Outpatient EEG for the Diagnosis of Epilepsy

December 2, 2011

Elson L. So, MD
Professor of Neurology
EEG & Epilepsy
Mayo Clinic
Rochester, MN
Disclosures

• Speakers Bureau – none

• Industry consultantship – none

• Non-FDA labeled drug use – none

• Intellectual Property – *Epilepsy Treatment Planning Software*, no financial proceeds

• Editorial Boards
  – Epilepsia
  – Epilepsy Research
  – Journal of Clinical Neurophysiology
Objectives

• Recognize the role and limitations of the outpatient EEG in epilepsy diagnosis and management

• Avoid the pitfalls of outpatient EEG

• Apply measures to increase yield of the outpatient EEG in epilepsy practice
EEG Issues in Sandy

• How useful is a “routine” outpatient EEG?

• How can we increase the yield of outpatient EEGs?
EEG Issues in Sandy

- How useful is a standard outpatient EEG?
- How can we increase the yield of outpatient EEGs?
Role of Interictal EEG in Epilepsy Diagnosis

Clinical impression of the probability of epilepsy (%)

Probability of epilepsy if EEG contains epileptiform activity (%)

Goodin, 1984
Role of Interictal EEG in Epilepsy Diagnosis

Goodin, 1984

Clinical impression of the probability of epilepsy (%) vs. Probability of epilepsy if EEG contains epileptiform activity (%)
Role of Interictal EEG in Epilepsy Diagnosis

Clinical impression of the probability of epilepsy (%)

Probability of epilepsy if EEG contains epileptiform activity (%)

Goodin, 1984
Role of Interictal EEG in Epilepsy Diagnosis

Probability of epilepsy if EEG contains epileptiform activity (%) vs. Clinical impression of the probability of epilepsy (%)

- Probability of epilepsy if EEG contains epileptiform activity (%)
- Clinical impression of the probability of epilepsy (%)

Goodin, 1984
Limitation of the Standard Outpatient EEG

Rates of interictal epileptiform discharges in epilepsy patients vary between \( \approx 30\% \) to 70\%.

Gilbert, 2002; Ajmone-Marsan, 1970; Salinsky, 1987
EEG Issues in Sandy

• How useful is a standard outpatient EEG?

• How can we increase the yield of outpatient EEGs?
You, the EEG reader
Meta-analysis of EEG test performance shows wide variation among studies

Donald L. Gilbert, MD; Gopalan Sethuraman, PhD; Uma Kotagal, MBBS; and C. Ralph Buncher, ScD

Abstract—Background: EEG results are used for counseling patients with seizures about prognosis and deciding on medications. Published sensitivities of interictal EEG vary widely. Objective: To account for variation in test characteristics between studies. Methods: Meta-analysis. Medline search, 1970 to 2000, of English language studies. Standard methods for meta-analysis of diagnostic test performance were used to determine the ability of EEG results to distinguish between patients who will and will not have seizures. Using linear regression, the authors assessed the influence of readers’ thresholds for classifying the EEG as positive, sample probability of seizure, percent of subjects with prior neurologic impairment, percent treated, and years followed. Results: Twenty-five studies involving 4,912 EEG met inclusion criteria. Specificity (range 0.13 to 0.99) and sensitivity (range 0.20 to 0.91) of epileptiform EEG interpretations varied widely and were heterogeneous by $\chi^2$ analysis ($p < 0.001$ for each). Diagnostic accuracy of EEG and the thresholds for classifying EEG as positive varied widely. In the multivariate model, differences in readers’ thresholds accounted for 37% of the variance in EEG diagnostic accuracy, and no other reported factors were significant. Conclusion: This analysis suggests that there is wide interreader variation in sensitivity and specificity of EEG interpretations, and that this variation influences the ability of EEG to discriminate between those who will and will not have seizure recurrences. In clinical practice, interpreting the degree to which a positive EEG result predicts increased seizure risk in an individual patient is difficult. Interpreting EEG with higher specificity yields more accurate predictions.

NEUROLOGY 2002;60:564–570
Meta-Analysis of EEG Test Performance Shows Wide Variation Among Studies

Differences in readers’ threshold was the only significant factor

Gilbert, 2002
Epileptiform

Diagnostic accuracy = 0.75 + -0.25
$r^2 = 0.37$

Gilbert, 2002
Wicket Waves
The Most Frequent Misleading Mimicker

Krauss, 2005; Benbadis, 2008
Meta-Analysis of EEG Test Performance Shows Wide Variation Among Studies

• Diagnostic accuracy of EEG and thresholds for classifying EEG as positive varied widely.

• Differences in readers’ threshold was the only significant factor (accounting for 37% of variance in the diagnostic accuracy).

• Interpreting EEG with higher specificity yields more accurate predictions.

Gilbert, 2002
Other Benign Variants that Mislead and Reduce Specificity

Westmoreland, 2003
Benign Sporadic Sleep Spikes (BSSS)
Referential Montage and Increased Time Scale

<table>
<thead>
<tr>
<th>Channel 1</th>
<th>Channel 2</th>
<th>Channel 3</th>
<th>Channel 4</th>
<th>Channel 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fs1 - F7</td>
<td>F7 - T7</td>
<td>T7 - P7</td>
<td>P7 - O1</td>
<td>P1 - TP12</td>
</tr>
<tr>
<td>F1 - FP12</td>
<td>F7 - TP12</td>
<td>T7 - TP12</td>
<td>P7 - TP12</td>
<td>P1 - TP12</td>
</tr>
</tbody>
</table>

\[ \wedge \]
6-Hertz Spike and Wave Bursts
14- and 6-Hertz Positive Bursts

M Age: 12 yrs

F7-A1
F8-A2
T7-A1
T8-A2
P7-A1
P8-A2
Lateral Rectus Muscle Spike
Mimickers of Epileptiform Discharges

Physiologic cerebral activities

- Benign variants
- Drowsiness and sleep activities
  - Hypnagogic hypersynchrony, POSTS, V waves especially in children
  - Quiet sleep sharp activities in neonates
- Neonatal EEGs – eg, frontal sharp transients

Artifacts

- Physiologic – eg, EKG, muscle
- Non-physiologic – eg, electrical, mechanical
Sleep Deprivation
Increase Yield of Outpatient EEG?
# Yield of Initial EEG and Repeat Sleep-Deprived EEG

<table>
<thead>
<tr>
<th>Clinically diagnosed epilepsy syndrome</th>
<th>Initial EEG epileptiform</th>
<th>Sleep-deprived EEG epileptiform</th>
<th>Total epileptiform</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized</td>
<td>17/25 (68%)</td>
<td>6/8 (75%)</td>
<td>23/25 (92%)</td>
</tr>
<tr>
<td>Partial</td>
<td>51/116 (44%)</td>
<td>19/60 (32%)</td>
<td>70/116 (60%)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>61/159 (38%)</td>
<td>30/90 (33%)</td>
<td>91/159 (57%)</td>
</tr>
<tr>
<td>Total</td>
<td>129/300 (43%)</td>
<td>55/158 (35%)</td>
<td>184/300 (61%)</td>
</tr>
</tbody>
</table>

King et al, 1998
(Excludes many acute seizure patients)
Pharmacologic Sedation
Increase Yield of Outpatient EEG?
## Sleep Deprivation (SD) + Chloral Hydrate (CH) versus Sleep Deprivation Only

<table>
<thead>
<tr>
<th></th>
<th>SD + CH (%)</th>
<th>SD only (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep recorded</td>
<td>85</td>
<td>86</td>
<td>NS</td>
</tr>
<tr>
<td>Awake epileptiform</td>
<td>27</td>
<td>35</td>
<td>NS</td>
</tr>
<tr>
<td>Sleep epileptiform</td>
<td>18</td>
<td>17</td>
<td>NS</td>
</tr>
</tbody>
</table>

Britton, 2010
The EEG record
Proportion of Children Attaining Sleep During EEG Procedure

IPS = intermittent photic stimulation; HV = hyperventilation

Kaleyias, 2006

Group I
IPS
n=48

Group II
HV
n=48

Group III
HV and IPS
n=48

Start
End

IPS
HV
IPS
HV and IPS

IPS = intermittent photic stimulation; HV = hyperventilation
Kaleyias, 2006
Duration of EEG Recording
How Long does it Need to be?
Cumulative Probability of 1st Epileptiform Discharge Appearing in 20 Patients in Whom Discharges were Detected

So, 1994
Timing of EEG Recording
Does it Really Matter?
EEG After Presenting Seizure

Timing of recording

With epileptiform discharge (%)

<table>
<thead>
<tr>
<th>Timing of recording</th>
<th>With epileptiform discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;24 hours</td>
<td>80/156 (51%)</td>
</tr>
<tr>
<td>&gt;24 hours</td>
<td>49/144 (34%)</td>
</tr>
</tbody>
</table>

95% CI for difference in proportion = 6-28%

Excludes acute seizures, but includes patients with previous seizures

King, 1998
Before seizure began
7 minutes after seizure ended
Seizures are often followed by long-lasting increases in spiking.

Increases in spiking before seizures have not been clearly documented.

Decreases in antiepileptic medication do not result directly in increased spiking.

Gotman, 1991
How about Ambulatory EEG?
Yield of Ambulatory EEG

- 24 hour Ambulatory EEG versus Routine EEG in 46 patients; EEGer’s blinded to clinical information
- Epileptiform activity seen 33% of Ambulatory versus 24% of Routine EEGs
- Seizures in 15% of AEEG, none in REEG
Summary of Epilepsy Metrics

1. Document seizure type and frequency of all seizure types at each visit
2. Document etiology or epilepsy syndrome at each visit
3. **At least one EEG needs to have been done or reviewed at some point during care of the patient**
4. At least one MRI or CT of the brain needs to have been done or reviewed during the course of care of the patient (except in those with idiopathic epilepsies)
5. Counsel and inquire about antiepileptic drug side effects at each visit
6. Surgical therapy to be considered in all patients with intractable epilepsy at least once every 3 years
7. Counsel regarding epilepsy safety issues at least once a year
8. Counsel all women with epilepsy of childbearing potential about implications of epilepsy and its treatment on contraception and pregnancy at least once a year

Fountain, 2011; Britton, 2011
How About for 1st Unprovoked Seizure?
Does EEG Help in Assessing Risk of Seizure Recurrence?
Cumulative Percent of Remaining Seizure Free After 1\textsuperscript{st} Unprovoked Seizure in Children

Scotini, 2004
Rates of Seizure Recurrence in Children 2 Years After a 1st Unprovoked Seizure

Abnormal EEG alone 48%
Remote symptomatic etiology 48%
If both absent 24%
If both present 65%

Berg, 1991
• “Routine EEG as part of the diagnostic evaluation was recommended.”

• EEG was the only test with Class I evidence for usefulness

Hirtz, 2000
Recurrence After 1\textsuperscript{st} Unprovoked Seizure in Adults with Normal versus Abnormal EEG

Schreiner, 2003

Follow-up (months)

Cumulative recurrence risk

P<0.001

Abnormal EEG

Normal EEG
• “EEG should be considered as part of the routine neurodiagnostic evaluation…”

• EEG has Level B evidence
Tips for Increasing Yield of Outpatient EEG in Epilepsy

• Avoid over-reading EEGs; beware of benign variants and artifacts
• Sleep deprive patient whenever possible; no need to sedate in most cases
• Perform EEG sooner than later after an episode
• Perform hyperventilation early in the procedure in children
• Extend EEG up to 1 hour if needed
References

Ajmone Marsan C, Zivin L. Factors related to the occurrence of typical paroxysmal abnormalities in the EEG records of epileptic patients. Epilepsia 1970;11:361-81


Goodin D, Aminoff M. Does the interictal EEG have a role in the diagnosis of epilepsy? Lancet 1984;1:1837-9


References

Scotini A, Manreza M, Guerreiro M. Recurrence after a first unprovoked cryptogenic/idiopathic seizure in children: a prospective study from Sao Paulo, Brazil. Epilepsia 2004;45:166-70


Additional References:
