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# Postoperative routine EEG correlates with long-term seizure outcome after epilepsy surgery

**Michelle Hildebrandt** [a], **Reinhard Schulz** [b], **Matthias Hoppe** [b], **Theodor May** [c], **Alois Ebner** [b,*]

[a] *Friedrich-Alexander University, Department of Neuropathology, Erlangen, Germany*
[b] *Bethel Epilepsy Centre, Clinic Mara, Department of Presurgical evaluation, Maraweg 21, 33617 Bielefeld, Germany*
[c] *Epilepsy Research Foundation, Bielefeld, Germany*

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**Summary** We investigated the correlation of interictal epileptiform discharges (IED) in routine EEG 6 and 24 months after epilepsy surgery with regard to long-term seizure outcome. In 148 patients (74% temporal lobe epilepsy (TLE), 26% extratemporal epilepsy) EEG results (IED present or absent) were correlated with the postoperative outcome using the Engel classification 6 and 24 months after resection (PO6m and PO2y, respectively). Self-evaluation was conducted 3 and 5 years after resection (PO3y and PO5y, respectively). Ninety-one patients (62%) were seizure-free 5 years after resection; 88% of them showed no IED in PO6m. Twenty-eight patients (19%) displayed IED in routine EEG 6 months after resection; 61% of them had recurrent seizures at PO5y, whereas of 120 patients without IED only 33% had recurrent seizures at PO5y; $p = 0.01$.

Absence of IED in PO6m and PO2y correlated with good outcome: 71% without IED remained seizure-free, whereas only 25% with IED at PO6m and PO2y remained seizure-free; $p = 0.001$.

Seizure-free patients (Engel 1) and patients with less favourable outcome (Engel 3–4) at PO6m and PO2y rarely changed categories of outcome during the following years ($p < 0.001$). Half of the patients with favourable seizure reduction (Engel 2) changed to seizure-free (Engel 1) or to a worse outcome category (Engel 3–4).

Postoperative routine EEG is a good prognostic instrument for the prediction of long-term seizure outcome, especially for TLE. It predicts the running up and down of fits in patients with rare seizures (Engel 2).


* Corresponding author. Tel.: +49 521 144 3400.
*E-mail address:* alois.ebner@evkb.de (A. Ebner).

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## Introduction

Follow-up studies in epilepsy surgery help to find predictive values and aid in advising patients in issues such as work, driving licence, family planning and discontinuation of antiepileptic drugs.[1,2]

Several studies investigated predictive factors for seizure outcome after epilepsy surgery. There are well-known preoperative predictors for good seizure outcome, for example, unilateral interictal epileptiform discharges IED,[3–6] detected lesions in the MRI,[3] hippocampal sclerosis[4,5] or tumor[7] as etiology, febrile convulsions in the history[5] and, regarding seizure semiology, complex partial seizures.[8] Generalised IED before or after resection were associated with worse outcome.[8] The absence of postoperative IED and no seizure in the first postoperative year correlate with good seizure outcome.[4,9] Persistence of IED after resection, as well as persistence of seizures longer than 2 months after resection[3,8] predict worse outcome.[10–14] Other factors such as electrocorticography (ECoG),[12] completeness of resection[7,14] age and duration of the epilepsy,[9] and etiology[9] were controversially discussed.

Most studies about the predictive value of postoperative EEG findings are about temporal lobectomy, because temporal epilepsy (TLE) is the focal epilepsy treated surgically most frequently.

McIntosh et al.[15] reviewed 126 articles about predictors after temporal lobectomy: good outcome was associated with preoperative hippocampal sclerosis, anterior temporal localisation of preoperative IED, absence of preoperative generalised seizures and absence of seizures in the first postoperative week. The presence of postoperative IED was associated with worse outcome. According to McIntosh, other factors such as the etiology or resection technique had inconsistent results in various studies.

Some studies compared the predictive value of postoperative IED after temporolobectomy with extratemporal resection.[9,13,14] Isolated studies about the outcome after extratemporal resections are rare. Boesebeck et al.[16] investigated the outcome after parietal resection and Janszky et al.[17] analysed frontal lobe resections. They found that the postoperative EEG is predictive for the postoperative seizure outcome.

Based on these findings we investigated the status of the postoperative routine EEG for the long-term seizure outcome. Other factors such as the localisation of the lesion (temporal versus extratemporal) and the etiology were also included.

Another important question addressed the stability of the early seizure outcome after 6 months over a period of 5 years, especially as to whether there were predictors of the so-called running up or down of seizures.[1,18]

## Methods

### Patient selection

We analysed follow-up data from patients involved in our epilepsy surgery program suffering from medically intractable partial epilepsy who underwent localised resection from the beginning of our programme in 1991 to 1996. In 148 patients there was reliable and complete data with respect to EEG-records and seizure outcome over a period of 5 years. The percentage rate of incomplete data was 10% due to inconsistent documentation in the first 2 years. Only patients aged 14 or older at the time of resection were included. Average at resection was 30.6, with a range from 14 to 57 years. Eighty (60%) patients were male.

### Data collection

General data such as the age at resection, sex and date of resection were collected. Our postoperative evaluation was standardised and contained two short clinical in-patient investigations 6 and 24 months after resection. At the first follow-up after 6 months (PO6m), routine EEG, MRI, clinical, neuropsychological, social and psychiatric examination were carried out. The second follow-up (PO2y) included another EEG and further clinical and social evaluation. If necessary, an additional MRI, psychiatric or neuropsychological examination could be conducted. Finally, we classified the seizure outcome with the Engel classification scale at the end of the two in-patient examinations (preliminarily at PO6m and finally at PO2y). The patients received a standardised questionnaire 3 (PO3y) and 5 (PO5y) years after resection. This included questions about seizure outcome, taking antiepileptic drugs and the quality of life. The questionnaire allowed only the possibilities ''seizure-free'' or ''recurrent seizures'' and ''auras present'' or ''absent''. Seizure-free was defined as seizures absent or auras only for 12 months and more. Further, we used preoperative video-EEG data and MRI findings, the resection protocol and the histological findings to define the localisation and etiology.

### EEG

Routine digital EEG (18 channels) lasting about 25 min including provocation with hyperventilation and photostimulation. The initiation of sleep was

desired but not demanded. The electrodes were placed following the 10-20-system including additional temporal electrodes (FT9/FT10) of the 10-10-system. Certified electroencephalographers interpreted the results (American board: AE, MH; German board: RS). We only defined sharp waves or spikes as interictal epileptiform discharges (IED) excluding slowing and breach rhythm which are regular findings in postoperative routine EEGs.

### Statistical methods

The statistical evaluation was performed using the Statistical Package for the Social Sciences (SPSS). For statistical analysis (extended) Fisher's exact tests and tests for trend (Cochran-Armitage test for linear trend) were performed. If not mentioned otherwise, two-sided tests were used and $p$-values $<0.05$ were considered as significant.

## Results

Ninety-one (62%) of 148 patients remained seizure-free 5 years after resection. One hundred and ten (74%) patients had TLE and 38 (26%) an extratemporal epileptogenic focus. Table 1 shows the distribution of localisation. The rate of seizure-free patients was higher in patients with TLE (64%) versus extratemporal epilepsy (55%), but this was insignificant (Table 2).

**Table 1** Frequency distribution of localisation.

| Localisation | $n$ | Percentage |
|---|---|---|
| Temporal | 110 | 74 |
| Frontal | 18 | 12 |
| Parietal | 4 | 3 |
| Occipital | 3 | 2 |
| Multifocal | 13 | 9 |
| Total | 148 | 100 |

**Table 2** Comparison between TLE and extratemporal localisation: rate of seizure-free patients 5 years after resection.

| Outcome | TLE | ExtraTL | Total |
|---|---|---|---|
| Seizure-free | 70 (64%) | 21 (55%) | 91 |
| Recurrent seizures | 40 (36%) | 17 (45%) | 57 |
| Total | 110 | 38 | 148 |

Not significant; Fisher's exact test, $p = 0.440$.

Twenty-eight patients had IED in the first EEG of whom 17 (61%) had seizures 5 years after resection, whereas of 120 patients without IED in the first EEG only 40 (33%) had seizures.

The relationship between the presence or absence of IED and the outcome was significant ($p = 0.01$).

The presence of IED at PO6m and PO2y was also significantly associated with outcome ($p = 0.001$; Table 3): 12 of 16 patients (75%) with IED at PO6m and PO2y had recurrent seizures at PO5y, whereas only 30 (29%) out of 103 patients without IED in PO6m and PO2y had recurrent seizures.

Separate analyses for different etiologies (Table 4) and localisation (temporal versus extratemporal) revealed no statistical significant relationship between presence or absence of postoperative IED and seizure outcome 5 years after resection. The major reason is probably the small number of cases with IED.

We classified the seizure outcome with the Engel classification scale at PO6m (preliminarily) and PO2y (finally). Between PO6m and PO2y, seizure-free patients (Engel 1) and patients in the worse outcome category (Engel 3–4) rarely changed their categories of outcome:

Eighty-six (87%) of 99 Engel 1 classified patients at PO6m did not change categories at PO2y, as was true for 24 (83%) of 29 Engel 3–4 classified patients ($p < 0.001$).

In contrast patients with good outcome but rare seizures (Engel 2) had a high tendency of changing categories between PO6m and PO2y:

Ten (50%) of 20 Engel 2 classified patients at PO6m did not change, but 5 (25%) changed to seizure-free (Engel 1) and 5 (25%) worsened (Engel 3–4).

**Table 3** Correlation between IED in routine EEG 6 months and 2 years after resection and seizure outcome 5 years after resection.

| IED | Seizure-free after 5 years, $n$ (%) | Not seizure-free after 5 years, $n$ (%) | $n$ (%) |
|---|---|---|---|
| Never | 73 (71) | 30 (29) | 103 (70) |
| At 6 month only | 7 (58) | 5 (42) | 12 (8) |
| At 2 years only | 6 (38) | 10 (62) | 16 (11) |
| Both dates | 4 (25) | 12 (75) | 16 (11) |
| Total | 90 (61) | 57 (39) | 147 (100) |

Fisher's exact test, $p = 0.001$.

**Table 4** Frequency distribution of etiology.

| Etiology | *n* | Percentage |
|---|---|---|
| Hippocampal sclerosis | 71 | 48 |
| Focal cortical dysplasia | 24 | 16 |
| Tumor | 33 | 22 |
| Other | 20 | 14 |
| Total | 148 | 100 |

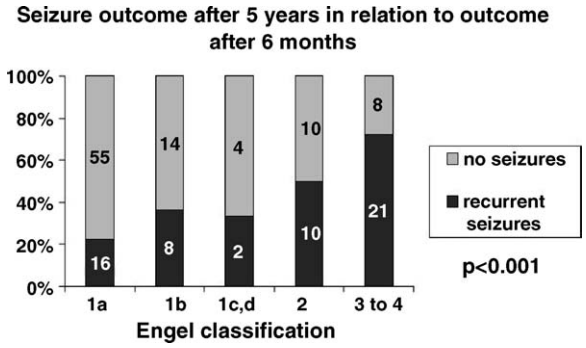


**Figure 1** Stability of seizure outcome 6 months and 5 years after resection (Fisher's exact test, $p < 0.001$).

Over the period of 5 years we saw similar results: Most of the seizure-free patients (Engel 1a—d) continued to be seizure-free and patients in the outcome category Engel 3—4 continued to have recurrent seizures 5 years after resection ($p < 0.001$). One-half of the patients with rare seizures (Engel 2) changed to the seizure-free category, the second-half worsened significantly (Fig. 1).

For the group with rare seizures, presence or absence of IED in PO6m and PO2y was predictive: 8 (75%) patients without IED at PO6m and PO2y became seizure-free after a period of 5 years. Four (100%) patients with IED at PO6m and PO2y worsened to frequent seizures ($p = 0.026$, one-sided test of trend) (Fig. 2).

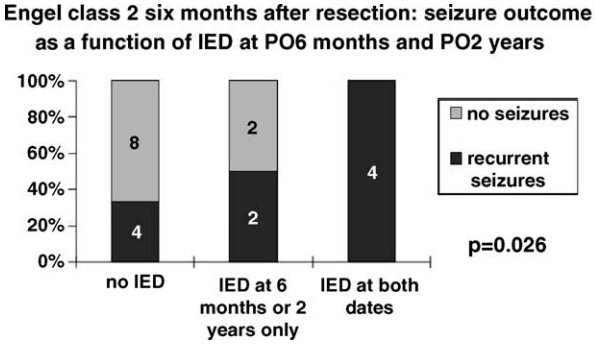


**Figure 2** Correlation of long-term seizure outcome of patients with favourable outcome (Engel 2) with interictal IED in PO6m and PO2y ($p = 0.026$, one-sided test of trend).

## Discussion

In our study we found the postoperative routine EEG to be a good prognostic instrument for the prediction of long-term seizure outcome, especially for TLE and FCD.

The outcome 6 months after resection remained stable over a follow-up period of 5 years.

Moreover, the presence or absence of postoperative IED predicts the running up and down of seizures in patients with rare seizures (Engel 2) after resection.

The percentage of seizure-free patients in our study (62% for all patients, 64% in patients with TLE, 55% with extratemporal epilepsy) is comparable to other investigations.[8,17] Our literature research predominantly included studies about temporal lobectomy.[7,8,15,18—21] Studies including extratemporal resections showed lower rates.[9,13,17] The definition of seizure freedom differed: The required seizure-free interval varied from 6 months[14,22] to 2 years.[23] Very common is the use of the category 1a—d of the Engel classification scale, allowing simple partial seizures, auras alone and seizures with medication withdrawal.[7,9,20] Especially the inclusions of occasional seizures with medication withdrawal poses methodological problems because drug levels and drug intake are mostly monitored in patients with seizure relapses but not in seizure-free patients. Consequently in our study, patients with seizures after drug reduction were classified as non-seizure-free. Velasco et al.[8] only defined the absence of seizures without antiepileptic medication as being completely seizure-free.

The correlation between postoperative IED and seizure outcome was investigated by several other authors.[4,7—17,24—26] Most authors found a significant correlation between postoperative IED and worse seizure outcome,[7,8,10—15,17,25] suggesting an incomplete resection of the epileptogenic zone. On the other hand, the absence of postoperative IED corresponded to good seizure outcome.[4,9,16]

All authors only regarded IED as postoperative EEG abnormalities, except for Patrick et al.[13] who included focal slowing. Patrick showed that focal slowing and IED together were more predictive for the seizure outcome than each factor alone. We excluded focal slowing because it is a common finding in the postoperative EEG caused by lost tissue and gliosis after resection and craniotomy, making it difficult to differentiate between normal and pathological focal slowing.

Methodology also differed in other aspects. The EEG duration varied from 20 min to 2 h in other investigations.[14,24] Hyperventilation was usually used as a method of provocation. Only Tuunainen

et al.[12] demanded sleep deprivation in the postoperative routine EEG and a more invasive EEG technique with sphenoidal electrodes. The first EEG took place postoperatively varying from 3 months[4,7–9] to 6 months[14] with controls after 12 and 18 months.[14,15]

The low percentage of 19% of all patients showing IED in the postoperative EEG corroborated Godoy et al.'s[14] findings of IED in 20% of patients. Patrick et al.[13] and Gates et al.[24] found IED in 71% and in 80% in the first postoperative EEG.

A reason for the low rate of postoperative IED in our study could be the predominance of TLE, which usually shows rare interictal IED in comparison to the frequent spiking in FCD[17] which is more often represented in extratemporal epilepsy.

Other studies showed that the early seizure outcome was relatively stable over a long-term follow-up period. Lüders et al.[22] found that the outcome 6 months after resection is predictive for the long-term seizure outcome. Other authors determined 1 year[4] or 2 years[20,21] as the follow-up period for the prediction of long-term seizure outcome.

Over a long follow-up interval, the rate at which patients are seizure-free decreases. In a review of 126 articles McIntosh et al.[15] found 70% of patients seizure-free after the second postoperative year compared to 52% after 5 years, similar to results found by Rougier and Salanova.[5,6,18] Seizure recurrence is possible after very long seizure-free periods. Paillas et al.[27] described relapses after 11–19 years of seizure freedom. However, the likelihood of seizure relapses decreases with the duration of the seizure-free period.[1,22] On the other hand, the possibility of developing repeated seizures increases, the earlier the first postoperative seizure appears.[20]

The group with rare seizures after resection (Engel 2) requires special comment. Fifty percent of patients in this group eventually became seizure-free in our study showing a high correlation with the EEG findings (Figs. 1 and 2). Postoperative running up and down of seizures has been described previously.[1,5,11,18,23]

To our knowledge our investigation is the first to show the role of the postoperative IED for the prediction of long-term seizure outcome in patients with rare seizures.

Other factors predictive for the running up and down of seizures in patients with TLE were reported by Salanova et al.[5]: the likelihood of becoming seizure-free was higher in patients with febrile convulsions in their history, preoperative unilateral IED and a young age at resection. Predictors for worse outcome were posterior lesions, a large lesion, head trauma or encephalitis in the history and preoperative bilateral IED.

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