SEIZURE SEMIOLOGY OF INFANTS AND YOUNG CHILDREN WITH LESIONAL EPILEPSY

Ph.D. thesis

András Fogarasi M.D.
Bethesda Children's Hospital of the Hungarian Reformed Church
Bethesda u. 3. H-1146 Budapest, Hungary

consultant: Prof. Péter Halász M.D., D.Sc.
program director: Prof. Zoltán Nagy M.D., D.Sc.

Budapest
2002
SUMMARY

Epilepsy is a broad category of recurrent paroxysmal episodes of brain dysfunction manifested by stereotyped alterations in behavior. Seizure semiology describes the clinical features of such an episode supporting its precise classification. Proper knowledge and frequent use of seizure semiology can greatly help in the adequate categorization of epileptic seizures and using their features in the localization and lateralization of the brain’s region involved in a certain attack.

There are several semiological studies of adulthood epilepsies in the medical literature; however, it lacks systematic semiological analysis of young children with lobe-specific epilepsies. My work tries to fill this gap.

Using independent multiobserver analysis of 304 videotaped seizures in 47 infants and preschool children with lobe-specific epilepsies and comparing these results with adulthood semiological studies from the literature, I found that childhood and adulthood seizures share a number of common clinical features; however, there are distinct age-dependent differences.

Daily seizure frequency, short duration of attacks, behavioral changes, epileptic spasms, and late oral automatisms are common, while complex motor automatisms and secondarily generalized seizures are rare manifestations in infants and young children. Because of young age and frequent associated disabilities, it is difficult to record definitive auras and sensory symptomatology, therefore videorecording-based analysis of semiology is a useful method in this age.

Studying lobe-specific features, I found that temporal lobe seizure semiology shows a gradual transition in preschool years and some of the lateralization signs described in adults have also lateralizing value in young children. Regarding to posterior cortex epilepsy, I described first some specific features for infants and young children with epilepsy of this region: ictal smile, ictal flush, and head nod were frequent symptoms; among them ictal smile also appeared as a lateralizing sign of the non-dominant hemisphere.

An appreciation of age- and lobe-specific seizure semiology in infants and young children should facilitate early diagnosis and improve medical and surgical treatment of therapy-resistant epilepsies leading to better neurologic outcome.
1. INTRODUCTION

Epilepsy is a broad category of recurrent paroxysmal episodes of brain dysfunction manifested by stereotyped alterations in behavior. Seizure semiology describes the clinical features of such an episode supporting its precise classification. Proper knowledge and frequent use of seizure semiology can greatly help in the adequate categorization of epileptic seizures and using their features in the localization and lateralization of the brain’s region involved in a certain attack. Since the advent of presurgical evaluation, especially long term video-EEG monitoring, our knowledge on seizure semiology has become much more exact. Repeated observation of a videotaped seizure can help us to notice even so subtle features, which might be easily missed by lay people or even experienced epileptologists. Moreover, the exact length of a seizure, the level of consciousness during the attack, postictal latent hemiparesis, or sensorial aphasia can be objectively judged only by videotaped and adequately tested seizures.

There are several semiological studies of adulthood epilepsies in the medical literature; however, it lacks systematic semiological analysis of young children with lobe-specific epilepsies. My work tries to fill this gap.

2. PURPOSES

1. The aim of my study is to create the first systematic semiological summary of infants and young children with
   - frontal lobe,
   - temporal lobe, and
   - posterior cortex epilepsy
   - based on a sufficient number of examined preschool children,
   - analyzing only videotaped seizures,
   - using multi-observer analysis, and
2. Beside a semiological description, I would like to compare my results with the semiological studies of adults, find possible similarities and differences, and check if the seizure semiology of young children show any lobe-specific feature.

3. I would like to study on the semiological changes within this young age range, especially the semiological transition in the temporal lobe group.

4. I would like to study on the different lateralizing signs in my group: to check if the features described in adults have also lateralizing value in childhood and look for age-specific lateralizing signs, too.

3. PATIENTS AND METHODS

3.1 Patients

There are only a few large epilepsy surgery centers in the world which could provide sufficient number of operated young children for a semiological study using the gold standard rule. Participating in a scientific cooperation between the Epilepsy Center Bethel (Bielefeld, Germany) and the Bethesda Children’s Hospital (Budapest, Hungary), I could study the archived seizures of infants and young children with different lesional epilepsies. Between 1990 and 2001, about 2300 patients underwent long term video EEG monitoring at the Epilepsy Center Bethel. In this study I included all children younger than 7 years in whom the presurgical evaluation showed frontal, temporal, or posterior cortex epileptic focus and after the resection of this focus they became either seizure-free or worthwhile improved.

My group consisted of 47 medically refractory patients, 23 girls and 24 boys. Age at first epileptic attack was between 2 days and 56 months (mean 10 months) and age at LTM was 3 to 81 (mean: 36) months. After surgical removal of the epileptogenic zone, 34 patients became seizure-free; the other 13 children showed worthwhile improvement. Duration of follow-up was between 3 and 92 (mean 36) months (only three children had a follow-up period shorter than one year. Postoperative seizure outcome was evaluated according to Engel’s classification system.
Histopathology of the resected tissue showed FCD (34 cases), benign tumor (10 cases), and hippocampal sclerosis (1 case), posttraumatic lesion (1 case), tuberous sclerosis (1 case).

Twenty-five children had right-sided, 23 of them had left-sided lesion.

3.2 Seizure classification

Three independent investigators reviewed 304 archived seizures of these 47 patients (mean 6, range 2-15 seizures per child). Each attack was analyzed by the authors independently by filling out a data-sheet especially designed for this study containing information on the behavioral, sensory, consciousness, autonomic, and motor spheres of the seizures, as well as the postictal period. The events of each sphere were classified using a time scale as onset, very early (<10 seconds), early (10-20 seconds) or late (>20 seconds after clinical seizure onset) events.

Seizures were recorded with a digital clock superimposed on video-images and transcribed in code on the electro-encephalogram (EEG) software, therefore we could evaluate the seizures without knowledge of EEG data. Patients were examined during and after the seizures by trained EEG technicians who assessed the level of consciousness by asking questions, giving tasks, and using external stimuli when needed. We used a wide-spread classification based on seizure semiology.

Beside seizure classification, I reviewed each patient’s medical charts and collected their most important clinical, imaging, seizure outcome, and semiology features.

3.3 Statistical analysis

Spearman rank correlation was used to test the hypothesis of an age-dependent change in the seizure semiology grouped as motor and nonmotor (psychomotor) components of lesional temporal lobe epilepsy (TLE) in young children.
4. RESULTS AND DISCUSSION

4.1 Age-dependent features

*Seizure frequency.* All patients had daily seizures with a frequency of 1-100 attacks per day, one-third of them showed seizure clusters. 43-100% of adults with frontal lobe epilepsy (FLE) has daily seizures, half of them with seizure clusters. In contrast to it, adults with TLE show only weekly-monthly seizure frequency and in adults with posterior cortex epilepsy (PCE) the mean seizure frequency was found to be typically only 10 per month with a range of 1-60 attacks monthly. It seems that seizure frequency is age-specific: the extremely intense childhood epilepsies become less active during the years. On the other hand, comparing lobe-specific groups of young children, temporal lobe seizures present less frequently already at this age. The high frequency of seizures may hinder cognitive development, therefore the proper pharmaco- or surgical therapy has a very important role in the early childhood.

*Duration of seizures.* Seizures’ length was in a range of 1-180 seconds. Although the shortest attacks presented in the FLE group (1-89, [mean: 29] seconds) comparing with TLE and PCE patients (mean: 62 and 67 seconds, respectively), all three groups had shorter mean duration than those of adults with seizures in the same localization. No statistical correlation was found between age and duration of seizure within any studied group.

*Aura.* While aura is frequently reported in adulthood semiological studies, only seven of my 47 children (15%) reported preictal warnings; four of them had non-specific (headache, nausea) and three had somatosensory aura. Although in an additional 47% of children I have recorded arousal, strange movement or behavioral change before seizure onset, I was cautious to define them as auras. Agreeing with earlier studies, I believe that because of their young age and special cognitive development, children have difficulty to report about their feelings before and during seizures.

*Behavioral change.* In 28 children (60%) a number of seizures started with behavioral change, a sudden arrest of preictal activity (i.e., playing, eating, sucking, etc.). Behavioral change was observed most frequently in the TLE group. By the end of these
seizures, children returned to their previous activity showing a very rapid postictal recovery. I think it is a characteristic non-convulsive phenomenon at this age, therefore it is important to know this phenomenon in case of differential diagnostic problems.

Late oral automatisms. Automatisms were recorded in 24 children (51%) with lesional epilepsy, mostly (in 20 cases) in oral form. Although the ratios of children with automatisms were different in the certain localization-related groups (i.e.: 87% in TLE, 21% in FLE), I can conclude that late oral automatism is a typical form at this age; 80% of children with automatism presented an oral form at least 20 seconds after seizure onset.

Epileptic spasm. In spite of their circumscribed seizure focus, eight children (17%) showed also generalized ES series among their seizures, most of them (five patients) from the frontal lobe group. Similarly to earlier studies, the asymmetric and asynchronous spasms were associated with a seizure focus contralateral to the behaviorally more involved side in my cases, too.

Vocalization. As it is described in adulthood studies, many children (49%) had ictal vocalization at least once during their seizures, mostly in the TLE, least frequently in the FLE group. Vocalization appeared in form of crying, whining, mumbling, or grumbling.

Secondarily generalized tonic-clonic seizures (SGTCS). It is generally accepted that SGTCS is a typical feature of adulthood and is reported in 61-91% of patients with different epilepsies. By investigating 304 attacks of young children and infants, I recorded only one seizure with an evolution to SGTCS and found this seizure component in the history of only four of them. Explanations for the rareness of secondary generalization may be the gradual maturation of the frontal lobe, the immature dendritic development and myelin formation, the imperfect synchronization of both hemispheres, as well as the relatively short interval between age at epilepsy onset and LTM of these patients (range: 2-66, mean: 34 months).

Etiology. In my series, histopathology showed most frequently dysplasia (73%) and benign tumor (21%) in the resected tissues, therefore the etiology of therapy-resistant epilepsies in early childhood seems to be different from that of adults where hippocampal sclerosis, tumor, and vascular malformations are the dominant lesions.
4.2 Localization-related features

4.2.1 Frontal lobe group

Nocturnal tendency. Similarly to adulthood FLE studies, a large part (37%) of preschool children's seizures started at night, while 47% of them occurred during sleep. This difference is most likely caused by children’s special sleep-wake rhythm: I observed a part of the seizures during daytime sleep.

Motor signs. As it was suspected, all children had motor seizures and only six of the analyzed 111 attacks (5%) showed no motor signs at all. Besides tonic seizures, clonic components and ES were the leading manifestations of the attacks.

Psychomotor seizures. I found that psychomotor seizures are rare clinical manifestations of young children with FLE. Only two patients (14%) had this form of attack with typical behavioral arrest and oral automatisms. Salanova et al. and Mihara et al. found that in FLE adults with psychomotor seizures the epileptogenic zones were largely in the anterior two thirds of the frontal lobe, whereas motor seizures originated from the posterior third of it. Psychomotor seizures were too infrequent in my group to extend these results to early childhood.

Automatisms. I did not observe any bimanual-bipedal or other complex motor automatism in this group, although in adults with FLE they are seen relatively frequently. I believe that the lack of such complex motor automatisms and hypermotor seizures reflects immature cortical connectivity and myelinization of the frontal lobe.

Short postictal confusion. As I already mentioned, because of the age of the children in this study, it was difficult to assess the level of consciousness. However, I observed that most of the verbalizing children -those who could cooperate well with our EEG technicians- showed a short postictal reorientation time, frequently less than 10 seconds.

4.2.2 Temporal lobe group

Semiological transformation. Temporal lobe seizure semiology appears to be significantly influenced by age-related mechanisms so that ictal features in young
children may not give much clue about the presence of this type of localization-related epilepsy. My study showed that this transformation occurred in a linear fashion ($r = -0.64; p < 0.01$) as a function of age during preschool years so that in the fourth year of life the nonmotor components of psychomotor seizures as the hallmark of limbic epilepsy as seen in adults was the dominant seizure manifestation.

By contrast, all patients under 42 months had a high ratio of motor features including tonic, clonic, myoclonic components, and ES compared to the overall observed seizure components. Beyond 42 months of age the rate of complex partial seizure semiology with behavioral arrest and automatisms increased and became the predominant feature in half of the children.

Animal studies investigating the ontogenetic expression of drug-induced limbic epilepsy in immature young rats shows a comparable age-dependent ictal behavior. Investigating kainic acid and pilocarpine-induced seizures in young rats during the first two postnatal weeks corresponding to a maturational age of the human infants, these rat pups developed hyperactivity, scratching, hyperextension of the limbs, tremor, head bobbing, and myoclonic movements. More mature rats aged above 2 weeks, in addition to prominent motor signs, produced limbic seizures consisting of rearing, akinesia, and masticatory movements. Further studies in hippocampal-kindled rat pups demonstrate that the afterdischarge thresholds (i.e., the lowest current intensity necessary to elicit an afterdischarge) are highest during the second to third postnatal week suggesting resistance of the limbic system to synchronization. These findings from animal studies appear to offer a reasonable explanation why temporal lobe seizures in immature humans only manifest more clearly with typical psychomotor features once the limbic system has matured from the fourth year of life.

The age-related motor component ratio was independent of the age at epilepsy onset. This is supported not only by my cross-sectional semiology study of the 15 patients but also the longitudinal follow-up of one child, who showed a definitive change of seizure semiology between the first and fourth year of her life. The ratio of motor seizure components depended on neither the mesial or lateral localization, the lateralization, nor the etiology (tumor, dysplasia, hippocampal sclerosis) in my patients. This corresponds to the results of a study on adult patients with mesial and neocortical TLE which
demonstrated no differences in the seizure semiology reflected involvement of the limbic system. Conversely, I can hypothesize that during the first three years of life, the immature limbic structures synchronize poorly and remain clinically silent at this age.

**Lateralization signs.** I observed two different lateralizing signs earlier described in adulthood TLE. Six patients produced ictal dystonic posturing of an arm; in five cases it was contralateral to the seizure focus, in one case it happened in both arms. Postictal nosewiping -an ipsilateral lateralizing phenomena in TLE- were recorded also in six children; in four cases it was ipsilateral to the seizure focus and twice it was observed by both hands. These results of my small group of patients are promising; however, an expansion of this series would give more reliable data.

### 4.2.3 Posterior cortex group

**Oculomotor features** -similarly to adults- were seen frequently (72%) in form of nystagmus (39%), eye deviation (33%), lid myoclonia (28%), and rapid, repetitive blinking (17%). Two patients also showed opsoclonic movements, a dyskinesia consisting of involuntary, arrhythmic, chaotic, multidirectional saccades without intersaccadic intervals.

**Ictal smile.** I observed ictal smile in five cases (28%). This phenomenon was previously reported only in a case report of adults with parietal and temporal lobe epilepsy, large surgical series of PCE did not mention it at all. According to my knowledge, this is the first reported group in childhood, despite ictal smile seems to be frequent in this group. The fact that all of my patients with ictal smile had right-sided epileptic focus, supports earlier findings that the subdominant hemisphere represents emotional facial expressions. Although right-sided focus was typical in my study, it would be helpful to check the lateralizing value of ictal smile in a larger patient population with PCE.

**Flush.** Five young children with PCE developed flush during their seizures, although this phenomenon is not mentioned in large adult surgical series at all. The reason for this difference can be my more detailed observing method with video recording.

**Head nod.** Myoclonic seizures most frequently appeared as head nodding; a rapid, symmetric inclination of head involving neck and occasionally shoulder muscles. This
phenomenon was very typical in my group; seven children (39%) produced head nods, three of them also in series. Large studies of adult PCE do not mention this seizure component. I think that head nod—similarly to epileptic spasm—is a generalized expression of epilepsy and could also be considered according to functional development of the brain.

**Automatisms.** Automatisms were recorded in 44% of my young children with PCE. According to large surgical series, 50-75% of patients with occipital lobe epilepsy show automatism; however, this phenomenon is observed in only 12% of parietal lobe epilepsy cases. This difference presented also in my group: from the 15 children with lesion involving also the occipital lobe, eight had automatism (53%), while in children with lesions exclusively in the parietal region this component did not appear at all.

**Longitudinal follow-up.** Two patients had video monitoring at two different ages; first with scalp electrodes, then in the second phase with subdural grids. Differences between the two phases were 31 and 49 months. The repeat studies showed very similar seizure semiology with the same oculomotor features in the two different points of time, which might support that posterior cortex seizure semiology is localization-specific and constant in this age range.
5. SUMMARY

Using independent multiobserver analysis of videotaped seizures in patients with lobe-specific epilepsies based on the gold standard rule, I found that childhood and adulthood seizures share a number of common clinical features; however, there are distinct age-dependent differences.

Daily seizure frequency, short duration of attacks, behavioral changes, epileptic spasms, and late oral automatisms are common, while complex motor automatisms and SGTCS are rare manifestations in infants and young children. Because of young age and frequent associated disabilities, it is difficult to record definitive auras and sensory symptomatology, therefore videorecording-based analysis of semiology is a useful method in this age. As an etiological factor, dysplasia is much more common in young children with therapy-resistant epilepsy than that in adults.

Studying lobe-specific features, I found that temporal lobe seizure semiology shows a gradual transition in preschool years and some of the lateralization signs described in adults have also lateralizing value in young children. Regarding to PCE, I described first some specific features for infants and young children with epilepsy of this region: ictal smile, ictal flush, and head nod were frequent symptoms; among them ictal smile also appeared as a lateralizing sign of the non-dominant hemisphere.

Because of the low number of operated infants and preschool children, my findings are based on a relatively small population. Therefore I plan to reconsider these statements in a larger patient population.

An appreciation of age- and lobe-specific seizure semiology in infants and young children should facilitate early diagnosis and improve medical and surgical treatment of therapy-resistant epilepsies leading to better neurologic outcome.
6. ACKNOWLEDGEMENTS

I wish to thank Professor Peter Wolf (Epilepsy Center Bethel, Germany) and Dr. Tamás Dizseri (Bethesda Children’s Hospital, Budapest, Hungary) who placed trust in me and rendered my field trip in the Epilepsy Center Bethel possible.

I also gratefully acknowledge my mentors, Dr. Ingrid Tuxhorn (Bethel) and Professor Péter Halász (National Institute of Psychiatry and Neurology, Budapest, Hungary) who supervised my research on childhood seizure semiology.

I am thankful to my bosses: Dr. Magdolna Neuwirth, Dr. Ágnes Herczegfalvi, and Dr. György Velkey (Bethesda Children’s Hospital) who showed me the clear and cordial thinking in pediatrics.

I am also grateful to my co-authors and friends: Dr. József Janszky (Budapest), Dr. László Bognár (Budapest), Dr. Péter Barsi (Budapest), Dr. Márta Hegyi (Budapest), Dr. András Sólyom (Budapest), Dr. János Vajda (Budapest), Dr. Hennric Jokeit (Zürich, Switzerland). Dr. Tom Pieper (Vogtareuth, Germany), and Eduardo Faveret (Rio de Janeiro, Brazil).

All my colleagues at the Bethesda Children’s Hospital, as well as all coworkers of the Epilepsy Center Bethel played an irreplaceable role in my studies. I also wish to thank the patience of my wife, daughters, son, parents, and brothers, who unselfishly helped me during preparing this work.

* * *

I dedicate this work to the memory of Dr. István Kovács (Budapest) and Dr. Hans-Erich Boenigk (Bethel) who taught me the love of sick and challenged children.
7. BIBLIOGRAPHY

7.1 Scientific publications


*Clin Neurosci/Ideggy Szle* 2001;54:89-104.

*Pediáter* 2002;11:5-12.

*Pediáter* 2002 (in press)

7.2 Free papers relating to the topic

1. **Fogarasi A**, Neuwirth M. Presurgical evaluation of epileptic children in the Epilepsy Center of Bethesda Children’s Hospital.  
*Nemzetközi Gyermekgyógyász Társaság XXII. világkongresszusa, Amszterdam, 1997.*

2. **Fogarasi A**. Epilepsziás gyermekek epilepszia sebészeti kivizsgálása Bethelben.  
*Budapest-Bethel Epilepszia Centrum továbbképző program, 2000.*

*Központi Fizikai Kutató Intézet, Budapest, 2000.*
*Magyar Ideg és Elmegyógyászati Társaság Kongresszusa, Budapest, 2000.*

*Magyar Gyermekorvosok Társasága Közép-magyarországi Területi Szervezetének tudományos ülése, Budapest, 2001.*

6. **Fogarasi A.** A PET szerepe a Rasmussen encephalitis korai diagnosztikájában.  
*Budapest-Bethel Epilepsia Centrum továbbképző program, 2001.*

*Magyar Gyermekneurológiai Kongresszus, Esztergom, 2001.*


9. **Fogarasi A.** Neuwirth M. Gyermekkori differenciál diagnosztikai problémák megoldása tartós videó-EEG monitorizálás segítségével (poszter).  

10. **Fogarasi A.** Siegler Zs, Neuwirth M. Videó-EEG monitorizálás gyermekkorban (poszter).  
*Magyar Gyermekorvosok Társasága Közép-magyarországi Területi Szervezetének tudományos ülése, Budapest, 2002.*