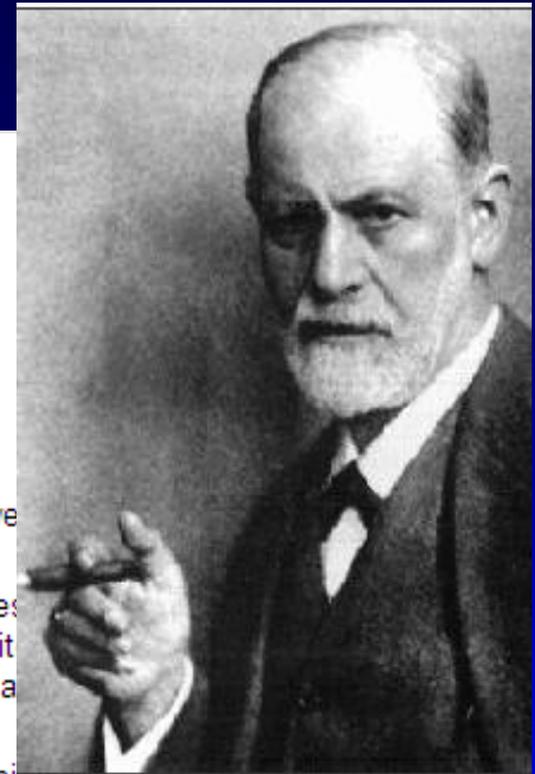
Dostoevsky and Parricide (1928)

Sigmund Freud

Four facets may be distinguished in the rich personality of Dostoevsky: the creative moralist and the sinner. How is one to find one's way in this bewildering complexity?

The creative artist is the least doubtful: Dostoevsky's place is not far behind Shakespeare. *Karamazov* is the most magnificent novel ever written; the episode of the Grand Inquisitor in the literature of the world, can hardly be overestimated. Before the problem of the creative artist, he has laid down its arms.

The moralist in Dostoevsky is the most readily assailable. If we seek to rank him high as a moralist on the plea that only a man who has gone through the depths of sin can reach the highest summit of morality, we are neglecting a



*“...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)

inpatient Epilepsy Monitoring Unit evaluations (% of admissions)

King et al	1982	20%
Bowman et al	1996	33%
Martin et al	2003	32%
Benbadis et al	2004	30%
Salinsky et al	2011	26%

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^{1,2}

◆ Relatively high rates of PTSD

- ◆ Estimates of 20%
- ◆ Established risk factor for PNES^{3,4}

◆ Compensation

- ◆ Illness behavior

¹Barry et al; Epilepsia 1998

²Westbrook et al; Epilepsia 1998

³Bowman and Markand, Am J Psychiatry 1996

⁴Rosenberg et al, Epilepsia 2000

Psychogenic Seizures (PNES)

U.S. Veterans

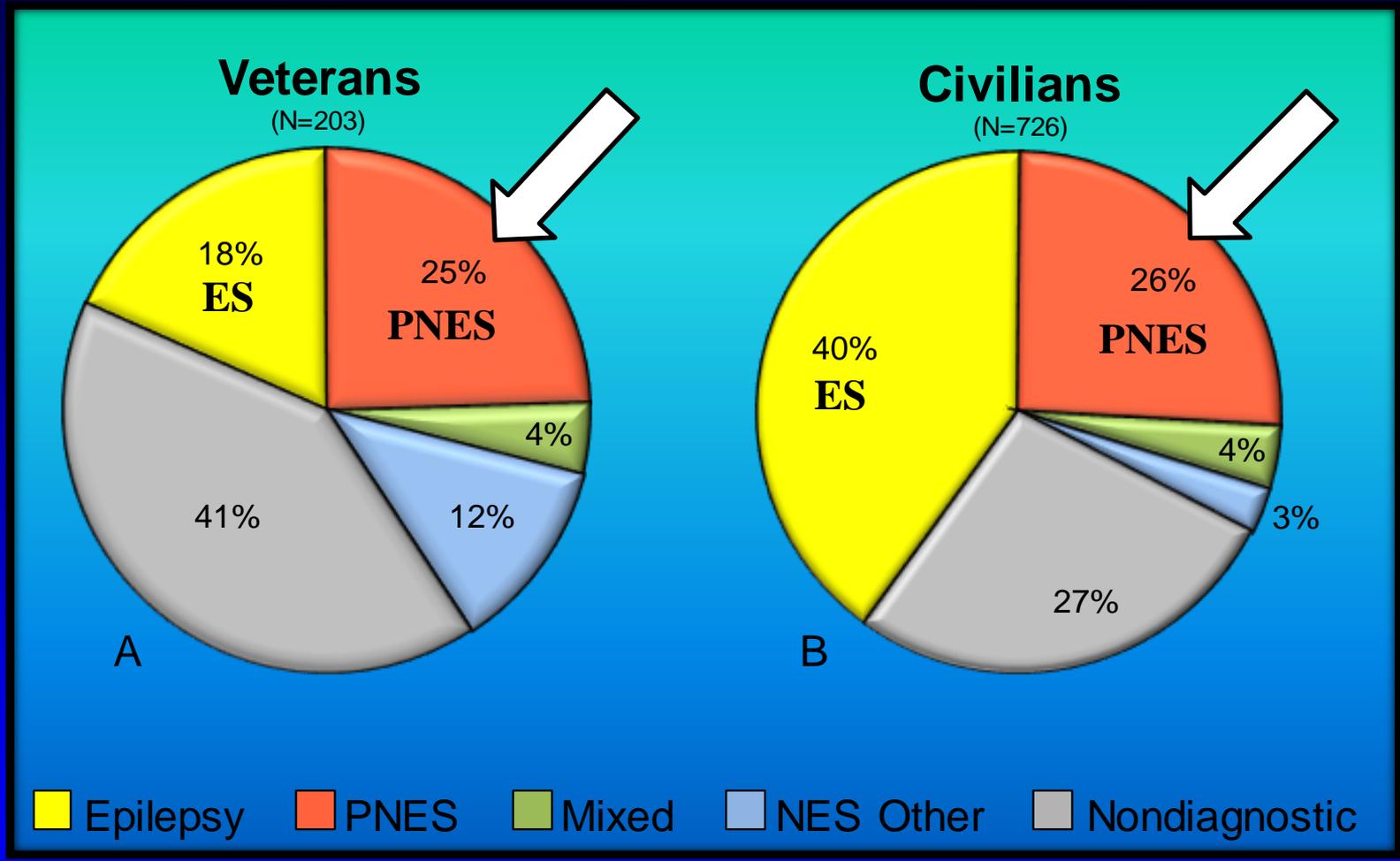
- ◆ **Are PNES more common in veterans than civilians?**
 - ◆ **Referred for inpatient epilepsy monitoring**
- ◆ **Is there a longer delay to diagnosis of PNES in veterans as compared to civilians?**
- ◆ **Do veterans with PNES have greater exposure to anti-epileptic drugs as compared to civilians?**

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

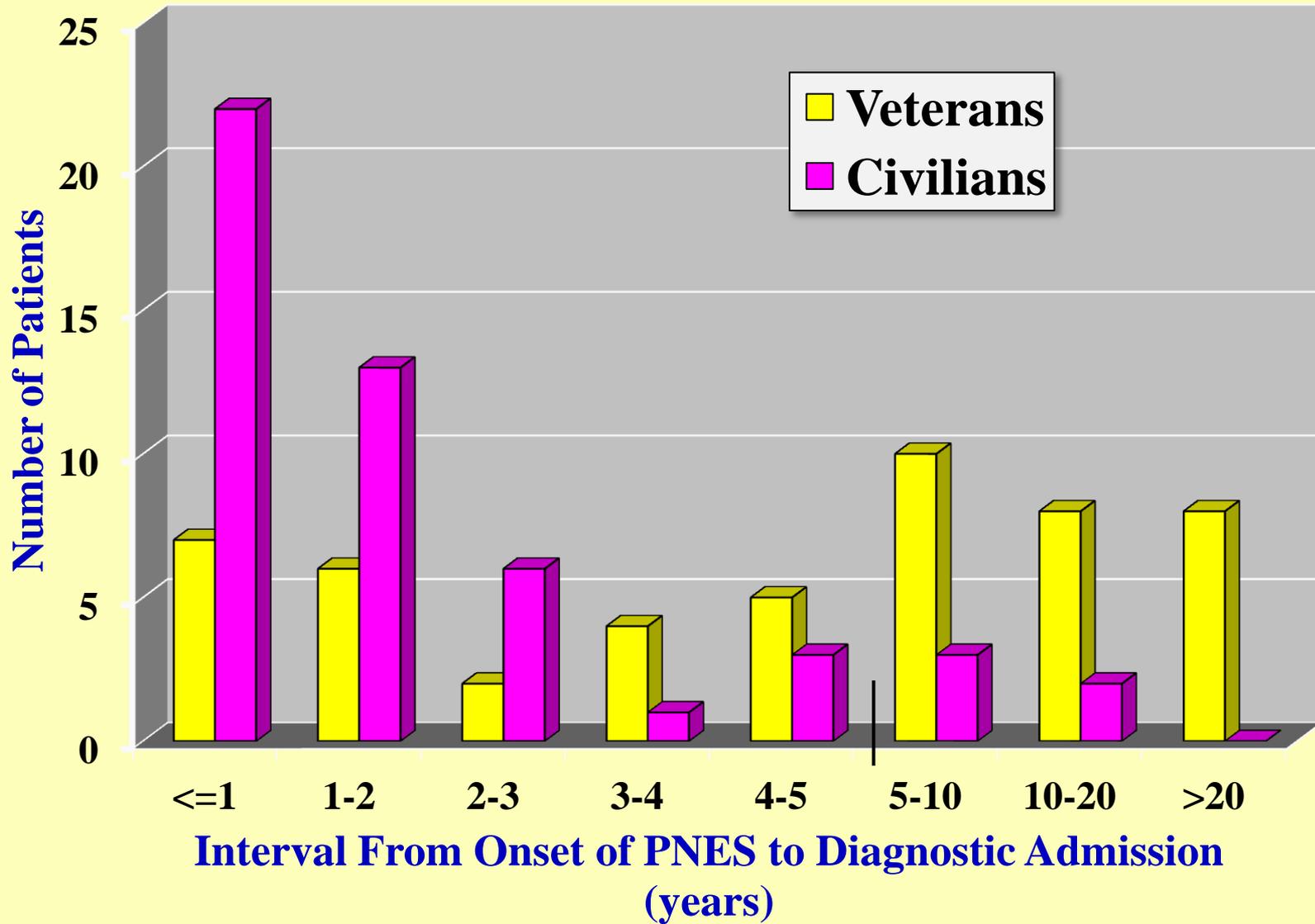


PNES – Psychogenic Non-epileptic Seizures
ES – Epileptic Seizures

Psychogenic Seizures Veterans Compared to Civilians

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

F – Fishers Exact test W – Wilcoxon test



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?

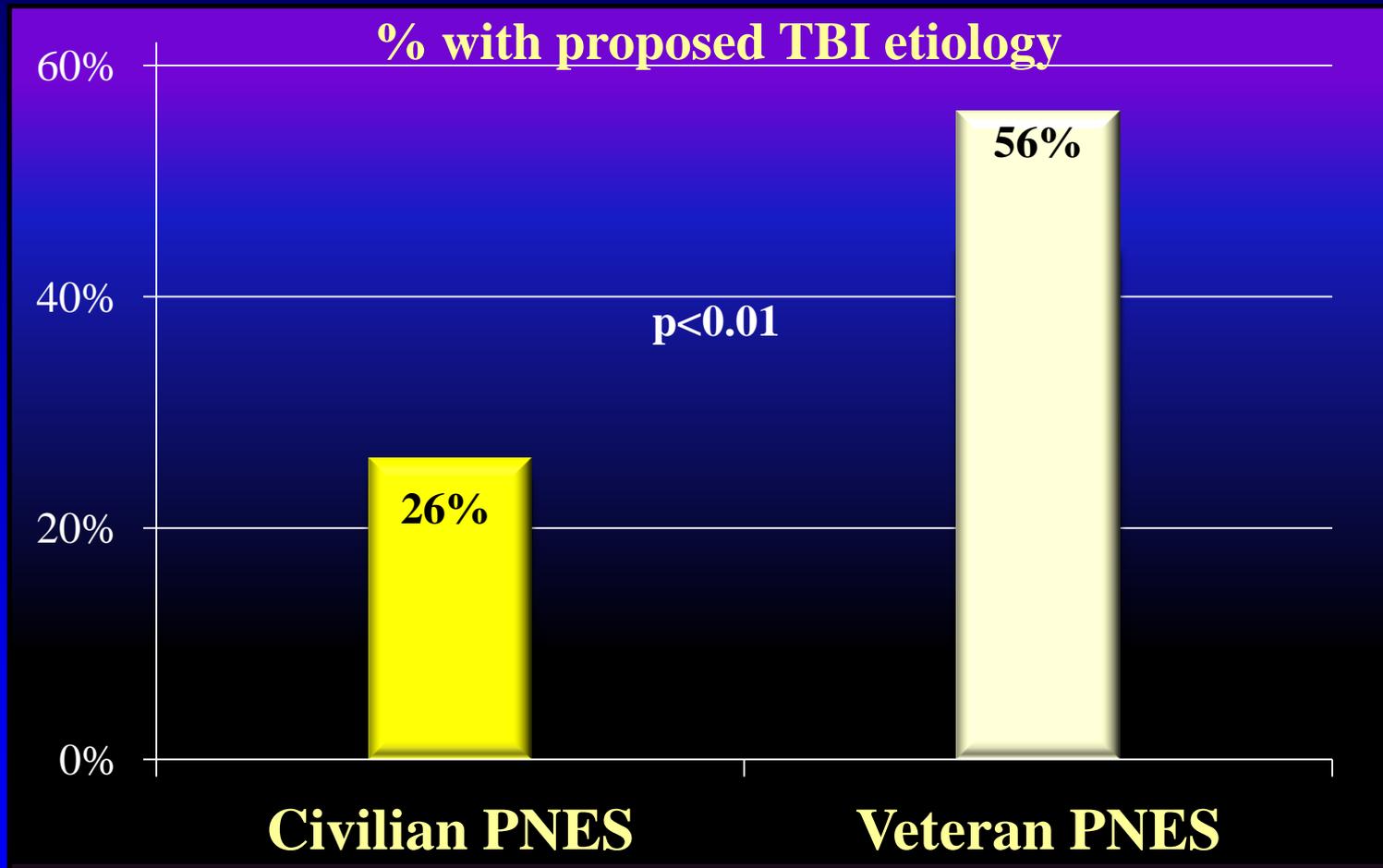
– 50% from states with no VA EMUs

– Epilepsy Centers of Excellence

» Acceptance of seizures related to TBI?

– Primary provider?

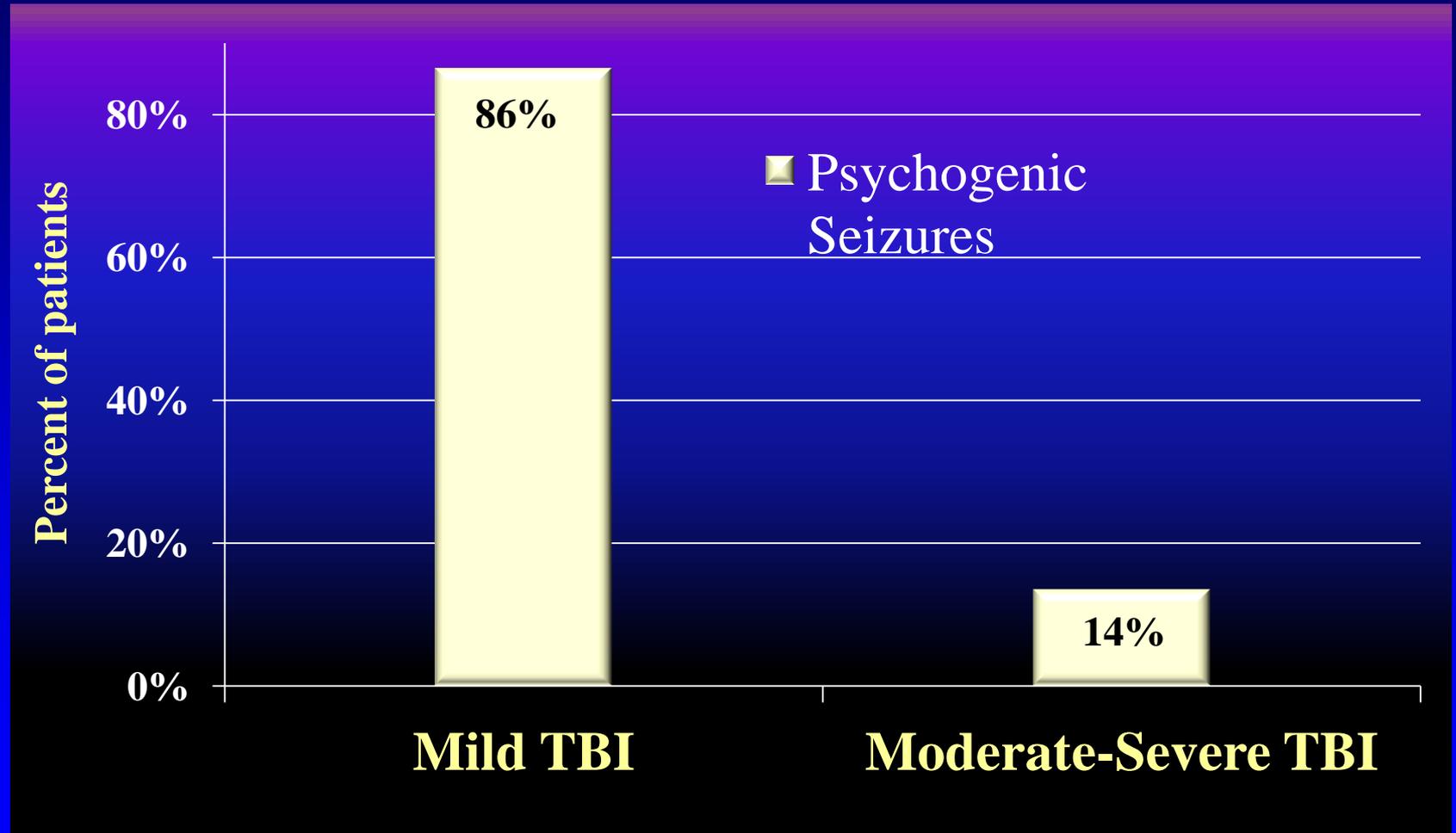
TBI as Proposed Cause of PNES Civilians vs. Veterans



For veterans - 50% of TBIs were military TBIs

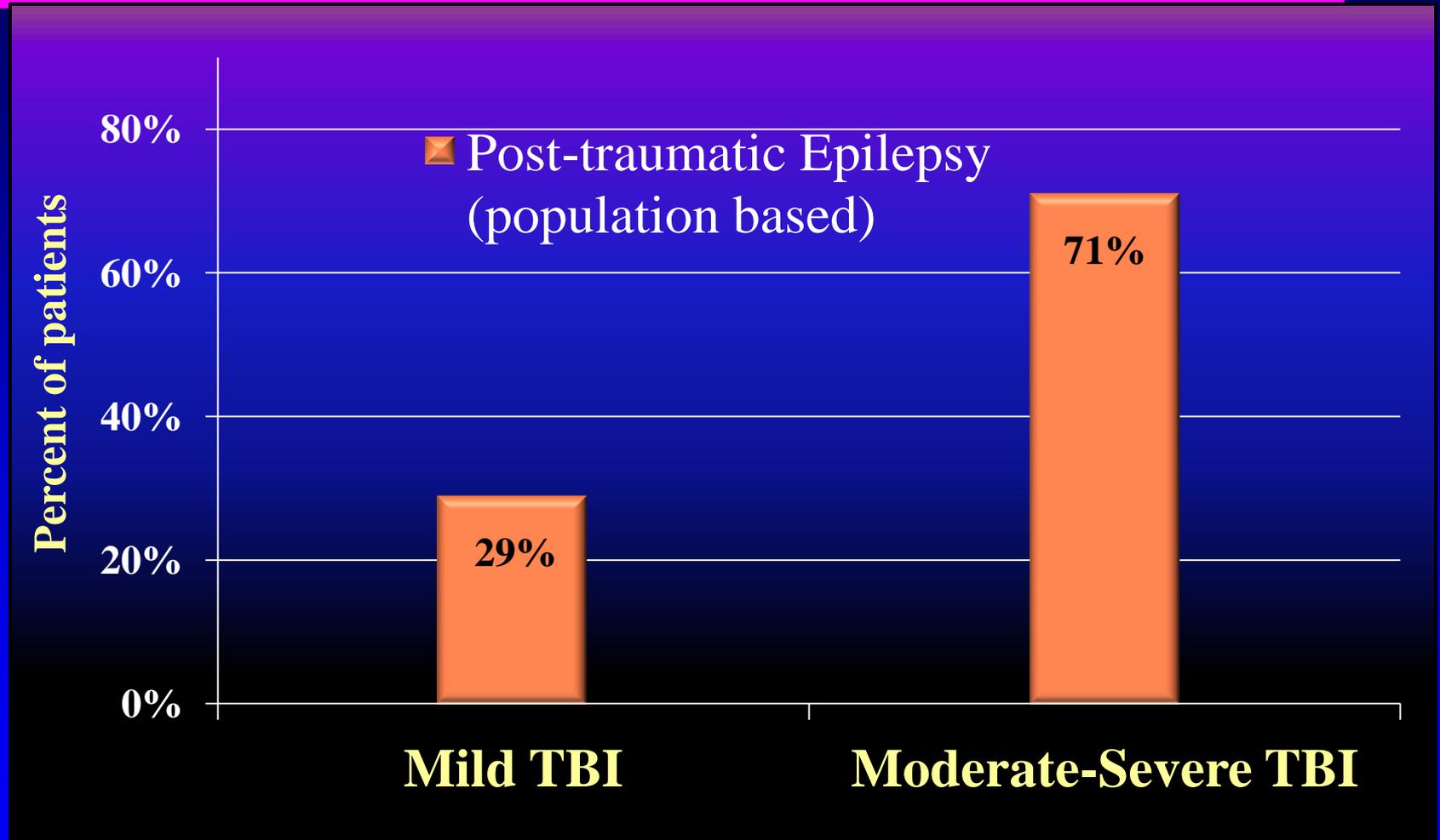
Veterans with PNES

TBI Severity

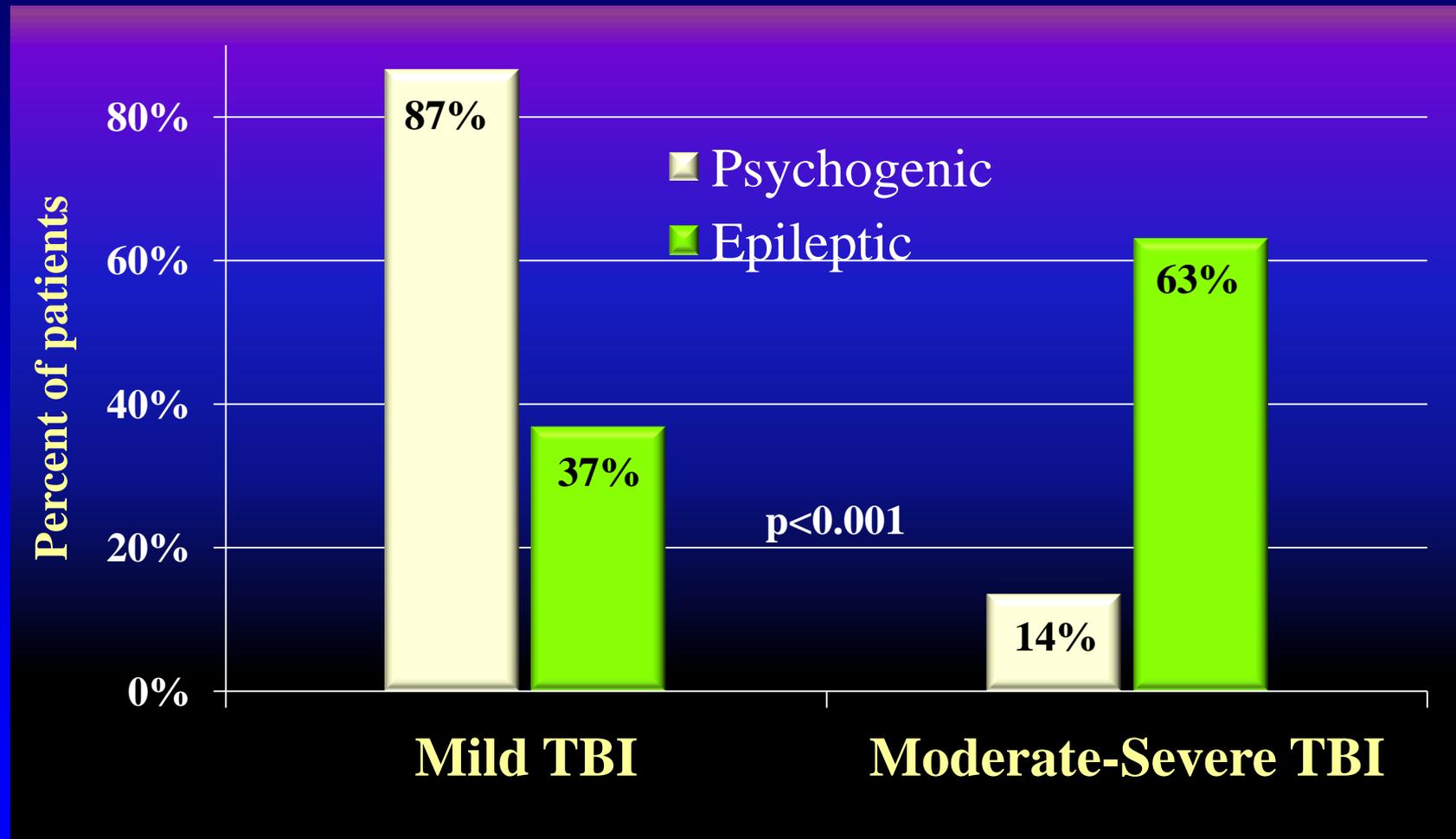


Mild TBI = Concussions or brief LOC (<30 min.)

Post-traumatic Epilepsy (civilians) TBI Severity



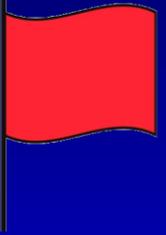
Veterans with PNES vs. Epilepsy TBI Severity



TBI Severity and Seizures

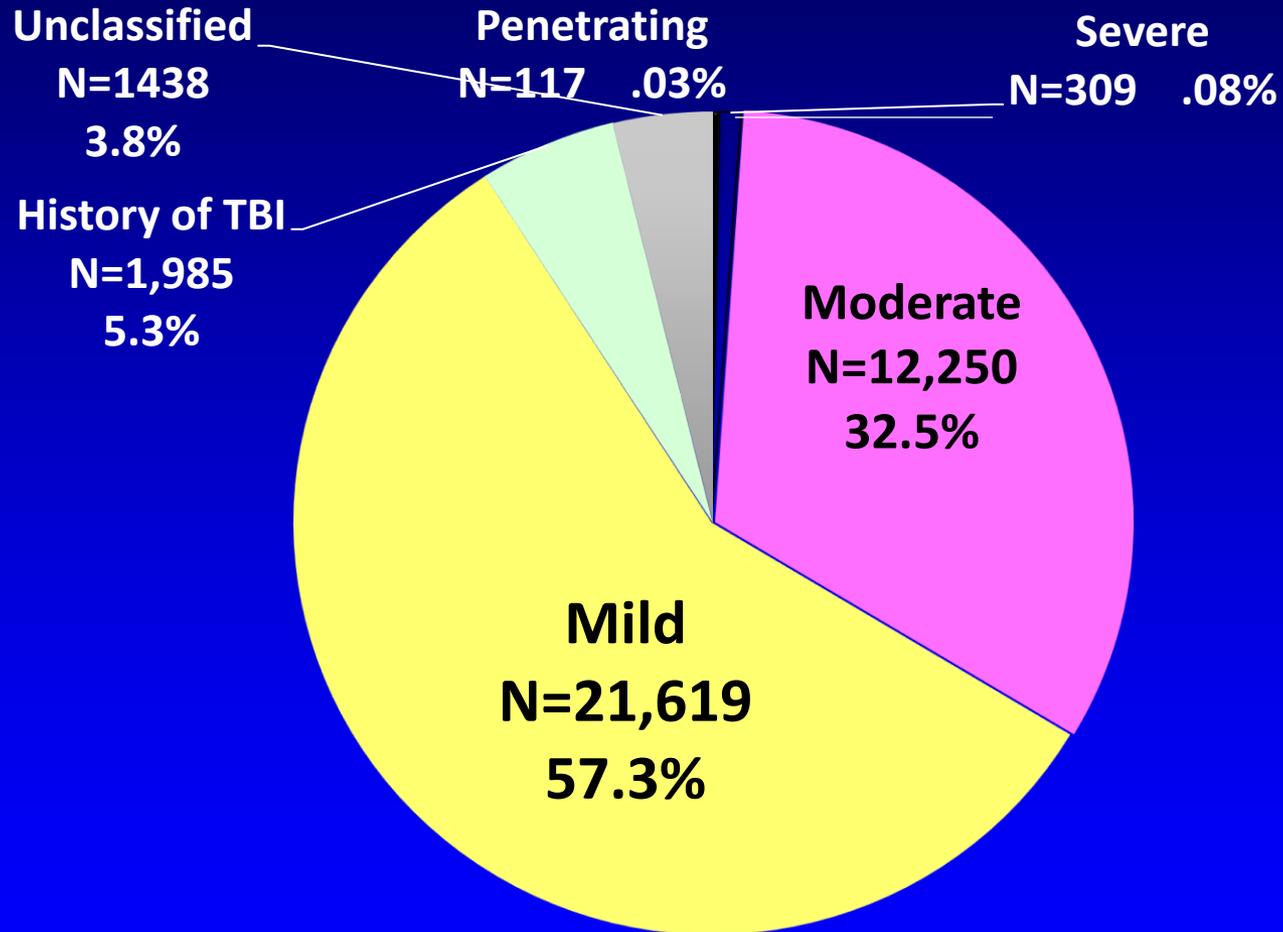
U.S. Veterans

◆ 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



Pugh, MJ; with permission

Psychogenic Non-epileptic Seizures (PNES), and Veterans

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

PNES in Veterans

◆ **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?

¹Bowman and Markand, Am J Psychiatry 1996

²Rosenberg et al, Epilepsia 2000

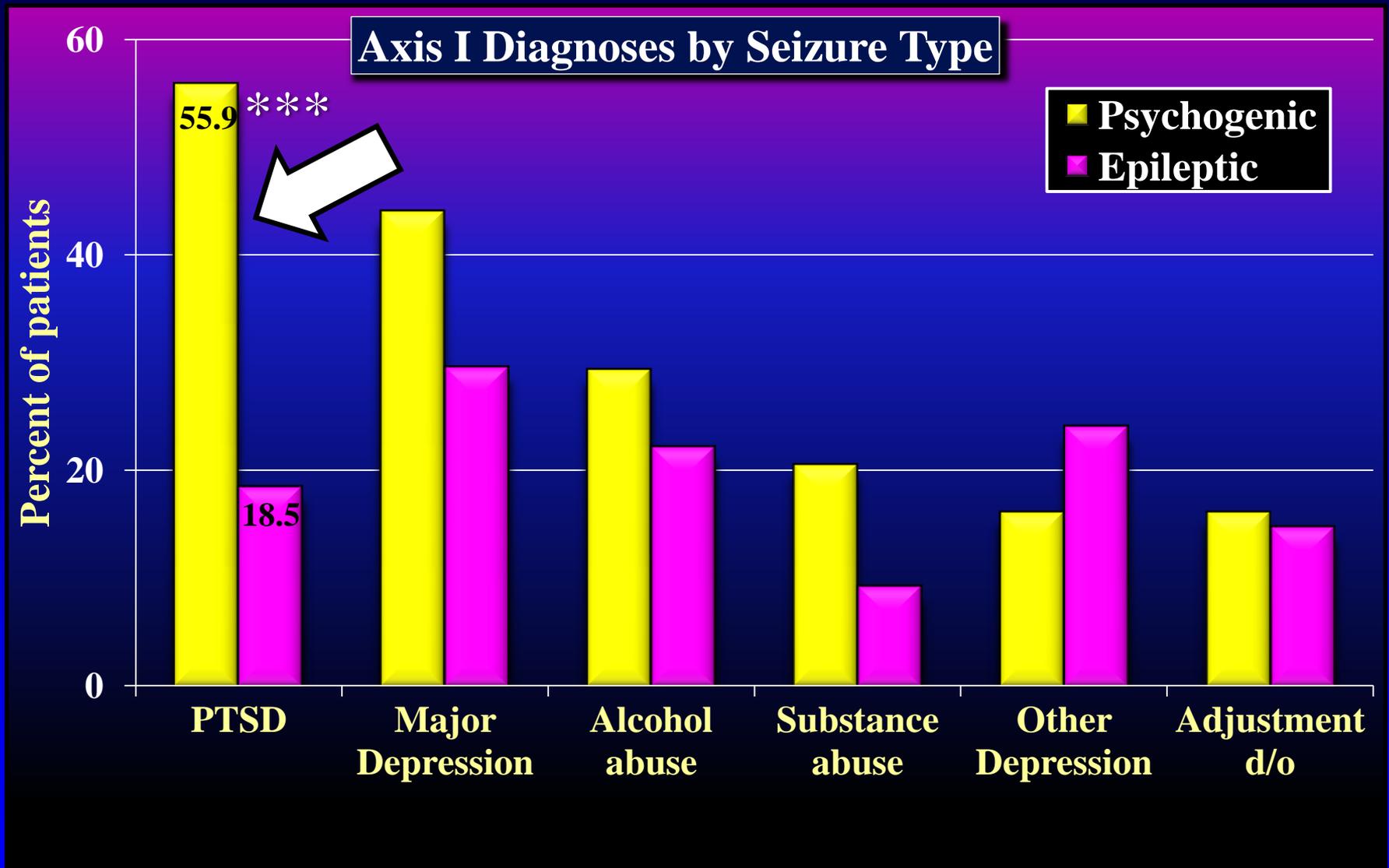
³Hoge et al, NEJM 2008

⁴Pietrzak et al, J Nerv Ment Dis 2009

⁵Zatzick et al, Arch Gen Psychiatry 2010

Veterans with PNES vs. ES Mental Health Evaluations

	Psychogenic	Epileptic	p
N	68	54	
Age at Admission	48.4	49.9	NS
Any Axis 1 Diagnosis (%)	77.9	66.7	NS
Number of Axis 1 Diagnoses	3 (0-8)	2(0-6)	0.01
Any Axis 2 Diagnosis (%)	27.9	16.7	NS

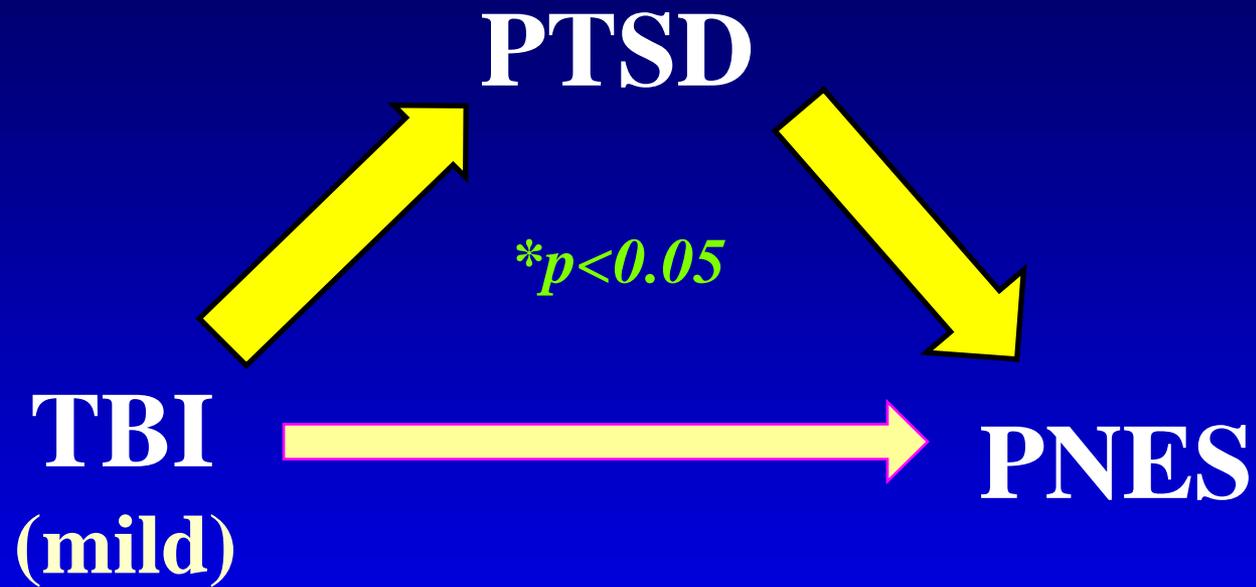


*** $p < 0.001$

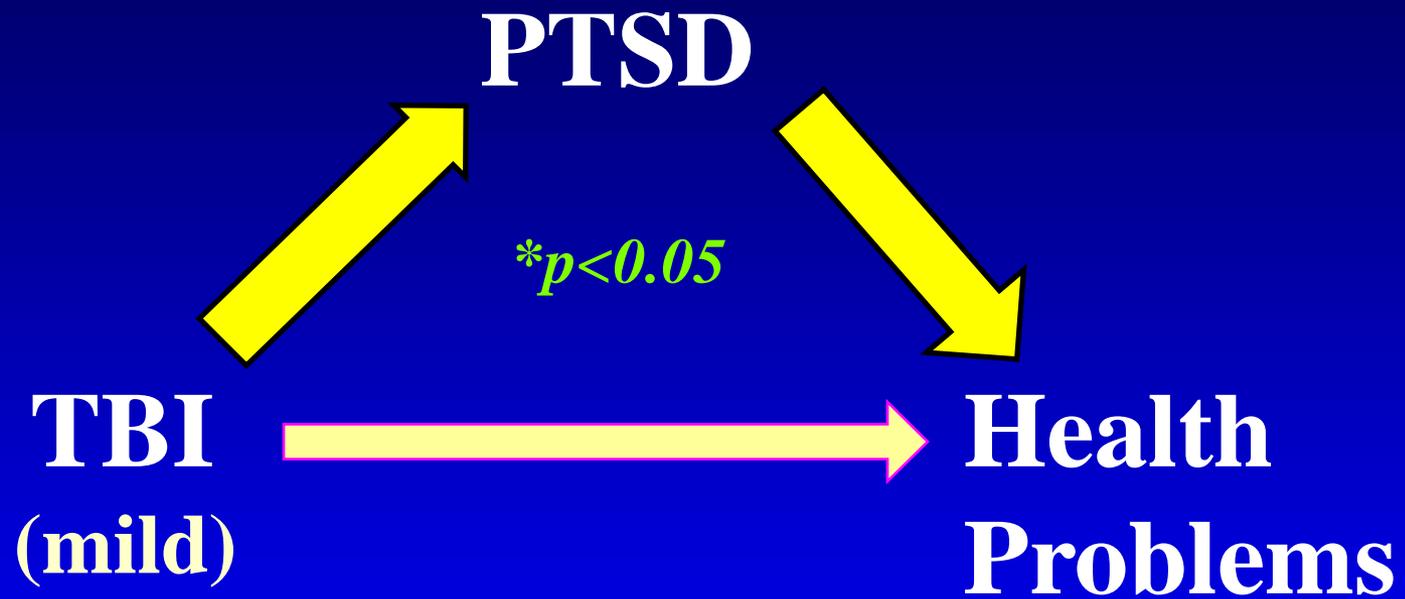
Veterans with PNES vs. Epilepsy Multivariate Analysis

Psychiatric	Historical
Total Axis I diagnoses	Age at admission
Any Axis II diagnosis	Sex
PTSD	Duration of seizures
Major depression	
Other depression	
Alcohol abuse	
Substance abuse	
Adjustment d/o	
Bipolar d/o	
Any Psychiatric Admit	
Number of Psychiatric Admits	

<i>Variables</i>	<i>Odds Ratio</i>	<i>p</i>
PTSD	5.7	<0.001



***Mediation analysis**



***Mediation analysis**

Hoge et al, NEJM; 2008

Pietrzak et al, J Nerv Ment Dis; 2009

Psychogenic Seizures - Treatment

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

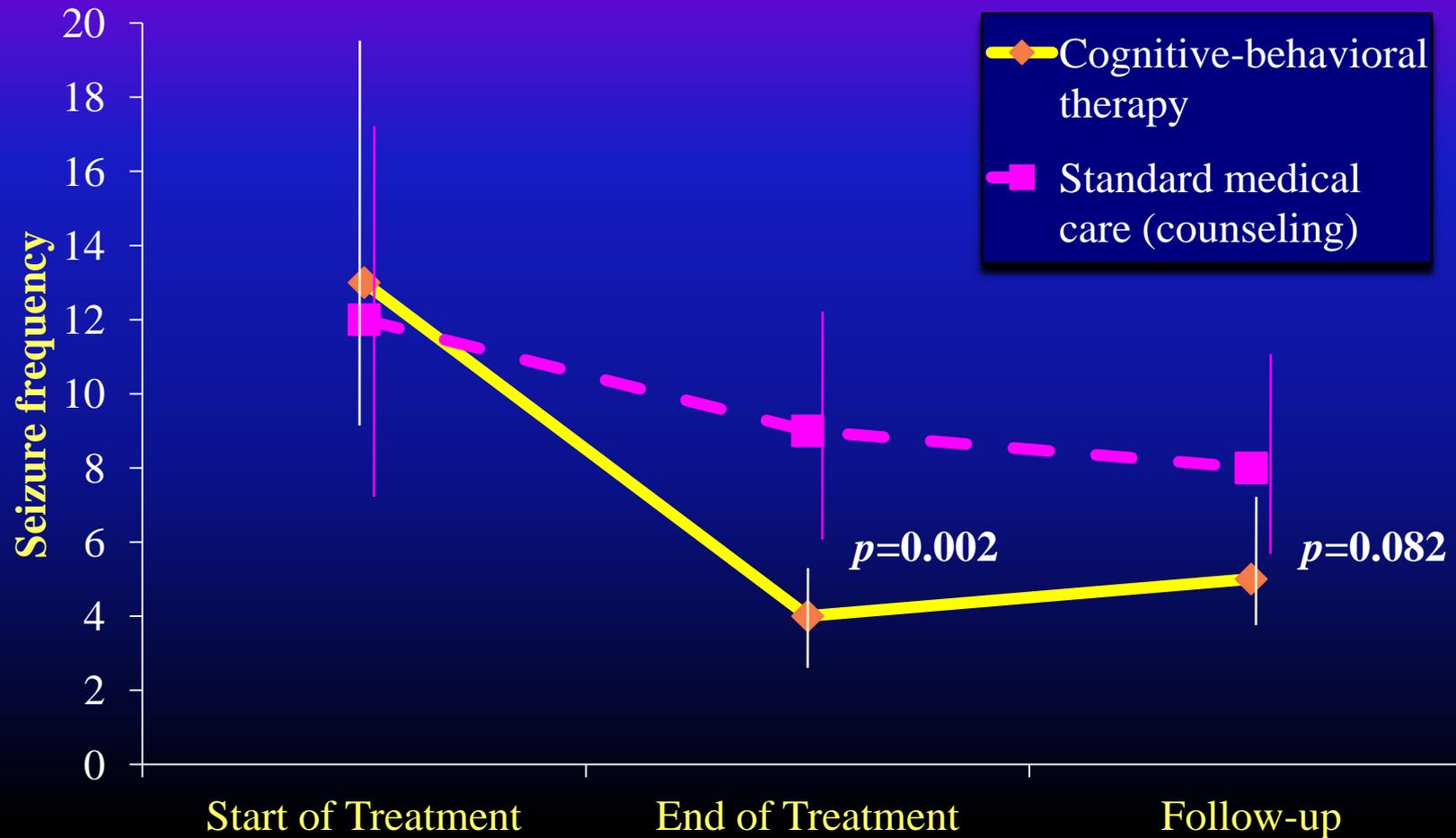
-Cochrane Review 2005

-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)



3 month treatment; 6 month follow-up

Goldstein et al, Neurology, 2010

Psychogenic Seizures

Outcome (diagnosis matters!)

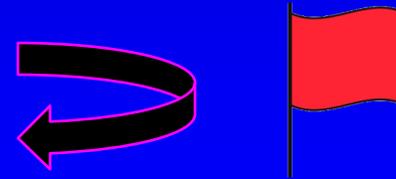
Author	N/ % f/u	f/u interval; months (SD)	Seizure free (interval)	AED free
Selwa, 2000	85/67	19-48	40% (?)#	68%
Kanner, 1999	45/100	6-26	29% (6 months)	?
Walczak, 1995	72/71	12-27	35% (6 months)#	53%
Ettinger, 1999	76/74	18 (10)	52% (?)	59%
Reuber, 2003	210/47	49 (3)	56% (?)#	48%
McKenzie, 2010	260/72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

#Shorter duration of illness at diagnosis correlated with better outcome

Psychogenic Seizures in Veterans

Key Points

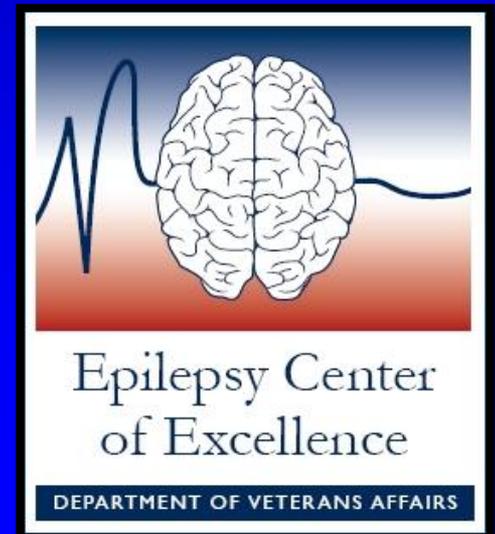
- ◆ **PNES are common in veterans**
 - » ~25% of EMU admissions (similar to civilians)
 - » ? rate in outpatients
- ◆ **Delayed diagnosis in veterans vs. civilians**
 - » Increased AED usage
 - » Prolonged disability; cost
 - » Worse prognosis (?)
- ◆ **Risk factors**
 - » Mild TBI as etiology
 - » History of PTSD



Portland VAMC

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