Paediatric Epilepsy surgery
Who, what and when?

J Helen Cross

UCL-Institute of Child Health, Great Ormond Street Hospital for Children NHS Foundation Trust, London & Young Epilepsy, Lingfield, UK
What is epilepsy surgery?

The removal or modification of part of the brain with the aim of alleviating seizures

• Children are investigated to determine
  where the seizures are coming from
  whether it is safe to remove that area with regard to function

• Requires multidisciplinary evaluation
  part of a comprehensive epilepsy service
  children require specific consideration
Myths

• ‘surgery is a last resort’
• inevitable functional compromise
• high rate of morbidity
• improved outcome in older children
• better to wait to enable participation in decision making
Types of Surgery

- Hemispherectomy
- Lobectomy
- Lesionectomy
- Corpus callosotomy
- Subpial transection
- Lobectomy
- Lesionectomy
Surgical procedures for Pediatric Epilepsy Surgery Patients Less Than 18 Years (ILAE Survey 2004; 20 Centers Europe, Australia, & USA; n=413)

- Hemispherectomy: 16%
- Multilobar: 17%
- Frontal: 17%
- Temporal: 23%
- Parietal
- Occipital
- Hypothalamic
- Electrodes Only
- Multiple Subpial Trans.
- Vagal Nerve Stim.: 16%
- Corpus Callosotomy

Harvey et al., Epilepsia 2008;49:146-155.
Aetiology/Substrates for Pediatric Epilepsy Surgery Patients Less Than 18 Years (ILAE Survey 2004; 20 Centers Europe, Australia, & USA; n=413)

- Cortical Dysplasia: 42.4%
- Tumor
- Atrophy/Stroke
- Hipp. Sclerosis
- Gliosis/NORMAL
- Tuberous Sclerosis
- Hypo. Hamartoma
- Sturge-Weber
- Rasmussen Syndrome
- Vascular

Harvey et al., Epilepsia 2008;49:146-155
# Surgical Procedures & Etiologies by Age in Pediatric Epilepsy Surgery Patients: 2004 ILAE Survey

<table>
<thead>
<tr>
<th></th>
<th>Birth to 4 Yrs</th>
<th>Over 4 to 8 Yrs</th>
<th>Over 8 to 12 Yrs</th>
<th>Over 12 to 18 Yrs</th>
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<tr>
<td><strong>Surgical Procedure</strong></td>
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<tr>
<td>Hemispherectomy</td>
<td>32%</td>
<td>15%</td>
<td>10%</td>
<td>8%</td>
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<tr>
<td>Multilobar</td>
<td>20%</td>
<td>11%</td>
<td>12%</td>
<td>10%</td>
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<tr>
<td>Lobar/Focal</td>
<td>35%</td>
<td>47%</td>
<td>49%</td>
<td>60%</td>
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<tr>
<td>Electrode Only</td>
<td>4%</td>
<td>2%</td>
<td>6%</td>
<td>9%</td>
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<tr>
<td>Palliative</td>
<td>9%</td>
<td>25%</td>
<td>23%</td>
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<td><strong>Etiology/Substrate</strong></td>
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<td></td>
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<tr>
<td>Cortical Dysplasia</td>
<td>60%</td>
<td>45%</td>
<td>32%</td>
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<tr>
<td>Tumor</td>
<td>10%</td>
<td>20%</td>
<td>24%</td>
<td>25%</td>
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<tr>
<td>Stroke/Atrophy</td>
<td>7%</td>
<td>8%</td>
<td>14%</td>
<td>12%</td>
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<tr>
<td>Hippocampal Sclerosis</td>
<td>1%</td>
<td>5%</td>
<td>9%</td>
<td>12%</td>
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<tr>
<td>Gliosis/Normal</td>
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<td>5%</td>
<td>8%</td>
<td>8%</td>
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<tr>
<td>Tuberous Sclerosis</td>
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<td>4%</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Hypothalamic Hamartoma</td>
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<td>6%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Sturge Weber</td>
<td>5%</td>
<td>3%</td>
<td>2%</td>
<td>2%</td>
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<tr>
<td>Rasmussen</td>
<td>2%</td>
<td>5%</td>
<td>2%</td>
<td>2%</td>
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</table>

Harvey et al., Epilepsia 2008;49:146-155.
How many should be suitable?

Frequency, prognosis and surgical treatment of magnetic resonance imaging structural abnormalities in childhood epilepsy

Anne T. Berg,1 Gary W. Mathern,2,3 Richard A. Bronen,4 Robert K. Fulbright,4 Francis DiMario,5 Francine M. Testa6,7 and Susan R. Levy6,7

1 Department of Biology, Northern Illinois University, DeKalb, IL 60115, USA
2 Department of Neurosurgery, The Mental Retardation Research Center and the Brain Research Institute, University of California,

127/1000,000 pharmaco-resistant epilepsy
27/1000,000 epilepsy related surgical procedure 21%
23/1000,000 resective surgery

8% ‘non-idiopathic’ group

Assume 6,000,000 children in Australia, 138 operations/year
Why are children special?

• Range of syndromes & aetiologies
• The effect of epilepsy on early brain development
• Heterogeneous presentation of focal epilepsy in childhood
• The potential for functional plasticity
• Potential to improve long term psychosocial outcome
Aims of epilepsy surgery

Primary outcome aims

*seizure freedom/reduction*

Secondary outcome aims

*neurodevelopmental gains*

*behavioural improvement*
Aims of epilepsy surgery

Primary outcome aims

seizure freedom/reduction

Secondary outcome aims

neurodevelopmental gains

behavioural improvement
Seizure Outcomes Pediatric Patients
Resective Cases (N=797); 2004 Outcome ILAE Survey

- 55% (72%)
- 3%
- 3%
- 3%
- 8%
- 4%
- 2%
- 2%
- 2%
- 8%
- 2%
- 8%
- 0.4%

Number of Cases
Seizure Free (1A) Off Medications Pediatric Patients-Resective Cases; 2004 Outcome ILAE Survey

- 68% percent
- 46% percent
- 10% percent
- 12% percent
- 0% percent
- 5% percent
- 3% percent
- 0% percent
- 6% percent
- 0% percent
- 4% percent
- 0% percent
- 0% percent
- 0% percent

Percentages for different categories:

- 1A
- 1B
- 1C
- 1D
- 2
- 3A1
- 3A2
- 3A3
- 3B
- 3C
- 4A
- 4B
- 4C
Aims of epilepsy surgery

Primary outcome aims
  *seizure freedom/reduction*

Secondary outcome aims
  *neurodevelopmental gains*
  *behavioural improvement*
What if no surgery?

Cognitive deficits progress over time

Longitudinal study of a cohort with epilepsy onset < 3 years

<table>
<thead>
<tr>
<th>Domain</th>
<th>Baseline, Mean (SE)</th>
<th>1 Year, Mean (SE)</th>
<th>2 Years, Mean (SE)</th>
<th>3 Years, Mean (SE)</th>
<th>P Value for Trend</th>
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<tbody>
<tr>
<td>Composite</td>
<td>92.0 (1.5)</td>
<td>86.6 (2.0)</td>
<td>82.9 (2.4)</td>
<td>81.5 (2.7)</td>
<td>&lt;.0001</td>
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<tr>
<td>Communication</td>
<td>93.4 (1.5)</td>
<td>90.4 (2.0)</td>
<td>87.2 (2.0)</td>
<td>85.2 (2.3)</td>
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<td>Daily Living</td>
<td>89.6 (1.4)</td>
<td>79.0 (1.6)</td>
<td>76.5 (2.0)</td>
<td>74.6 (2.4)</td>
<td>&lt;.0001</td>
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<td>Motor</td>
<td>94.4 (1.7)</td>
<td>90.0 (2.2)</td>
<td>83.1 (2.5)</td>
<td>80.5 (3.3)</td>
<td>&lt;.0001</td>
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<tr>
<td>Social</td>
<td>96.1 (1.7)</td>
<td>92.7 (2.0)</td>
<td>90.0 (2.2)</td>
<td>88.8 (2.4)</td>
<td>.0015</td>
</tr>
</tbody>
</table>

**Berg et al Pediatrics 2004;114: 645-650**

Longitudinal study to 8-9 years following seizure onset <8 years

Dichotomous IQ indicator strongly correlated with age at onset in pharmacoresistant group (p<0.0001), not pharmacoresponsive group (p=0.61)

**Berg et al Neurology 2012;79:1384-1391**
Epileptic Encephalopathy

‘the epileptic activity itself contributes to cognitive and behavioral impairments beyond that expected from the underlying pathology alone (e.g. cortical malformation)’

Reversible?  
Or at the very least preventable?
Early & late recovery


Roulet –Perez et al Epilepsia 2010;51:1266-1276

Skirrow et al Neurology 2011;76:1330-1337
IQ improves after AED withdrawal following paediatric epilepsy surgery

Boshuisen et al Ann Neurol 2015; 78: 104-114

301 children; 11 centres
Effect of withdrawal of medication on IQ and change in IQ

Patients starting AED withdrawal a significantly higher postoperative IQ

Complete discontinuation of AEDs significantly related to a higher IQ and IQ gain

The number of AEDs that had been reduced postoperatively linearly related to IQ and change in IQ: the more drugs withdrawn, the higher postoperative IQ and the more increase in IQ
Behaviour disorder

Temporal lobe epilepsy
60 children; temporal lobe resection
83% at any time; 72% preoperatively & 72% post operatively

Extratemporal epilepsy
71 children; extratemporal resection
52.1% at any time; 43.7% preoperatively & 45.1% post operatively

Mclellan et al Dev Med Child Neurol 2005;47:666-672

Colonnelli et al Dev Med Child Neurol 2012;54:521-526
Proposed criteria for referral and evaluation of children for epilepsy surgery

• ‘Paediatric Specialist Epilepsy Unit’
• No minimal expertise/infrastructure requirements
• Certain subgroups should be referred to unit with experienced multidisciplinary personnel, access to advanced technologies
  – Infants and toddlers
  – Hemispherectomy
  – Multilobar resecton

Cross et al 2006  Epilepsia 2006;47:952-959
Focal resection

Seizures arise from one functionally silent area from the brain; drug resistance
Ictal onset

Fp2-F4
Fp1-F3
F4-C4
F3-C3
C4-P4
C3-P3
P4-Oz
P3-Oz
Fp2-F8
Fp1-F7
F8-A2
F7-A1
A2-T6
A1-T5
T6-Oz
T5-Oz
*ECG
*R.Deltoid
*L.Deltoid

1 sec
100 µV

Cries
L arm extends

Brain MRI scan
Visibility of lesions with brain maturation

Age 4m

Age 18m
Hemisindrome

Seizures arise from structurally abnormal side of the brain; contralateral pre-existent hemiplegia
Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies

*1 Patrick Kwan, †Alexis Arzimanoglou, ‡Anne T. Berg, §Martin J. Brodie, ¶W. Allen Hauser, #2 Gary Mathern, *‡Solomon L. Moshe, ††Emilio Perucca, ‡‡Samuel Wiebe, and §§2 Jacqueline French

Level 1: ‘Rule of three’

A seizure free duration that is at least three times the longest seizure free interval prior to starting a new intervention required.

Level 2: Drug resistant epilepsy may be defined as a failure of adequate trials of two tolerated and appropriately chosen and used AED schedules, whether as monotherapies or in combination, to achieve sustained seizure freedom
Special considerations

*Specific ‘surgical’ syndromes in childhood epilepsy*

- Rasmussens Syndrome
- Tuberous sclerosis
- Sturge Weber syndrome
- Polymicrogyria
- Hypothalamic Hamartoma
- *Common pathologies with specific phenotype*
Resective surgery: Aims of evaluation

Localisation of responsible tissue

- Clinical evaluation
- Interictal EEG
- Video EEG ictal recording
- Optimised structural MRI
- Functional imaging

Localisation of function

- Clinical evaluation
- Neuropsychology
- Functional MRI

Evaluation of outcome aims

- Neuropsychiatric evaluation

Cross et al
2006 Epilepsia
2006;47:952-959
Pre-Surgical Investigations for Pediatric Patients
2004 ILAE Survey

Harvey et al., Epilepsia 2008; 49:146-155
Can we now revisit?

30 participants, representing all continents

Reviewed clinical studies of utility of diagnostic tests for specific cohorts

No class 1, insufficient class 2 data

Recommendations through consensus
### Aetiologies reviewed

<table>
<thead>
<tr>
<th>Cohort</th>
<th>II EEG</th>
<th>Video EEG</th>
<th>MRI</th>
<th>3D EEG/MEG</th>
<th>PET</th>
<th>SPECT</th>
<th>ECoG</th>
<th>IEM</th>
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<td>H</td>
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<td>M/H</td>
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<td>Consider possibility of dual path</td>
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<td>Post-infec/Ischemic</td>
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<td>Lesions may be bilateral</td>
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<tr>
<td>No Function</td>
<td>M*</td>
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<td>Possible EEG false lateralization</td>
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<td>H</td>
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<td>O/H</td>
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<td>Rasmussen</td>
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<td>H</td>
<td>H</td>
<td>Serial Tests</td>
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Epilepsy surgery in childhood

- The spectrum of paediatric epilepsy surgery candidates is wide

- Primary aim remains seizure freedom
  - BUT secondary aims include improvement in psychosocial functioning

- Presurgical evaluation aimed at determining whether area of brain can be removed without detriment to further function
  - Multidisciplinary approach

- Outcome goals of surgery will be individual and require full exploration prior to surgery