Risk Factors for Epilepsy

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Epilepsy Risk Factors

• Established risk factors for epilepsy
  – Traumatic brain injury
  – Stroke
  – CNS infections
  – Degenerative diseases
  – Hypoxia in infants
  – Mental retardation/Cerebral palsy/Autism

• Psychiatric disorders

• Migraine
Civilian traumatic brain injury and risk for unprovoked seizures

Standardized Incidence Ratio

Annegers et al Neurology 1980

*- n.s.
Military traumatic brain injury and risk for unprovoked seizure

The risk for TBI after epilepsy onset

• The risk for concussion is increased in people with epilepsy
  – Generalized seizures HR 6.8; 95% CI 1.1–42.6 adjusting for age, sex, disability and country
  – Myoclonic seizures and absence seizures have also been associated with concussion
  – Generally the concussions are mild

Beghi et al Epilepsia 2002; Wirrell et al, Arch Neurol 1996
## The Bidirectional relationship between stroke and epilepsy

<table>
<thead>
<tr>
<th>Direction</th>
<th>SMR</th>
<th>OR</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke ---&gt; epilepsy</td>
<td>3</td>
<td>7.6</td>
<td>Hauser et al, Epilepsia 1983</td>
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<tr>
<td>Epilepsy ---&gt; stroke</td>
<td>7.6</td>
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<td>Shinton et al, Lancet 1987</td>
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<tr>
<td>Epilepsy ---&gt; stroke</td>
<td>2.3</td>
<td></td>
<td>Cleary et al, Lancet 2004</td>
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</tbody>
</table>
Central Nervous System Infection and risk for unprovoked seizure

Dementia and risk for unprovoked seizures

Hesdorffer et al, Neurology 1996
Risk for epilepsy after hypoxia in infants > 2500 g at birth

Bergamasco et al. 1984
Mental retardation, cerebral palsy and risk for epilepsy

- 3-6 children per 1,000 live births have moderate to severe MR or CP or both
  - About 1/3 will develop epilepsy
  - Risk for epilepsy persists into adulthood

Nelson and Ellenberg 1986; Van den Berg and Yerushalamy 1969
Autism and risk for epilepsy

Tuchman and Rapin 2002
Migraine as a risk factor for unprovoked seizures and epilepsy in children


<table>
<thead>
<tr>
<th></th>
<th>Migraine</th>
<th>Migraine with aura</th>
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<tbody>
<tr>
<td>All seizures</td>
<td>3.7</td>
<td>8.2</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>3.3</td>
<td>6.9</td>
</tr>
</tbody>
</table>
ADHD and Incident Unprovoked Seizures in Icelandic children aged 3-16 years

Hesdorffer et al 2004

Odds Ratio

ADHD: 1.1-5.5
ADHD-Inattentive: 1.1-13
ADHD-Hyperactive: 0.6-5.7
ADHD-Combined: 0.3-18
Any inattention: 1.1-10

Hesdorffer et al 2004
Depression as a risk factor for epilepsy

Odds Ratio

Overall: 1.9 (1.2-2.9)
MDD: 1.7 (1.1-2.7)
Bipolar: 8 (0.9-72)
Idiop..: 1.9 (1.1-3.3)

Hesdorffer et al Annals of Neurology 2006
Premorbid Depression: FDA RCTs of SSRIs and SNRIs

- Assessment of seizure incidence for patients with MDD randomized to SSRIs, SNRIs and placebo in regulatory studies in major depression (N=70,465)
  - SSRIs and SNRIs associated with 50% lower seizure incidence relative to placebo
  - Placebo group experienced a 19-fold higher incidence of seizures than expected in the general population

Alper et al., Biol Psychiatry, 2007
Suicide attempt as a risk factor for epilepsy

324 cases with epilepsy aged 10 years and older
641 controls age and gender matched

Adjusted for:
Age, gender, SES, MDD, and cumulative alcohol consumption

Odds ratio for developing epilepsy

- Suicide attempt: 5.1 (2.2-11.5)
- Adjusted SA: 3.5 (1.5-8.6)
- MDD only: 1.5 (0.9-2.5)
- SA only: 11.1 (1.3-92)
- Both: 3.6 (1.4-9.2)

Suicide attempt: Risk for recurrent attempt and for completed suicide

  • 30% had recurrent attempt
  • 10% died by suicide, most shortly after hospital discharge

– 3,690 admitted to hospital with suicide attempt and followed for 10 years
  • 28.1% with recurrent attempt
  • 4.6% died by suicide
Conclusions

• The risk for developing epilepsy is known to be increased by TBI, stroke, CNS infections, dementia, hypoxia, MR, CP, and autism
  – For TBI, stroke and autism the relationship is bidirectional

• Migraine with aura is associated with an increased risk for epilepsy in children

• There is a bidirectional relationship between psychiatric disorders and epilepsy
  – Competed suicide in epilepsy may represent recurrence of a suicide attempt that occurred before the onset of epilepsy