Psychiatric Comorbidity in Children & Adolescents with Epilepsy

David Graeber, MD

April 16, 2014

Epilepsy - Definitions

Seizure: Disturbances in the electrical activity of the brain. May manifest with motor (muscle activity) but not always

Epilepsy: Two or more unprovoked seizures separated by at least 24 hours

Epilepsy includes a spectrum of disorders

- Many different types of seizures
- Many causes

Seizure Classification

1. Partial Seizures:

- Simple partial (focal, local)
- Complex Partial (impaired consciousness, simple evolving to impaired consciousness)
- Partial evolving to generalized seizures

2. Generalized Seizures

- Absence
- Myoclonic
- Tonic-Clonic
- Atonic

Seizure Types

- A seizure is determined by the patient's behavior and EEG pattern during the ictal event

- An epileptic syndrome is defined by:

  seizure type(s)

  natural history

  EEG (ictal and interictal)

  Response to treatment

  Etiology

Epilepsy Epidemiology

- Occurs in 1% of the population
- 3rd most common neurologic syndrome in the US behind Alzheimer disease and stroke (4th if migraine is included)
- Equal to the combined prevalence of cerebral palsy, multiple sclerosis and Parkinson disease

Epilepsy Epidemiology

- Most common childhood neurologic disorder
- Affects .5% to 1% of youth < 16 years of age
- More than 326,000 children <15 have epilepsy
- 90,000 of these have poorly controlled seizures
- Behavioral and cognitive functioning also negatively affected in many youth in addition to seizures

Psychiatric Comorbidity in Epilepsy

2007 survey: 977 of 91,605 reported epilepsy/seizures

Children with epilepsy/seizures

- Depression (8 vs 2%)
- Anxiety (17 vs 3%)
- ADHD (23 vs 6%)
- Conduct problems (16 vs 3%)
- DD (51 vs 3%)
- ASD (16 VS 1%)
- Headache (14 vs 5%)
- Epilepsy/seizure group poorer education, social outcome

Russ, Larson, Halfon: Pediatrics, 2012

Psychiatric Comorbidity in Epilepsy

- Frequent finding: lifetime prevalence of depression and anxiety disorders 30%-35%
- Associated with worse response to AEDs and surgery and worse medication tolerance
- Affective disorders increase the completed suicide risk by 32-fold

Bateman, et al, Ep Currents, 2012

Psychosocial Outcomes in Epilepsy

	CAE patients (%)	JRA patients (%)	Odds ratio (CI)
No high school grad	36	14	3.7 (1.3-10.4)
Special classes	16	3	5.7 (1.1-40.5)
Repeated a grade before diagnosis	20	3	7.6 (1.4-52.8)
Ever considered a behavior problem	41	10	6.4 (2.2-19.9)
Unplanned pregnancy	34	3	19.3 (2.3-426.1)
Psychiatric or emotional problems	54	31	2.6 (1.1-5.9)
Unskilled laborer	53	16	5.9 (1.6-24.0)
Not employed in area of training	50	14	5.7 (1.2-33.9)

Wirrell et al, 1997.

Psychiatric Comorbidity in Epilepsy

Most common psychiatric conditions co-occurring with epilepsy are:

- ADHD
- Depressive Disorders
- Anxiety Disorders
- Psychosis

Psychiatric Comorbidity in Epilepsy - ADHD

Epilepsy may affect:

- Attentional problems
- Hyperactivity
- Impulse control problem

Attentional problems affected by:

- Epileptiform activity
- Medication effects
- Repeated seizures

Comorbidity in Epilepsy – ADHD

- ADHD appears to be prevalent in children newly diagnosed with epilepsy and in those with chronic epilepsy
- Attentional problems are often reported prior to onset of seizures
- ADHD rate in children with epilepsy range from 15% to 40%
- ADHD rate in children in the general population range from 5% to 7%

Psychiatric Comorbidity in Epilepsy – ADHD

- ADHD in epilepsy more likely to be the inattentive subtype
- Most common subtype in general population is combined type
- ADHD in epilepsy effects boys and girls equally
- ADHD in general population is 4 – 5X more likely in boys

Psychiatric Comorbidity in Epilepsy – ADHD

Medication issues:

Antiepileptic medications associated with:

- Attention
- Cognitive slowing
- Difficulty concentrating

Psychiatric Comorbidity in Epilepsy – ADHD

Medication issues:

- Stimulant warning:

  Seizure disorder: Use with caution in patients with a history of seizure disorder; may lower seizure threshold leading to new onset or breakthrough seizure activity.

- Has led to significant reluctance to treat ADHD in patients with epilepsy with stimulants

Psychiatric Comorbidity in Epilepsy – ADHD

Medication issues:

- Stimulant warning:

  Seizure disorder: Use with caution in patients with a history of seizure disorder; may lower seizure threshold leading to new onset or breakthrough seizure activity.

- Has led to significant reluctance to treat ADHD in patients with epilepsy with stimulants

Psychiatric Comorbidity in Epilepsy – ADHD

Only a few open trials and 2 small placebo controlled studies of stimulants in children with epilepsy and use of stimulants.

Randomized Clinical Trial:

N = 10; Ages 6 to 10 years of age

On single Antiepileptic medication – well controlled

.6 mg/kg dose of methylphenidate

Statistical improvement of ADHD on multiple measures

No seizures; no change in EEG's

Am J Dis Child. 1989

Psychiatric Comorbidity in Epilepsy - Depression

- Depression under-recognized in youth with epilepsy
- Depression prevalence in youth with epilepsy is up to 30% (11% in General Population)
- Some mistakenly view depression as an expected result of the negative impact of seizures on youth
- Depression may more negatively affect quality of life more than epilepsy

Psychiatric Comorbidity in Epilepsy – Depression

- Depression not linked to seizure type or severity in youth
- Associated with negative attitude toward epilepsy and problems in family
- Depression is a risk factor for developing epilepsy
- Icelandic study showed children and adults 1.7X more likely to have pre-seizure depression

Psychiatric Comorbidity in Epilepsy – Depression

- No RCT of antidepressants in depressed youth with epilepsy – excluded from studies
- SSRI's and CBT recommended
- Drug-Drug interactions with seizure medications not uncommon

Psychiatric Comorbidity in Epilepsy - Anxiety

- Anxiety disorders more common in epilepsy than general population
- Youth with complex partial or absence seizures more likely to have anxiety
- Need to distinguish from ictal fear – phenomena associated with seizure activity in some youth

Psychiatric Comorbidity in Epilepsy – Anxiety

Treatment recommendations:

- SSRI
- Buspirone
- CBT

Psychiatric Comorbidity in Epilepsy - Psychosis

- Psychosis is relatively rare in youth with epilepsy

- Some reports of illogical thinking and hallucinations without apathy/negative affect in youth with chronic complex partial seizures

Psychiatric Comorbidity in Epilepsy – Psychosis

Ictal and postictal psychosis:

- May occur after prolonged or cluster of seizures
- Psychotic symptoms stereotyped
- Youth often cannot remember hallucination content
- Associated with some antiepileptic medications

Psychogenic Non-Epileptic Seizures

- Historically labeled hysteria; more recently pseudoseizures
- Current Terminology: Psychogenic Non-Epileptic Seizures
- Associated with depression, anxiety, histories of trauma and PTSD
- Associated with seizure disorder as well

Dickinson,Looper: Epilepsia, 2012

Paroxysmal Non-Epileptic Events Children & Adolescents

PNES in 15.2% of those monitored

- 2 months to 5 years: 26 patients

  Stereotypical movements, hypnic jerks, parasomnias, Sandifer Syndrome (Torticollis and GER)

- 5-12 years: 61 patients

  Conversion disorder (psychogenic seizures), inattention/daydreaming, stereotyped movements, hypnic jerks, paroxysmal movements (15 with concomitant epilepsy)

- 12-18 years: 48 patients

  Conversion disorder (40/83%; 9 concomitant epilepsy)

Kotegal, Pediatrics, 2002

Epilepsy, Anti-Epileptic Drugs and Suicidality (FDA Alert 2008)

- AEDs: Suicidal thoughts/behavior risk: 0.43 vs. 0.22 (placebo)
  Estimated 2.1/1000 more patients on AEDs vs. placebo
  Not specific to single drug/class

- Recommendations: Class warning.
  Balance risk for suicidality with clinical need for AED
  Be aware of possibility of emergence or worsening of depression, suicidality, or unusual changes in behavior
  Inform patients, their families, and caregivers of the potential risk.

Epilepsy, Anti-Epileptic Drugs and Suicidality (FDA Alert 2008)

- Symptoms such as anxiety, agitation, hostility, mania and hypomania may be precursors to emerging suicidality.
- Suicide rate increased in epilepsy
- Suicide rate increased in adolescents

Epilepsy and Suicidality

- History of attempt strongest predictor
- Comorbid psychiatric disorders increased risk 14x
  Mood – 32x
  Anxiety – 12x
- Risk greatest in the initial 6-months following diagnosis of epilepsy

Kanner, 2009