

„Not small adults“

**Specific aspects of pediatric
epilepsy surgery**

Pavel Kršek

Department of Pediatric Neurology

Motol Epilepsy Centre

Prague



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neurologie



Outline

■ Identification of pediatric candidates

- *Re-defining medical intractability*
- *Timing of surgery*
- *Modified goals of epilepsy surgery*
- *Epilepsy surgery in epileptic encefalopatias*

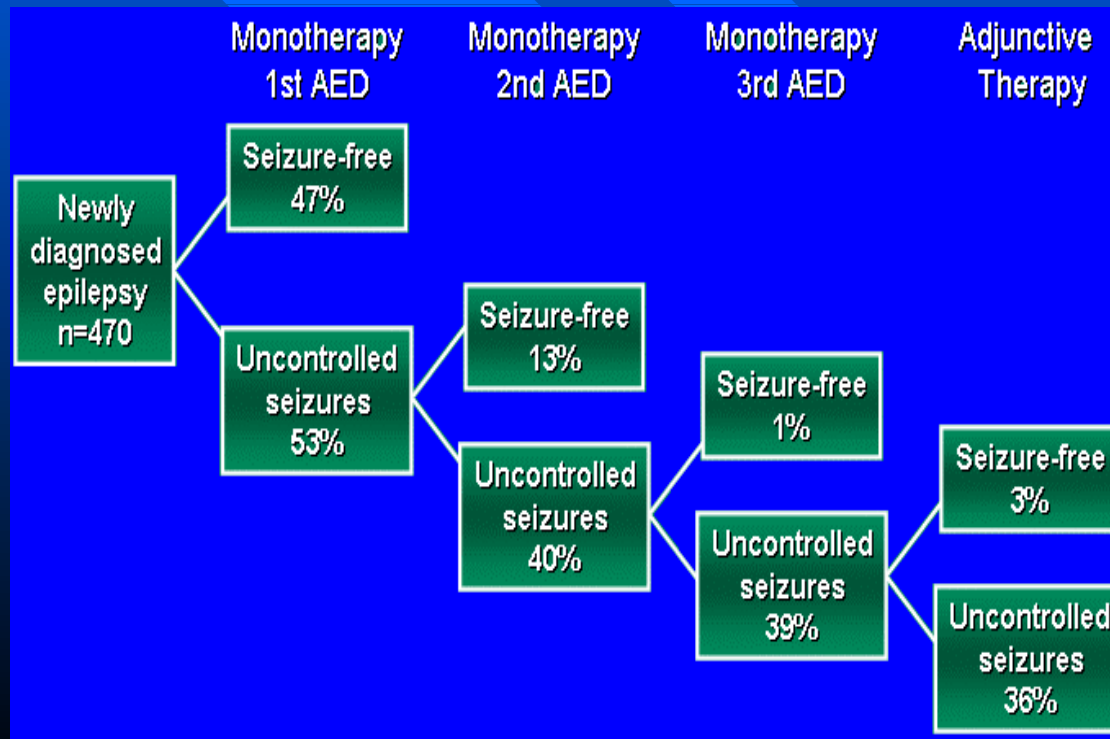
■ Specific diagnostic aspects in children

- *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*



Kwan & Brodie,
N Engl J Med, 2000

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

<i>Disorder</i>	<i>Series</i>	<i>N</i>	<i>SF (%)</i>
Sturge-Weber syndrome	Hoffman et al, 1979	7	5 (71)
Tuberous Sclerosis	Koh et al, 2000	13	9 (69)
Infantile Spasms	Chugani et al, 1990	23	15 (65)
Hemimegalencephaly	Vigevano & DiRocco, 1990	5	5 (100)
Cortical Malformation	Edwards et al, 2000	35	17 (49)

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 encephalopathies

- 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 signaling 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*

Acharya, Wyllie, Lüders et al. 1997

Development of Seizure Manifestations

	<u><2 Yrs</u>	<u>2-6 Yrs.</u>	<u>6-12 Yrs.</u>
<i>Staring</i>	8 (72%)	5 (71%)	7 (88%)
<i>Motor**</i>	10 (91%)	5 (71%)	5 (63%)
<i>Automatisms</i>	8 (72%)	5 (71%)	7 (88%)
<i>Smiling</i>	0	0	2 (25%)
<i>Fear</i>	0	0	1 (13%)
<i>Autonomic</i>	0	0	2 (25)

Jayakar & Duchowny, 1990

** p < 0.05

Development of Seizure Manifestations

Automatisms

	<u>< 2 Yrs</u>	<u>2-6 Yrs.</u>	<u>6-12 Yrs.</u>
<i>Oroalimentary</i>	8 (72%)	3 (43%)	6 (75%)
<i>Facial</i>	6 (55%)	1 (14%)	4 (50%)
<i>Gestural</i>	5 (45%)	5 (71%)	6 (75%)
<i>Axial**</i>	0	3 (43%)	6 (75%)
<i>Stereotypy**</i>	1 (9%)	4 (57%)	6 (75%)

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 (hypsarrythmia, 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

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

MRI finding	Engel I	Engel II	Engel III	Engel IV
Abnormal (n=82)	45 (55%)	10 (12%)	6 (7%)	21 (26%)
Normal (n=26)	14 (54%)	2 (8%)	1 (4%)	9 (34%)

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 I

- *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

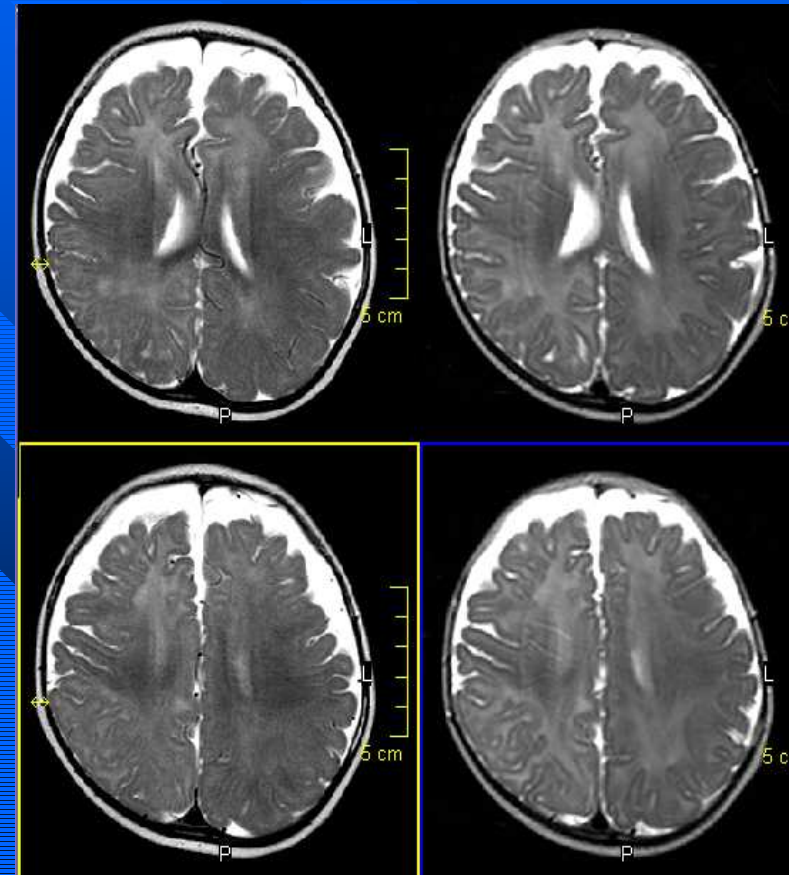
- *Least frequent, usually less pronounced abnormalities described in FCD type I*

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*



10 months

5 months

Specific diagnostic aspects in children

■ 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*
- *Promising new tracers: **alpha-[¹¹C] methyl-L-tryptophan** may differentiate between epileptogenic and nonepileptogenic tubers in TSC patients*
(Chugani et al., Ann Neurol, 1998)

Specific diagnostic aspects in children

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