Seizure semiology and its changes in temporal lobe epilepsy

Ph.D. thesis

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ABBREVIATIONS

ARBS: Ability to react before seizure

ATLP: Asymmetric tonic limb posturing

CPS: Complex partial seizure

EEG: Electroencephalography

fMRI: Functional MRI

ILAE: International League Against Epilepsy

MRI: Magnetic resonance imaging

MTS: Mesial temporal sclerose

SGTCS: Secondarily generalized tonic-clonic seizures

TLE: Temporal lobe epilepsy

UMA: Unilateral manual automatism

INTRODUCTION

Epilepsy is the second most common neurological disorder. Seizures comprise the main symptomatology of patients with epilepsy. The quality of a patient's life depends in large part on the type of seizures they have.

In this thesis we discuss from different points of view the clinical signs and symptoms of seizures (ictal semiology) of the temporal lobe epilepsy syndrome, which is considered to be the most common type of epilepsy in adulthood. We describe in our literary overview the importance of seizure semiology in epileptology, which is also marked by the evolution of epilepsy classification. With reference to this, we give the definition of **temporal lobe epilepsy (TLE)**.

TLE is considered to be the most frequently occurring epilepsy that can be treated by surgery. We give a brief summary of the aim and the course of the **pre-surgical assessement of epilepsy** and we discuss in detail the information gained through the use of **video-EEG monitoring**, which is considered to be the gold standard in the assessement of seizure semiology, and we will also discuss its application in clinical practice.

Subsequently, we present our three studies (based on the methods of pre-surgical assessement, with video-EEG monitoring included) all of which investigate certain aspects of **seizure semiology of temporal lobe epilepsy**.

In our first study we investigated the pathophysiology of patients' ability to react during the conscious phase of complex partial seizures originating from temporal lobe. We concluded that the ***ability to react before CPS*** is associated with a circumscribed region involved at seizure onset and spread and with a seizure-free postoperative outcome.

In our twice study we analysed ***the lateralising value of unilateral manual automatism (UMA)***, its relation to contralateral dystonia and the hand by which the UMA was performed. We found that the UMA with contralateral dystonia has a high lateralising value to the ipsilateral hemisphere and left-sided UMA without contralateral dystonia has a lateralising value to the left hemisphere. Right-sided UMA without contralateral dystonia has no lateralising value.

We have only limited knowledge about ***changes in seizure semiology during ageing***. In other words, the possibility of clinical progression or regression in epilepsy is unknown. In children, brain maturation significantly influences clinical seizures, resulting in changes in the seizure semiology over time. To our knowledge, no study has investigated these

phenomena in adults yet. In our third, longitudinal study, we investigated whether seizure semiology in temporal lobe epilepsy changed over time and whether surgery had an effect on this change. We concluded that seizure semiology may show some changes over time: psychic aura and oral automatisms became less frequent over time. In patients who underwent surgery, ictal version and ictal unilateral limb cloni occurred less frequently, while psychic aura appeared more frequently over time. We suggest that the clinical picture of epilepsy and epileptic seizures is not static over time even in adult epilepsy, especially if the patient undergoes epilepsy surgery where the changed seizue semiology can be explained by having cut off the pathways for extratemporal seizure spread.

In our three study, all patients had consecutively undergone presurgical evaluations with ictal video-EEG recordings and high-resolution MRI, had had epilepsy surgery (except for six patients in study 3.) due to intractable temporal lobe epilepsy with psychomotor (complex partial) seizures due to unilateral temporal lobe lesions. The clinical assessment, treatment and postoperative controls of patients involved in the investigation were made in the Epilepsy Center Bethel, Bielefeld, Germany. This institution houses one of the highest-standard departments of epilepsy surgery and pre-operative diagnostics in the world (Department of Intensive Diagnostics and Epilepsy Surgery). Throughout its operation - from 1992 until the present day– an extensive, unified and well-recorded patient-documentation procedure has been established, capable of immediately responding to the current demands of modern epilepsy surgery and also the pre-surgical assessement of epilepsy. As such, we intended to draw upon this documentation for the purposes of our study. Scientific processing from which we have gained our topics took place between 2005 and 2007 in the framework of the joint scientific work of our Clinic and the Epilepsy Center Bethel.

I. PATIENT ABILITY TO REACT BEFORE COMPLEX PARTIAL SEIZURES

I.1. Background

Up to ninety-six percent of patients with medial TLE have auras appearing some seconds before the onset of ictal unconsciousness (French et al., 1993). To react during auras is highly important for epileptic patients. The ability to react before seizures of complex partial type (ARBS) may prevent the patients from serious injuries occurring in 30% of drug-resistant epilepsies (Neufeld et al., 1999). During vagus nerve stimulation (VNS) therapy, patients are usually provided with a magnet allowing additional stimulation to be commanded by the patient during aura phase (Boon et al., 2001). The capability of reacting during the conscious phase of seizures is a prerequisite for patients to use additional VNS stimulation by magnet and aura interruption techniques.

I.2. Aims

To our knowledge, no study has systematically investigated the patients' ability to react during the conscious phase of complex partial epileptic seizures. In order to describe clinical features, surgical outcome and understand the pathophysiology of preictal reactivity, we reviewed video-taped seizures of 130 patients and correlated the clinical features with preictal reactivity.

I.3. Patients and methods

Patients

In this retrospective study, we reviewed video-recordings of 130 patients (77 women, aged 16-59, mean age: 34.5±10, mean age at epilepsy onset: 10.9±8) who had consecutively undergone our adult presurgical evaluation program with ictal video-EEG recordings from 1995 to 2002, and had had epilepsy surgery due to intractable medial temporal-lobe epilepsy with video-recorded complex partial seizures (CPS) due to unilateral medial temporal-lobe lesions. Altogether 285 archived seizures were analyzed.

Methods

Patients underwent continuous video-scalp EEG monitoring lasting >2 days. All patients were clearly instructed by the medical staff to push the alarm button if they felt an aura. We defined reaction ability (ARBS) during aura phase before CPS if the patient pushed the alarm button during at least one of his/her recorded seizures. Performing this task requires conscious reaction.

We analyzed whether ARBS was associated with the patients' clinical variables, secondary generalisation, lateralisation of epileptic activity, and seizure-free postoperative outcome.

Statistical methods

For statistical evaluation of categorical variables, Chi-square and Fisher's exact tests were carried out. For analysing age and age at epilepsy onset, independent samples t-test were carried out and for analysis of seizure frequency, the Mann-Whitney U test was used. To identify which variables are associated with ARBS independently, a logistic regression analysis was performed for variables demonstrating a significant effect in univariate analyses. Error probabilities of <0.05 were considered to be significant.

I.4. Results

According to our inclusion criteria, all patients reported that they had auras before their seizures. However, only 77 patients (59%) was able to push the alarm button before their seizures. Patients who pushed the alarm button were significantly younger ($p=0.01$), had lateralised EEG seizure pattern more often ($p=0.04$), had the experience of isolated auras more often ($p=0.01$), and had a better postoperative outcome ($p<0.01$). Patients who did not push the alarm button, had secondarily generalised seizures after the initial complex partial phase more often. This multivariate analysis showed that only the ARBS was associated with the surgical outcome *independently* ($p<0.01$).

I.5. Discussion

We found that patients with ARBS were significantly younger, had lateralised EEG seizure pattern more often, had the experience of isolated auras more often, and had a better postoperative outcome than those who did not. The presence of secondarily generalised seizures showed an association with lack of ARBS. Multivariate analysis revealed that ARBS was independently associated with a lack of secondarily generalised seizures after the initial complex partial phase and with a seizure-free postsurgical outcome, while the other variables were not independent of these variables. The association between ARBS and favourable surgical outcome was independent of other variables supposed to have an effect on surgical results.

Amnesia for auras is associated with bilateral epileptic EEG activity of temporal lobes. The lack of aura experience may be caused by postictal amnesia due to transient bilateral mesiotemporal disturbance (Schulz R et al., 1995). The phenomenon of ARBS is obviously

differs from postictal amnesia; however, we also found that a unilateral seizure pattern showed an association with ARBS, but the bilateral interictal activity did not.

Although preserved consciousness during temporal-lobe seizures with automatism as well as the presence of isolated auras is associated with right-sided seizure activity (Ebner et al., 1995; Janszky et al., 2004), ARBS showed no association with the laterality of epileptic focus, suggesting that the underlying mechanism of ARBS is independent of these phenomena.

Our results suggest that the ARBS is associated with a more circumscribed region involved at seizure onset as we found that it was associated with a lateralised seizure onset. Moreover, ARBS is probably associated with seizure spread because those patients who could react during seizure onset had fewer secondary generalised seizures. This study is in accordance with a recent study that found that consciousness during seizures was usually impaired in patients with bitemporal and left temporal seizure activity (Lux et al., 2002).

We found that ARBS was associated with a seizure-free postoperative outcome. This fact may be very helpful in selecting patients for surgery because the presence of ARBS can probably be extracted during patient history, even before the presurgical evaluation. Our previous studies also demonstrated that seizure semiology has a prognostic value in predicting the postoperative seizure outcome (Boesebeck et al., 2002).

II. UNILATERAL HAND AUTOMATISMS IN TEMPORAL LOBE EPILEPSY

II.1. Background

Hand automatisms is one of the principal characteristics of complex partial (psychomotor) seizures (Commission on Classification and Terminology of the International League Against Epilepsy, 1981) occurring in >80%. In 9-40% of patients, hand automatism occur in one hand only and are called unilateral manual automatism (UMA) (Chee et al., 1993; Fogarasi et al., 2006; Yen et al., 1998; Saygi et al., 1994; Marks et al, 1998).

Although this is one of the most frequently seen unilateral phenomenon during seizures, the lateralising value of UMA is controversial. Some studies did not find it as a reliable lateralising sign (Berkovic et Baldin, 1984), whereas others found it as a sign frequently indicating an ipsilateral epileptic focus (Chee et al., 1993; Fogarasi et al., 2006; Yen et al., 1998; Marks et al., 1998; Wada 1982). Kotagal et al. found UMA to be a lateralising sign to the ipsilateral hemisphere only when it was accompanied by contralateral hand dystonic posturing (Kotagal et al., 1989). It is unclear whether ictal automatisms are caused by spreading ictal epileptic activity (Jasper, 1964; Talairach et al., 1973) or may be considered to be a release phenomenon (Loddenkemper and Kotagal, 2005).

II.2. Aims

In our twice study, we wanted to systematically investigate the lateralising significance of the very frequently seen phenomenon, the manual automatism, in complex partial seizures, and its relation to ictal dystonia and the side of epileptogenic zone. For this purpose, we re-evaluated video-documented seizures looking for the lateralising value of this phenomen, its relation to contralateral dystonia and the hand by which the UMA was performed.

II.3. Patients and methods

Patients

In this retrospective study, we reviewed video recordings of 141 patients (81 women, aged 16-59, mean age 34.1±10, mean age at epilepsy onset 10.9±8.1, mean epilepsy duration 23.2±11) who had consecutively undergone presurgical evaluations with ictal video-EEG recordings from 1995 to 2002, had had epilepsy surgery due to intractable

medial temporal lobe epilepsy with complex partial seizures due to unilateral medial temporal lobe lesions. Only patients who had long-term video-EEG and recorded psychomotor (complex partial) seizures were included. Epilepsy surgery was performed on the left in 76 patients and on the right side in 65.

Methods

Altogether 310 archived seizures were analysed. Patients underwent continuous video-scalp EEG monitoring lasting >2 days. Ictal hand dystonia was defined as sustained unnatural posturing of one upper extremity with a rotational component in the arm during the seizure (Kotagal et al., 1989; Talairach et al., 1973). Hand automatism was defined as involuntary ictal movements of one or two hands such as picking at bedclothes, repetitive movements of fingers, pillrolling, fumbling, grasping, or repetitive raising and lowering of upper extremities (Chee et al., 1993; Yen et al., 1998). If hand automatism occurred in one hand only we defined it as UMA (Chee et al., 1993). Ipsilateral UMA was defined if UMA was ipsilateral to the EF and there were no seizures where the UMA was contralateral to the epileptogenic focus. We categorized UMA as non-ipsilateral UMA if any UMAs occurred in the hand contralateral to the epileptic focus during one of the recorded seizures. Positive predictive value (PPV) indicates the ratio of true positive cases divided by all positive cases. Considering previous studies, true positive cases were defined as ipsilateral UMA.

Statistical methods

For statistical evaluation, binomial, Chi-square and Fisher's exact tests were carried out. Error probabilities of <0.05 were considered to be significant.

II.4. Results

Hand automatism was present in 122 (86.5%) of 141 included patients. UMA occurred in 75 (53%) of 141 patients and in 128 (41%) of 310 seizures. UMA was ipsilateral to the EF in 53 patients (PPV = 75%, $p = 0.001$) and 94 seizures (PPV = 73%, $p < 0.001$). UMA was accompanied by contralateral ictal hand dystonia in 27 patients (19% of all patients and 36% of patients with UMA) and 39 seizures (13% of all seizures and 30% of seizures with UMA). UMA with accompanying dystonia has a PPV = 85% ($p = 0.001$) and PPV = 90% considering seizures ($p < 0.001$). UMA without accompanying dystonia occurred in 48 patients and 89 seizures. UMA without accompanying dystonia has a 63% PPV considering patients ($p = 0.11$, non significant) and 66% PPV considering seizures ($p = 0.003$). Comparing the lateralising value (PPV) of UMA with versus without accompanying dystonia, the difference was significant considering patients ($p = 0.03$) and

seizures (p = 0.006). Thus, we concluded that UMA with accompanying dystonia has a reliable lateralising value, while UMA without dystonia has only limited information as to the side of epileptic focus.

According to our working hypothesis, for the further evaluation we investigated only those patients in whom UMA occurred without dystonia and examined whether its lateralising value depended on which hand was involved: whether the left-sided UMA differed from the rightsided UMA. Comparing the lateralising value (PPV) of left-sided vs. right-sided UMA without dystonia, the difference was highly significant considering patients (p = 0.001) and seizures (p = 0.001).

II.5. Discussion

The origin of ictal manual automatisms is controversial. By stimulating the anterior gyrus cinguli and mesiotemporal structures oral and hand automatisms can be evoked (Jasper 1964; Talairach et al., 1973) indicating that automatisms may be caused by spreading ictal activity. Others suggest that automatisms may be release phenomena during partially disturbed consciousness (Loddenkemper and Kotagal, 2005; Ebner et al., 1995).

We can speculate that the different lateralising values of left versus right UMA may be caused by handedness, such as right-handed patients independent of EF tend to use their right hand in a semipurposeful or purposeless manner during disturbed consciousness and this phenomenon is seen as automatism. This kind of UMA has no lateralising value as it depends on handedness and not on the EF.

We hypothesize that UMA occurring in left hand is probably independent of handedness and lateralises to the left hemisphere as it may be a truly bilateral automatism, but automatisms contralateral to EF are overridden by contralateral ictal paresis as suggested by Kotagal et al. Thus, there may be two mechanism of UMA:

one is caused simply by general hand preference, while the other by contralateral dystonia or paresis (Kotagal et al., 1989). The right-sided predominance of UMA may also support this theory. The non-lateralising nature of right-sided UMA supports the hypothesis that ictal automatisms (or at least one kind of ictal automatism) may be a release phenomenon and not caused directly by the ictal activity.

III. CHANGES IN SEIZURE SEMIOLOGY OF TEMPORAL LOBE EPILEPSY – A LONGITUDINAL VIDEO-EEG STUDY

III.1. Background

We have only limited knowledge about changes in seizure semiology during ageing. In other words, the possibility of clinical progression or regression in epilepsy is unknown. In children, brain maturation significantly influences clinical seizures, resulting in changes in the seizure semiology over time (Fogarasi et al., 2007). To our knowledge, no study has investigated these phenomena in adults yet.

To precisely analyze the changes in seizure semiology, cross-sectional studies may provide only limited data because they cannot demonstrate the clinical changes in the same patient. This problem is compounded by the diversity of epilepsy types as epilepsy is a highly heterogeneous disorder. Conversely, there are only case reports where the changes of seizure semiology was investigated in longitudinal studies because repeated video-recorded seizures at different times in the same patient are extremely rare (Specht, 1994; Seino, 1994; Boas, 1994; Fogarasi et al., 2002). Apart from these case reports, there are no longitudinal studies systematically evaluating the seizure semiology over time.

III.2. Aims

In this longitudinal study, we investigated whether seizure semiology in TLE changed over time and whether surgery had an effect on the seizure semiology if the seizures persisted postoperatively. For this purpose we included those patients who had ictal video recordings at separate times.

III.3. Patients and methods

Patients

We included all patients (1) who underwent our adult presurgical evaluation program due to pharmacoresistant TLE with psychomotor (complex partial) seizures at the Epilepsy Center Bethel between 1990 and 2006; (2) who had at least two separate video-EEG monitoring examinations with ictal recordings; (3) whose two video-EEG monitoring sessions were > 5 years apart; (4) who had no epilepsy surgery between the two monitoring sessions or who had temporal lobe resections within 6 months after the first monitoring.

According to the latter inclusion criteria we divided patients into two groups. The non-surgical group consisted of patients who did not undergo epilepsy surgery while the

surgical group consisted of patients in whom surgery was performed after the first monitoring but the surgery failed.

Methods

Patients underwent continuous video-scalp EEG monitoring lasting 2-10 days. All patients had high-resolution MRI examinations made on 1.5 Tesla Siemens Magnetom MR machines using special protocol for detecting epileptogenic lesions.

If the patients had >2 video-EEG monitoring sessions then we considered the first monitoring session and the last monitoring only and the last monitoring was defined as "second monitoring session" for our study. We defined the semiological manifestations according to previous studies (Wyllie et al., 1986; Kotagal et al., 1989; Bleasel et al., 1997; Leutmezer et al., 1998; Janszky et al., 2000; Janszky et al., 2001).

We investigated the following variables: (1) aura data based on patient self-report (presence of auras, presence of isolated auras, number of different auras, aura types), (2) semiological data based on video inspection (oral and manual automatisms, dystonic posturing, head version, vocalization, limb cloni, postictal nose wiping, presence of secondarily generalized tonic clonic seizures, seizure duration).

Statistical methods

To examine the effects of time and surgery on the dependent variables we implemented generalized linear models with repeated logistic design, which allows for investigation of differences in a binary outcome given that the same subjects are measured at different time points. Time, as a continuous variable, surgery, as a dummy variable, and their interaction term were included in these models. The interaction term referred to the difference in change of the dependent variables over time among operated and non-operated patients, and thus, indicated the effect of surgery. We also used multivariable models with which we adjusted for potential confounders, i.e. age, presence of hippocampal sclerosis, gender, and lateralization of the epileptic focus.

III.4. Results

The Table 4. shows the occurrence and changes of investigated clinical phenomena over time. Psychic aura became less frequent over time. The odds ratio (OR) was 0.89 with an 0.86-0.91 confidence interval (CI), that is, the occurrence of psychic aura decreased by 11% each year. Similarly, oral automatism occurred less often over time; the OR was 0.74 (CI:0.57-0.91). In other words, its frequency decreased by 26% each year.

Table 4. The occurrence of the analyzed variables, their changing over time and the effect of surgery. The interaction term refers to the difference in change of the dependent variables over time among operated and non-operated patients, thus, indicating the effect of surgery. In the multivariable models potential confounders, i.e. age, presence of hippocampal sclerosis, gender, and lateralization of the epileptic focus were controlled. The surgery*time interaction was interpreted as the effect of surgery. The dependent continuous variables (seizure frequency, seizure duration, and number of different aura types) were categorized and analyzed according to their median split.

	Presence during the first monitoring	**Significance level for changes over time in the non-surgical group (p)**		**Significance level for surgery*time interaction (p)**	
		Univariate model	Multivariate model	Univariate model	Multivariate model
Presence of aura	87%	0.22	0.09	0.91	0.90
Presence of isolated auras	73%	0.65	0.64	0.28	0.27
Abdominal auras	57%	0.22	0.35	0.63	0.85
Psychic auras	13%	**<.0001**	**<.0001**[*]	**0.03**	**0.04**[*]
Number of aura types	Median: 1 Range: 0-4	0.71	0.57	0.58	0.49
Oral automatisms	53%	**0.03**	**0.02**[**]	0.10	0.07
Manual automatisms	37%	0.83	0.85	0.48	0.45
Secondarily generalized tonic-clonic seizures	20%	0.19	0.18	0.40	0.38
Ictal dystonia	20%	0.75	0.94	0.69	0.86
Cloni	36%	0.12	0.13	**0.03**	**0.046**[***]
Ictal version	30%	0.12	0.14	**0.009**	**0.02**[****]
Ictal vocalization	17%	0.25	0.14	0.88	0.90
Seizure duration	78±77 sec	0.20	0.16	0.66	0.52
Postictal nose wiping	33%	0.85	0.53	0.50	0.53
Monthly seizure frequency	Median: 9 Range: 2-270	0.53	0.30	0.21	0.10

[*]Psychic aura became less frequent over time. The odds ratio (OR) was 0.89 with an 0.86-0.91 confidence interval (CI). That is, the occurrence of psychic aura decreased by 11% each year. In the surgical group there was a relative increase in psychic auras as compared to the non-surgical group. The OR for surgery*time interaction was 1.19 (CI: 1.01-1.41).

[**] OR=0.74 (CI:0.57-0.91) for oral automatisms

[***] OR=0.80 (CI:0.64-0.99) for cloni in the surgical group

[****] OR=0.75 (CI:0.60-0.95) for head version in the surgical group

There were 30 patients (19 men) who fulfilled the inclusion criteria. Their ages at the first monitoring were 14-54 (mean 28.6±9) years. Epilepsy surgery was performed in 24 patients after the first monitoring, whereas the remaining 6 patients did not undergo epilepsy surgery between the two monitoring sessions. The time between the first and second monitorings spanned 5-14 (mean 8.7±3) years.

We found statistically significant effects of surgery for psychic aura, unilateral cloni, and ictal head version. That is, in the surgical group there was a relative increase in psychic auras compared to the non-surgical group. The OR for surgery' time interaction was 1.19 (CI:1.01-1.41). In the surgical group both cloni and head version showed a relative decrease in occurrence compared to the non-surgical group. The ORs were 0.80 (CI:0.64-0.99) and 0.75 (CI:0.60-0.95) for cloni and ictal head version, respectively (for more details see the Table 4).

We could not detect changes over time or effect of surgery for the following variables: presence of any aura type, presence of isolated auras, number of different auras, presence of gastric auras, manual automatisms, dystonic posturing, vocalization, postictal nose wiping, secondary generalization, or the duration of the seizure (see the Table 4.).

III.5. Discussion

Here we performed the first longitudinal study which systematically analyzes whether seizure semiology changes over time in epilepsy. We investigated patients with adult TLE who had at least two ictal video-recordings in intervals > 5-years. The main finding of our study is that seizure semiology may show some changes over time, especially if the patient undergoes epilepsy surgery. We found that in TLE (1) psychic aura and oral automatisms became less frequent over time, (2) in patients who underwent surgery, ictal version and ictal unilateral limb cloni occurred less frequently, while psychic aura appeared more frequently over time.

Our findings regarding the changes in seizure semiology might suggest that TLE is not a static condition. Indeed, some data suggest that TLE is a progressive disorder. After an initial childhood precipitating injury (for example, febrile seizures), the first unprovoked seizure only appears some years later after a silent period (French et al., 1993; Wieser&ILAE, 2004). After the first unprovoked seizure it takes some additional years for epilepsy to become pharmacologically resistant (French et al., 1993; Berg et al., 2003). Recently, we provided evidence that after pharmacological intractability it takes further years for TLE to become surgically intractable (Janszky et al., 2005). The mechanism whereby chronicity of seizures imparts poor outcome is uncertain, but this may suggest that secondary epileptogenesis at sites distant to the lesion may develop with years of uncontrolled seizures. It is hypothesized that an initial precipitating injury (for example, febrile seizures) causes hippocampal damage, and after this initial damage, a progressive synaptic reorganization takes place in the hippocampus, which progressively evolves into

hippocampal sclerosis and TLE. Moreover, this process does not stop at the development of TLE. Systematic follow-up studies suggest that recurrent afebrile seizures damage the hippocampus (Fuerst et al., 2003; Briellmann et al., 2002).

On the other hand, our data did not indicate a clear progression in the clinical picture because neither the seizure frequency nor its duration changed over time. Moreover, psychic auras and oral automatisms became *less frequent* over time which suggests only a change (a natural course of the disorder) and not a progression.

Seizures in temporal lobe epilepsy (TLE) are characterized by typical auras (mainly gastric or psychic), oral and manual automatisms, or altered consciousness which reflects the activation of temporo-limbic structures (French et al., 1993). However, there are some seizure elements which may be activated due to extratemporal structures such as ictal dystonia involving basal ganglia (Kotagal et al., 1989; Newton et al., 1992), head version involving premotor versive areas (Wyllie et al., 1986), unilateral cloni involving the motor cortex (Janszky et al., 2001) or postictal nose wiping involving the rhinal cortex (Leutmezer et al., 1998). We found that head version and ictal limb cloni became less frequent after temporal surgery, suggesting that even unsuccessful temporal lobe resections may prevent the extratemporal (presumably the frontolateral) seizure spread. Conversely, unsuccessful surgery might not affect the mesiotemporal seizure activity since we could not detect the effect of surgery in seizure elements indicating mesiotemporal activation. Moreover, psychic auras became more frequent postoperatively compared to patients who did not undergo temporal resections.

THESES

I. This is the first study which systematically analyzes the clinical features of the ability to react before seizures of complex partial type (ARBS).

Patients with preictal reactivity were significantly younger, had lateralised EEG seizure pattern more often, and had a better postoperative outcome. Patients, who did not push the alarm button, had secondarily generalised seizures more often.

Ability to react before CPS is associated with a circumscribed region involved at seizure onset and spread and with a seizure-free postoperative outcome.

II. We first demonstrated that UMA could be a lateralizing sign in temporal lobe epilepsy, if occured with contralateral dystonia or in the left hand.

Left-sided UMA without contralateral dystonia has a lateralising value to the left hemisphere. Right-sided UMA without contralateral dystonia has no lateralising value.

III. We performed the first longitudinal study which systematically analyzes whether seizure semiology changes over time in epilepsy. We investigated patients with adult TLE who had at least two ictal video-recordings in intervals > 5-years. The main finding of our study is that seizure semiology may show some changes over time, especially if the patient undergoes epilepsy surgery. We found that in TLE psychic aura and oral automatisms became less frequent over time, in patients who underwent surgery, ictal version and ictal unilateral limb cloni occurred less frequently, while psychic aura appeared more frequently over time.

We suggest that the clinical picture of epilepsy and epileptic seizures is not static over time even in adult epilepsy, especially if the patient undergoes epilepsy surgery where the changed seizue semiology can be explained by having cut off the pathways for extratemporal seizure spread.

LIST OF PUBLICATION

Publications related to the thesis:

I.

Gyimesi C, Fogarasi A, Kovacs N, Toth V, Magalova V, Schulz R, Ebner A, Janszky J. Patients' ability to react before complex partial seizures. *Epilepsy Behav* 2007;10:183-6. **IF:2.026**

II.

Janszky J, Fogarasi A, Magalova V, **Gyimesi C**, Kovacs N, Schulz R, Ebner A. Unilateral hand automatism in temporal lobe epilepsy. *Seizure*, 2006; 15(6):393-6. **IF:1.384**

III.

Gyimesi C, Janszky J, Janszky I, Fogarasi A, Schulz R, Ebner A. Changes in seizure semiology of temporal lobe epilepsy – a longitudinal video-EEG study. *Epilepsy Behav* elbírálás alatt.

Poster presentations:

Gyimesi C, Janszky J, Fogarasi A, Schulz R, Ebner A. Are There Any Changes in Seizure Semiology over Time? – A longitudinal Video EEG Study.
60th Annual Meeting of American Epilepsy Society, December 1-5, 2006, San Diego, USA

Gyimesi C, Janszky J, Janszky I, Fogarasi A, Schulz R, Ebner A.
Changes in seizure semiology of temporal lobe epilepsy - a longitudinal video-EEG study.
1st International Epilepsy Colloquium, Marburg, Germany, Jun 22-25, 2008

Publications unrelated to the thesis:

1. Spike Frequency is Dependent on Epilepsy Duration and Seizure Frequency in Temporal Lobe Epilepsy
   Janszky J, Hoppe M, Clemens Z, Janszky I, **Gyimesi C**, Schulz R, Ebner A
   Epileptic Disorders 2005; 7(4):1-5. IF:1.074

2. Distribution of Spatial Complexity of EEG in Idiopathic Generalized Epilepsy and Its Change After Chronic Valproate Therapy
Kondakor I, Toth M, Wackermann J, **Gyimesi C**, Czopf J, Clemens B
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3. Peri-ictal vegetative symptoms in temporal lobe epilepsy
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6. Brain lateralization and seizure semiology: ictal clinical lateralizing signs
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