„Not small adults“

Specific aspects of pediatric epilepsy surgery

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Outline

- **Identification of pediatric candidates**
  - Re-defining medical intractability
  - Timing of surgery
  - Modified goals of epilepsy surgery
  - Epilepsy surgery in epileptic encephalopathies

- **Specific diagnostic aspects in children**
  - Seizure semiology
  - EEG
  - Invasive monitoring
  - MRI
  - Functional imaging
Identification of candidates

- Medical intractability
  - The majority of patients who have epilepsy that is uncontrolled by two AEDs will not be controlled with additional AEDs

Identification of candidates

- Medical intractability and timing of surgery in children
  - No lower age-limit to surgical referral
  - Many pediatric epilepsy syndromes have a known long-term prognosis (e.g. lesional epilepsies, Rasmussen’s syndrome, focal cortical dysplasia)
  - Medical intractability can often be established rapidly; „standard“ criteria may be waived
  - Epileptic encephalopathy - special indication
Identification of candidates

- Specific aspects of pediatric epilepsy surgery candidates
  - The underlying seizure disorder is often different from adults
  - Seizures are usually more frequent
  - Surgery is more likely to be extratemporal
  - „Non-lesional“ cases might be suitable candidates
  - Negative impact of seizures on development
  - Negative impact of AEDs on development
  - Importance of developmental plasticity in children
Identification of candidates

- Sub-groups of patients treated in pediatric epilepsy surgery centers
  - 0-6 years  Uniquely pediatric
  - 4-10 years  Transitional group
  - > 10 years  Similar to adults

- Different pathologic substrates of epilepsy in children
  - Hippocampal sclerosis much less important
    (found in 12-15% of cases)
  - Focal cortical dysplasia and low-grade (developmentally-based) tumors are the predominant etiologic factors
Identification of candidates

- Pediatric syndromes with potential surgical cure
  - West Syndrome
  - Lennox-Gastaut syndrome
  - Ohtahara syndrome
  - Focal cortical dysplasia
  - Hemimegalencephaly
  - Tuberous sclerosis complex
  - Sturge-Weber syndrome
  - Hypothalamic hamartoma
  - Hemifacial spasms
Identification of candidates

- Pediatric syndromes with palliative goals
  - Landau-Kleffner Syndrome
  - Autistic regression

- Pediatric syndromes not presently amenable to surgical intervention
  - Dravet syndrome
  - Migrating partial seizures in infancy
  - Lissencephaly / Agyria
Epilepsy surgery in epileptic encephalopathies

- Epileptic condition associated with a deterioration resulting from intense epileptic activity, marked either by seizures or only by EEG alterations.
- Psychomotor regression in these patients provides a rationale for early surgical intervention.
- Families faced with frank regression of a child and its prognostic implications often pressure the surgical team to consider intervention.
- A balance between clinical urgency and surgical reality should be found.
Epilepsy surgery in epileptic encephalopathies

- Surgically-induced deficits more acceptable in an encephalopathic child
- Palliative procedures desirable if accompanied by cessation of encephalopathy
- Commisural disconnection procedures utilized more frequently
- High proportion of patients are not straight-forward cases:
  - Multilobar / hemispheric extent of pathology
  - Discordant diagnostic findings common
  - Significant proportion of non-lesional / uncertain lesional / multi-lesional cases
Epilepsy surgery in epileptic encephalopathies

Selected Series

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Series</th>
<th>N</th>
<th>SF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sturge-Weber syndrome</td>
<td>Hoffman et al, 1979</td>
<td>7</td>
<td>5 (71)</td>
</tr>
<tr>
<td>Tuberous Sclerosis</td>
<td>Koh et al, 2000</td>
<td>13</td>
<td>9 (69)</td>
</tr>
<tr>
<td>Infantile Spasms</td>
<td>Chugani et al, 1990</td>
<td>23</td>
<td>15 (65)</td>
</tr>
<tr>
<td>Hemimegalencephaly</td>
<td>Vigevano &amp; DiRocco, 1990</td>
<td>5</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Cortical Malformation</td>
<td>Edwards et al, 2000</td>
<td>35</td>
<td>17 (49)</td>
</tr>
</tbody>
</table>
Epilepsy surgery in epileptic encephalopathies

*Case reports*

- **Lennox-Gastaut syndrome**
  - Angelini et al, 1979 (*astrocytoma*)
  - Quarato et al, 2002 (*DNET*)

- **Ohtahara Syndrome**
  - Pedespan et al, 1995
  - Hirofumi et al, 1999
  - Hamiwka et al, 2004

- **Hemifacial Seizures**
  - Harvey et al, 1996
  - Chae et al, 2001
  - Arzimanoglou et al, 2003
Epilepsy surgery in epileptic encephalopaties

- Will successful epilepsy surgery reverse or improve the encephalopathy?
  - *Left functional hemispherectomy at age 44 months in a child with continuous LH inter-ictal discharging leads to dramatic improvement in language acquisition* (Rosenblatt et al, 1998)
  - *Above-average intelligence after left* (Smith & Sugar, 1975) or *right* (Damasio & Damasio, 1975) *hemispherectomy*
  - *Improvement in IQ scores, cessation in deterioration after hemispherectomy in 17 patients* (Lindsay et al, 1987)
Goals of epilepsy surgery in catastrophic epilepsies

- Developmental outcome is of paramount importance
- Modified goals of surgery in epileptic encephalopathies
  - Relief of the catastrophic course of a condition
  - Resumption of developmental progression
  - Improvement in behavior
- Sometimes may be reached even in the absence of complete seizure freedom
Specific diagnostic aspects in children

- Seizure semiology in infants and children
  - Clinical features of focal seizures are frequently different from adult cases
  - Generalized (bilateral symmetric) manifestations may have focal origin
  - Seizure characteristics signalizing localized onset may be absent or unidentifiable (auras)
  - ILAE classification of seizures is usually not applicable to infants younger than 3 years
Specific diagnostic aspects in children

- Seizure semiology in infants under 2 years of age
  - Seizures characterized by decrease in behavioral motor activity with indeterminate level of consciousness and minimal or no automatisms ("hypomotor" seizures) arise from temporal, temporoparietal, or parieto-occipital regions
  - Seizures with localized or bilateral clonic, tonic, or atonic motor phenomena arose predominantly from frontal, frontocentral, central, or frontoparietal areas
  - Infantile spasms occur from either location

## Development of Seizure Manifestations

<table>
<thead>
<tr>
<th>Type</th>
<th>&lt;2 Yrs</th>
<th>2-6 Yrs.</th>
<th>6-12 Yrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staring</em></td>
<td>8 (72%)</td>
<td>5 (71%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td><em>Motor</em>**</td>
<td>10 (91%)</td>
<td>5 (71%)</td>
<td>5 (63%)</td>
</tr>
<tr>
<td><em>Automatisms</em></td>
<td>8 (72%)</td>
<td>5 (71%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td><em>Smiling</em></td>
<td>0</td>
<td>0</td>
<td>2 (25%)</td>
</tr>
<tr>
<td><em>Fear</em></td>
<td>0</td>
<td>0</td>
<td>1 (13%)</td>
</tr>
<tr>
<td><em>Autonomic</em></td>
<td>0</td>
<td>0</td>
<td>2 (25%)</td>
</tr>
</tbody>
</table>

Jayakar & Duchowny, 1990  
**p < 0.05**
### Development of Seizure Manifestations

#### Automatisms

<table>
<thead>
<tr>
<th>Type</th>
<th>&lt; 2 Yrs</th>
<th>2-6 Yrs.</th>
<th>6-12 Yrs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oroalimentary</td>
<td>8 (72%)</td>
<td>3 (43%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>Facial</td>
<td>6 (55%)</td>
<td>1 (14%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Gestural</td>
<td>5 (45%)</td>
<td>5 (71%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>Axial**</td>
<td>0</td>
<td>3 (43%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>Stereotypy**</td>
<td>1 (9%)</td>
<td>4 (57%)</td>
<td>6 (75%)</td>
</tr>
</tbody>
</table>

Jayakar & Duchowny, 1990

**p < 0.05**
Specific diagnostic aspects in children

- Scalp EEG in infants and children
  
  - Within the first 2 years of life, focal lesions frequently manifest as generalized scalp EEG patterns (hypsarrhythmia, burst-suppression)
  
  - EEG findings which may help to identify a region of cortical abnormality:
    
    - Predominance of spikes over one region
    - Localized slowing / decreased background activity / absent sleep spindles over one region
    - Unilateral electrodecremental events
    - Asymmetric EEG seizures

Gupta & Wyllie, 2004
Specific diagnostic aspects in children

- Invasive EEG monitoring in children
  - With rapid advances in neuroimaging, the need for chronic intracranial monitoring has diminished significantly
  - It has however regained its utility in complicated pediatric epilepsy surgery candidates
    - Normal MRI studies
    - Discordant findings of noninvasive tests
    - Proximity of a lesion to the eloquent cortex
  - Subdural electrodes most suited for pediatric cases
    - Allow coverage of large areas of the neocortical convexity and of basal and interhemispheric surfaces
  - Depth electrodes necessary to document seizure origin from the hippocampus or other deep-seated lesions
Specific diagnostic aspects in children

- Functional cortical mapping in children
  - Although electrode implantation is usually well tolerated in young children, cortical mapping might not always be successful
    - No response to widely used paradigms of cortical stimulation in children under the age of 4 years
    - Even older children rarely demonstrate consistent regions of sensorimotor function
  - The threshold for both ADs and sensorimotor responses was found to have an inverse linear correlation with age
  - Specific stimulation protocols are necessary in infants and young children
Specific diagnostic aspects in children

- MRI in infants and children
  - A critical component of surgical strategy, especially in cases with non-localizing seizure semiology and EEG
  - Should be enhanced by use of high-resolution imaging, specialized protocol with thin sections, and experience of the reader
  - Still an open question whether a focal epileptogenic lesion on the MRI indicates a better postoperative seizure outcome

  - Yes Zentner et al., Epilepsia, 1996
  - No Krsek et al., Neurology, submitted

<table>
<thead>
<tr>
<th>MRI finding</th>
<th>Engel I</th>
<th>Engel II</th>
<th>Engel III</th>
<th>Engel IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal (n=82)</td>
<td>45 (55%)</td>
<td>10 (12%)</td>
<td>6 (7%)</td>
<td>21 (26%)</td>
</tr>
<tr>
<td>Normal (n=26)</td>
<td>14 (54%)</td>
<td>2 (8%)</td>
<td>1 (4%)</td>
<td>9 (34%)</td>
</tr>
</tbody>
</table>
MRI findings in pediatric focal cortical dysplasia

- **Distinctive features of FCD type II**
  - *Focal cortical thickening*
  - „Transmantle“ sign
  - Abnormal gyral and sulcal patterns
  - *Prominent blurring of the gray/white matter junction*
  - *Signal changes in both gray and white matter*

- **Distinctive features of FCD type II**
  - *Less prominent gray/white matter junction blurring*
  - *Signal changes predominantly in white matter*
  - *Prominent lobar hypoplasia / atrophy*

- **MRI findings in mild malformation of cortical development**
  - *Least frequent, usually less pronounced abnormalities described in FCD type I*  

  Krsek et al., Ann Neurol, in press
MRI findings in pediatric focal cortical dysplasia

- MRI picture of FCD may change with brain maturation

1. *The initial study might be normal, later shows the high T2 signal in the white matter, the high T1 signal in the cortex and the gray/whitter matter junction blurring*

2. *An early study in an infant may show a low T2 signal in the white matter that will disappear on subsequent studies*
PET in infants and children

- In a series of infants with infantile spasms, Chugani et al. (1990) found localized regions of hypometabolism corresponding to FCD even without MRI abnormalities.

- Majority (65%) of infants with cryptogenic infantile spasms show more areas of cortical hypometabolism without correlation with EEG and are not ideal surgical candidates.

Specific diagnostic aspects in children

- $^1$H MR spectroscopy in infants and children
  - *It has not been extensively studied in children*
  - *We recently showed that $^1$H MRS correctly lateralizes and frequently also localize epileptogenic zone in children with MRI-negative focal cortical dysplasia*
  - $^1$H MRS changes co-localized with ictal SPECT findings and ictal onset zone according to invasive EEG mapping

Krsek et al., Eur Radiol, 2007