Insular lesionectomy for refractory epilepsy: management and outcome

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Surgical treatment of deep-seated insular lesions causing refractory epilepsy is thought to be difficult due to the complicated accessibility and close proximity of eloquent areas. Here we report our experience with insular lesionectomies. Twenty-four patients (range 1–62 years, mean 27) who underwent epilepsy-surgery for a lesion involving the insular region, were identified from the epilepsy surgery data bank. We analysed pre-surgical diagnostics, surgical strategy and postoperative follow up concerning functional morbidity and seizure outcome (range 12–168 months, mean 37.5). Eight patients had pure insular lesions, in 16 cases the lesion extended either to the frontal (n = 3) or temporal lobe (n = 8) or was multilobar (n = 5). Sixteen resections (66.7%) were done on the right side. Six patients required invasive EEG-recording, three patients received intra-operative electrocorticography. In seven patients only subtotal resection of the insular lesion was possible due to involvement of eloquent areas. Thirty patients suffered from glial/glioneural tumours (WHO grades I–III), 11 from non-neoplastic lesions. Postoperatively, one patient had a hemihypesthesia and one patient had a deterioration of a pre-existing hemiparesis; two patients had a hemianopia as calculated deficit (mild permanent morbidity 16.6%). According to the ILAE-classification, 15 patients were completely seizure free (62.5%, ILAE 1). Around 79.2% had satisfactory seizure outcome (ILAE 1-3). In selected patients an individually tailored lesionectomy of insular lesions can be performed, which is acceptably safe and provides a high rate of satisfactory seizure relief. Even subtotal resection can result in good seizure control.

Keywords: insular lobe; epilepsy surgery; seizure outcome

Abbreviations: EEG = electroencephalogram; ILAE = International League against Epilepsy; LAO = Last available outcome; MRI = Magnetic resonance imaging; NF = Neurofibromatosis; PET = positron emission tomography; SPECT = Single photon emission computed tomography; WHO = World Health Organization

Introduction

Although there have been rapid advances in imaging and surgical techniques in the last two decades, epilepsy surgery of the insula is not generally accepted as a treatment option. Operative strategies and outcome results from surgically treated patients with epilepsy due to insular lesions are mostly presented as case reports or in very small series (Roper et al., 1993; Cukiert et al., 1998; Duffau and Fontaine, 2005; Duffau et al., 2006; Kaido et al., 2006). The largest series report was of 11 patients suffering from epilepsy due to low-grade gliomas (Duffau et al., 2002). Little is known about long-term seizure outcome after insular lesionectomies. Semiology of seizures generated by insular lesions is often described as similar to temporal (Isnard et al., 2000) and frontal (Ryvlin et al., 2006) semiology. Nevertheless, there are some specific characteristics of insular seizures like vegetative, viscero- and...
somatosensory symptoms (Isnard et al., 2004; Rossetti et al., 2005; Britton et al., 2006; Catenoix et al., 2008) according to the complex physiology and extensive connections of the insular cortex (Bamiou et al., 2003; Frot and Mauguiere, 2003; Krolak-Salmon et al., 2003). On the other hand some aspects of temporal lobe seizures may be related to an involvement of the insular cortex (e.g. an epigastric aura). For a complete functional and anatomical review we refer to articles of Shelley and Ture et al. (1999), Duffau et al. (2000), Trimble (2004) and Tanriover et al. (2004).

The close connections with other potentially epileptogenic areas like temporomesial structures or the frontal/central cortex can be considered as a reason for misleading findings in electrophysiological and imaging investigations (Isnard et al., 2000; Bouilleret et al., 2002; Isnard et al., 2004). The distance of the insular cortex to the surface and the overlying cortex lead to imprecise results of surface EEG recordings or even of subdural EEG. Thus, the implantation of depth electrodes is preferred by some investigators to evaluate an involvement of the insular cortex (Isnard et al., 2004; Nguyen et al., 2008).

We report our experience with pre-surgical work-up, surgical techniques, functional and seizure outcome in patients suffering from refractory focal epilepsy due to insular lesions.

Methods

Patients

Out of the 2010 patients who underwent resective epilepsy surgery in the Bonn Epilepsy Surgery Program between 1989 and September 2007, we identified 24 patients who suffered from medically intractable epilepsy originating from the insular cortex. We reviewed the pre- and postoperative data for medical history, pre- and postoperative neurological status, semiology and frequency of pre and postoperative seizures, pre- and—if available—postoperative MRI-findings and pre- and intra-operative electrophysiological results.

Preoperative procedures

Pre-surgical work up was performed as previously described (Clusmann et al., 2006) with simultaneous video-EEG-recording, high-resolution MRI (Urbach, 2005) and neuropsychological assessment (Helmstaedter, 2004). All seizures recorded during surface-EEG-video-monitoring were categorized following EEG data by an epileptologist (J.W., Table 1) and semiology was classified for this study with respect to the particularities of insular seizures (J.W., Table 2). In cases with only rudimentary documentation of EEG or semiology, the original tapes were reviewed (J.W.).

Wada tests (Wellmer et al., 2005) and fMRI (Weber et al., 2006) were performed to identify speech dominance in 11 and 2 patients, respectively.

Surgery and histopathology

Operative details included side and extent of the resection (pure insular or extending to adjacent regions). Histopathological examinations were performed according to a routine protocol for epilepsy cases (Wolf and Wiestler, 1993). Tumours were classified according to the revised WHO classification (Kleihues and Sobin, 2000). Different types of dysplastic cortical malformations were grouped together as cortical dysplasias. For lesions with clear-cut features of focal cortical dysplasias (FCD Ila/Ilb) we used the classification of Palmini and Lueders (2002).

Follow up

Follow-up information regarding seizure outcome and neurological status was obtained from the last regular yearly outpatient visit or from standardized telephone interviews (M.v.L.). Patients were assigned to six different outcome classes according to the ILAE classification (Wieser et al., 2001). Patients were classified annually after surgery, so that changes over time could be documented. To describe an overall outcome, the last available outcome was considered. For the purpose of statistical analyses, the seizure outcome classes ILAE 1–3 were grouped together representing satisfactory outcome

Table 2 Classification of insular seizure semiology (initial symptoms)

<table>
<thead>
<tr>
<th>Class</th>
<th>Leading semiological features at seizure onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Viscerosensory or emotional or undetermined,</td>
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<tr>
<td></td>
<td>including the experience of fear</td>
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<tr>
<td>2</td>
<td>Somatosensory</td>
</tr>
<tr>
<td>3</td>
<td>Motor</td>
</tr>
<tr>
<td>4</td>
<td>Auditory</td>
</tr>
<tr>
<td>5</td>
<td>Visual</td>
</tr>
<tr>
<td>6</td>
<td>Vegetative</td>
</tr>
<tr>
<td>7</td>
<td>Initial loss of consciousness without further precision</td>
</tr>
</tbody>
</table>

Table 1 Categories of ictal surface-EEG data acquired according to the international 10–20 system

<table>
<thead>
<tr>
<th>EEG category</th>
<th>Main focus of ictal rhythmic activity at seizure onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Temporo-mesial</td>
<td>T1, T3, F7 with phase reversal over T1–T3 or T3a</td>
</tr>
<tr>
<td>B Fronto-temporal</td>
<td>As above, but additionally F3, Fp1a or Fz</td>
</tr>
<tr>
<td>C Frontal/fronto-central</td>
<td>F3, F7, Fp1a, Fz or Cz</td>
</tr>
<tr>
<td>D Temporo-occipital/-parietal</td>
<td>T1, T3, T5, O1a</td>
</tr>
<tr>
<td>E Occipital/parieto-occipital</td>
<td>O1, P3a</td>
</tr>
<tr>
<td>F Diffuse/generalized amplitude suppression</td>
<td>Diffuse, not localizable ictal rhythmic activity or bilateral ictal rhythmic activity; general amplitude suppression</td>
</tr>
<tr>
<td>G No surface-EEG, no ictal EEG-correlate or artefacts only</td>
<td></td>
</tr>
</tbody>
</table>

a Or right hemispheric equivalents.
and classes ILAE 4–6 represented unsatisfactory outcome, similar to previous studies (von Lehe et al., 2006).

**Statistics**

Dichotomous discrete variables were analysed using the chi-squared test or Fisher’s Exact test. A P-level of 0.05 was accepted for the indication of statistical significance in two-tailed testing.

**Results**

**Demographic and clinical parameters**

Mean age at operation was 27 years (range 1–62), 15 were female (62.5%), 16 (66.7%) resections were done on the right side; mean duration of epilepsy prior to surgery was 7 years (range 1–55); mean follow up after surgery was 37.5 (range 12–168) months. Patients’ data are summarized in Table 3.

Two patients had previous resections for insular tumours (oligodendroglioma WHO II in both cases) and two other patients suffered from neurofibromatosis (NF Type 1, ganglioglioma WHO I and pleomorphic astrocytoma WHO III, respectively).

Four patients suffered from mental retardation (three patients with dysplastic lesions and one with gliosis as histopathological diagnosis) and one had a mild hemiparesis preoperatively due to a perinatal Rhesus-factor incompatibility and intracerebral fronto-insular haemorrhage (histopathological diagnosis: gliosis).

**Pre- and intra-operative procedures**

At least one seizure was recorded—mostly with surface EEG—in all but one patient. In this case, with oligodendroglioma and a low seizure frequency (three per year), no seizure was recorded preoperatively. Invasive EEG-monitoring with subdural and/or depth electrodes were applied in six cases (25%), five times after non-invasive video-EEG, and in one case without antecedent surface video-EEG. Depth electrodes were inserted into the suspected lesion in four cases; in one additional patient, the depth electrode was close to the lesion but not within. Intra-operative electrocorticography (ECoG) was used in three patients (12.5%).

Neuronavigation was used in seven cases (29%) and intraoperative electrophysiological monitoring (continuous MEP/SEP recording and phase reversal) in 12 cases (50%).

In case of additional temporal resection (eight patients, 33%), the temporomesial structures were included in four patients.

**Electrophysiological and semiological findings**

Locations of the lesion, according to the preoperative MRI, and seizure origin, to be detected in surface-EEG, were not closely correlated. Of 21 patients with surface-EEG seizure recording, 12 did not show a clear seizure origin (in three patients no surface-EEG data were available). In the remaining, there were five temporomesial EEG-patterns, two fronto-temporal, one fronto-central and one temporo-occipital pattern. Most (seven of nine) of the circumscribed EEG-seizure onsets were found in patients with temporo-insular lesions, and one in a fronto-temporo-insular and a pure insular lesion each. Vice versa, six of seven patients with temporo-insular lesions and surface EEG-recording had a circumscribed seizure origin. Most patients with seizure recording and with pure insular (six of seven), fronto-insular (three of three) or fronto-temporo-insular lesions (two of four) had seizures without clear onset in EEG (diffuse seizure origin, artefacts, or no ictal patterns in EEG despite absence of artefacts).

The most frequent symptoms were those of Class 1 (viscerosensory, emotional or undetermined, including the experience of fear, n = 13). Two patients initially experienced somatosensory symptoms. Motor symptoms were the first experienced or detected in six patients (one patient had both Class 1 and 3 seizures). Auditory or visual phenomena (combined with motor symptoms) were described by one patient. None of the patients in our series reported vegetative phenomena as the initial symptom (Class 6). Three patients had initial loss of consciousness and no further specified symptoms (Class 7).

Class 1 symptoms were not exclusively described by patients with extension of the lesion into the temporal lobe: four out of seven pure insular lesions, one out of two fronto-insular lesions, three out of four fronto-temporo-insular lesions and five out of eight temporo-insular lesions were characterized with initial Class 1 semiology. Somatosensory symptoms (Class 2) were reported by one patient with pure insular, and one with temporo-insular lesions. Motor symptoms (Class 3) were found in two patients with pure insular, and each one with temporo-insular, fronto-insular or fronto-temporo-insular lesions. Auditory (Class 4) and visual (Class 5) phenomena were reported by two patients with temporo-insular lesions.

**Morphological and functional imaging**

In all cases, a circumscribed structural lesion was detectable on preoperative MRI (Table 4, see Figures 1–3). Four of the eight temporo-insular lesions involved the temporo-mesial structures and one lesion of the temporo-insular lesions extended into the basal ganglia. One of the two patients with a cavernoma had multiple supra- and infratentorial cavernomas.

Five of eight patients with lesions in the left hemisphere and 7 of 16 patients with a lesion in the right hemisphere had further investigations for speech dominance [Wada-test (n = 11) and/or fMRI (n = 2)]. Additional PET- or SPECT-imaging were performed in five and one patients, respectively.

Two patients with a lesion in the presumed dominant left hemisphere were not able to cooperate for these procedures. If the clinical data was not suggestive for an atypical speech-dominance in the right hemisphere further investigations were not considered.

**Surgical procedures**

Two thirds of the insular resections were in the right hemisphere, but two of these had a right dominance for speech representation. Six of the eight resections in the respective dominant hemisphere were pure insular or temporo-insular. In one case of additional frontal resection in the dominant hemisphere, brain mapping with an implanted grid-electrode of the eloquent area (Broca
<table>
<thead>
<tr>
<th>Pat Nr</th>
<th>Sex</th>
<th>Age</th>
<th>Dur</th>
<th>Location</th>
<th>Inv.</th>
<th>Side</th>
<th>Classification of initial semiology</th>
<th>Category of ictal surface EEG</th>
<th>Appr</th>
<th>OP</th>
<th>Postoperative course</th>
<th>FU (months)</th>
<th>ILAE (LAO)</th>
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<td>R</td>
<td>1, 3</td>
<td>F</td>
<td>tc</td>
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<td>7</td>
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<td>–</td>
<td>R</td>
<td>1</td>
<td>A</td>
<td>ts</td>
<td>Lx (w AH)</td>
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</tr>
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<td>F</td>
<td>4</td>
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<td>Insular</td>
<td>–</td>
<td>–</td>
<td>7</td>
<td>F</td>
<td>ts</td>
<td>subtotal resection</td>
<td>164</td>
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<td>S, G</td>
<td>L</td>
<td>4</td>
<td>G</td>
<td>ts</td>
<td>Lx (w/o AH)</td>
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<td>S, D</td>
<td>L</td>
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<td>A</td>
<td>ts</td>
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<td>M</td>
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<td>–</td>
<td>R</td>
<td>1, 5</td>
<td>A</td>
<td>tc</td>
<td>Lx (w/o AH)</td>
<td>Hemianopia (calculated deficit)</td>
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<td>R</td>
<td>1</td>
<td>G</td>
<td>ts</td>
<td>Lx</td>
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<td>L</td>
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<td>A</td>
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<td>Transient dysphasia and HP</td>
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<td>G</td>
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<td>L</td>
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<td>G</td>
<td>tc</td>
<td>Lx</td>
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<td>2</td>
<td>F</td>
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<td>Lx (w/o AH)</td>
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<td>R</td>
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<td>F</td>
<td>tc-ts</td>
<td>subtotal resection, transient HP</td>
<td>Hemianopia (calculated deficit), transient HP</td>
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<tr>
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<td>9</td>
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<td>ECoG</td>
<td>R</td>
<td>7</td>
<td>F</td>
<td>tc-ts</td>
<td>subtotal resection</td>
<td>Transient HP</td>
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<tr>
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<td>ECoG</td>
<td>L</td>
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<td>B</td>
<td>tc</td>
<td>Lx</td>
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<td>D</td>
<td>R</td>
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<td>F</td>
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<td>Lx</td>
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<td>D</td>
<td>R</td>
<td>3</td>
<td>C</td>
<td>ts</td>
<td>Lx (w AH)</td>
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<td></td>
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<td>R</td>
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<td>G</td>
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<td>12</td>
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<td>L</td>
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<td>D</td>
<td>ts</td>
<td>Lx (w/o AH)</td>
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<td>ts</td>
<td>Lx</td>
<td>Second OP for completion of Lx</td>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

**Dur** = Duration of epilepsy in years; **EEG** = Electroencephalogram; **Inv.** = Invasive EEG-Diagnostics, **S** = Strip-electrode(s), **G** = Grid-electrode(s), **D** = Depths-electrode(s), **ECoG** = Intra-operative Electrocorticography; **Appr** = Approach, **tc** = transcortical, **ts** = transsylvian; **Lx** = Lesionectomy, **AH** = Amygdalal hippocampectomy; **HP** = Hemiparesis; **FU** = Follow up period; **ILAE LAO** = Last available outcome according to the ILAE classification.

a For definition of classification of semiology and EEG categories see Table 1.
b For definition of classification of semiology and EEG categories see Table 2.
and primary motor cortex) was carried out. The other patient (4 years old, epilepsy since third month of life, mentally retarded) had a large fronto-temporo-insular dysplasia in the presumed Broca area. Due to his young age at seizure onset, we hypothesized a transfer of speech representation.

The transsylvian approach was used to resect seven of eight pure insular lesions. In one patient the lesion was in the posterior insular cortex, covered by the parietal operculum. In this case we chose a combined transsylvian-transcortical (parietal) approach.

In case of pure insular lesions we performed a lesionectomy in different parts of the insular cortex in seven of eight cases: Four patients had resections in the posterior part and three in the anterior part of the insular cortex. A 1-year-old boy with a catastrophic seizure situation (hundreds of seizures per day) and a dysplastic lesion of the whole insular cortex had an ‘insular lobectomy’ via a transsylvian approach. Post operation he had nocturnal seizures only (ILAE4) and continues to develop well.

Seven of eight patients with temporo-insular lesions were operated via a transsylvian approach including all four patients with additional temporomesial resections. With multilobular involvement (five patients with fronto-temporo-insular lesions) the lesions were resected via a transcortical approach, in one case combined with a transsylvian approach.

Table 4 Location and extension of the lesions derived from MRI

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
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</thead>
<tbody>
<tr>
<td>Pure insular</td>
<td>8 (33.3)</td>
</tr>
<tr>
<td>Fronto-insular</td>
<td>3 (12.5)</td>
</tr>
<tr>
<td>Temporo-insular</td>
<td>8 (33.3)</td>
</tr>
<tr>
<td>Fronto-temporo-insular</td>
<td>5 (20.8)</td>
</tr>
<tr>
<td>n</td>
<td>24 (100)</td>
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In general, we always aimed to perform complete lesionectomies plus extension to include a rim of surrounding epileptogenic cortex. Complete lesionectomies were achieved in 17 cases. In 12 patients an extended lesionectomy was possible. However, due to widespread lesions or involvement of eloquent areas, complete removal or relevant extension was not possible in 12 cases. The reason for incomplete resection \((n=7)\) was involvement of the basal ganglia \((n=3)\), the peri-rolandic cortex \((n=3)\) or primary speech areas \((n=1)\), respectively.

With complete lesionectomy 13 of 17 patients became seizure-free \(76.5\%\), ILAE1) and with additional extension 9 of 12 patients had complete seizure control \(75\%\), ILAE1), whereas only two of seven patients with subtotal resection were completely seizure-free \(29\%\); six of seven had satisfactory seizure outcome \(86\%\), ILAE1-3).

### Histopathology

The results of histopathological examination are summarized in Table 5. Five patients with dysplastic lesions had focal cortical dysplasias (four FCD IIb and one FCD IIa) (Palmini and Luder, 2002). One patient harboured a grey–white-matter differentiation abnormality.

Beyond two dysembryoplastic neuroepithelial tumours (DNTs) and six gangliogliomas (WHO I) we found five other typical long-term epilepsy-associated neuroepithelial tumours (Luyken et al., 2003): Two oligoastrocytomas (WHO I/II), one astrocytoma (WHO II/III), one oligodendrogloma (WHO II/III) and one pleomorphic xanthoastrocytoma (WHO III).

### Postoperative morbidity

In one of 24 patients a pre-existing hemiparesis was slightly aggravated and one patient suffered from a new hemihypesthesia (together 8.3%). Two patients suffered from a calculated hemianopia which had been preoperatively discussed with the patients. Taken together, the rate of mild permanent morbidity was 16.7%. Temporary morbidity, which had resolved before discharge from hospital, was noted in two patients \(8.3\%\): two mild hemiparesis, in one case combined with transient aphasic symptoms.

There was no statistical correlation between side, age, extent of resection or site of the lesion and postoperative morbidity. One of six patients with pure insular lesion had a hemihypesthesia. One patient with a temporo-insular lesion of the dominant hemisphere suffered from a transient dysphasia. The other three patients with temporary or permanent morbidity (except the two with hemianopia) had an involvement of the frontal lobe.

There was one postoperative aseptic inflammatory meningeal response.

### Seizure outcome

Seizure outcome, according to the ILAE-classification, is summarized in Table 6 (last available outcome, LAO): 79.2% of the patients had a satisfactory seizure outcome (ILAE1-3). Less favourable results were achieved in five patients \(20.8\%\), ILAE 4). However, all patients had some benefit with respect to seizure control.

After 4 years, outcome data were available from 12 patients: satisfactory seizure outcome was found in 10 cases \(83.3\%). After 8 years, six of nine remaining patients \(66.6\%)\) had a satisfactory seizure situation.

There was no statistically significant correlation between side and location with seizure outcome. However, \(75\%\) of the patients with pure insular lesions had excellent seizure control postoperatively \(6\) patients ILAE 1 and 2 patients ILAE 4). All patients with (fronto-)temporo-insular resections, without hippocampal involvement, became seizure free \(5\) patients, ILAE 1). On the other hand, two of the four patients who underwent temporo-insular resections with amygdalal hippocampectomy had unsatisfactory seizure outcome (ILAE 4) and one patient continued to have auras (ILAE 2). With multilobar involvement, only two out of five patients \(40\%)\) became seizure free. The others still have seizures \(ILAE 3 and 4\), respectively). The three patients with fronto-insular resections had excellent seizure outcome \(ILAE 1 or 2\).

Even with subtotal resection seizure, six of seven patients achieved satisfactory seizure control \(ILAE 1–3\): two patients were seizure-free, two suffered from auras only and one has up to three seizure days per year.

Potentially predictive parameters like age, duration of epilepsy or histopathological results had no influence on seizure outcome.

### Discussion

Focal epilepsy due to an insular lesion is rare: 1% of the patients who underwent resective procedures in our epilepsy surgery...
program harboured an insular lesion. However, the exact number of patients who had insular lesions, but were not referred to surgery or in whom the resection was offered but refused by the patients can not be determined *post hoc*. The precise reasons for refusing a surgical intervention cannot be identified due to the retrospective character of the study.

**Preoperative management**

Allocating the epileptogenic zone in the insula is challenging. In our study, neither ictal surface EEG nor seizure semiology showed features delineating insular seizure origin with sufficient certainty against temporal or frontal lobe seizure origin. We did not find typical semiological criteria for insular epilepsy. There are some reports of patients with frontal (Duffau et al., 2006; Ryvlin et al., 2006) or temporal (Cukiert et al., 1998) semiology who were seizure free after insular lesionectomy. Nevertheless, other studies proved insular epileptogenic discharges with invasive EEG-recording in a patient presenting with ictal vomiting (Catenoi et al., 2008) or in a patient presenting with ictal dysgeusia and contralateral somatosensory phenomena (Rossetti et al., 2008). Isnard et al. (2004) describes typical insular stereotype semiology in a group of patients with laryngeal constriction and paresthesias.

The reason why some patients with circumscribed (or extended) insular lesions do not show clear insular semiology may lie in the extensive connections of the insular cortex and rapid spread of seizure activity to surrounding structures. The fact that, with insular epilepsy, different kinds of semiology occurred points to different networks in which the insular cortex is involved [fronto-mesial/temporo-mesial (limbic) and perisylvian] (Isnard et al., 2008). The fast spread of ictal rhythmic activity in extensively connected anatomical structures like the insula may lead to an overestimation of the size of the seizure onset zone and therefore to unnecessary large resection in this critical surrounding. On the other hand, failure of epilepsy surgery might be caused in an unrecognized insular focus (Nguyen et al., 2008).

Even subdurally implanted grid or strip electrodes cannot sufficiently contribute to the localization of the seizure onset zone located in the deep-seated insula. Proof of insular seizure origin is only possible via depth electrode placement. Isnard et al. (2000) studied 21 patients with multiple transopercular depth electrodes for the invasive pre-surgical work-up, one third with non-lesional MRI. These patients represented a subgroup of patients suffering from temporal lobe epilepsy and had some clinical or electrophysiological signs of insular lobe involvement. Most patients in their study showed insular propagation from a temporal focus. After different kinds of temporal resections, 14 patients had an excellent seizure outcome (66.7% Engel Class I). The two patients with unsatisfying outcome (Engel Class IV) were those in whom pre-operative evaluation had shown seizures originating from insular cortex. Consequently, the authors draw the conclusion that additional ‘insulectomy’ would be needed for optimal surgical results.

Our preoperative approach in insular epilepsy was different. Our aim was to identify potentially epileptogenic lesions with high-resolution MRI (currently 3.0 Tesla). If no lesion could be detected visually, we performed MRI postprocessing (Huppertz et al., 2005). If a lesion was detected, our aim was to verify that seizure semiology and ictal, as well as interictal EEG-data, support—or at least do not contradict—the assumption of a peri-lesional insular seizure origin. If features consistent with insular seizure origin were detected, a resective strategy was worked out. In cases with two or more alternative seizure onset hypotheses, invasive recordings were performed including at least one depth electrode targeting the insular lesion.

The fact that all MRI showed a clear lesion explains the low rate of supplementary imaging procedures. PET and SPECT were used only in exceptional cases for the confirmation of an insular seizure origin. Patients with suspected cryptogenic, i.e. non-lesional insular epilepsy, have so far not been considered as candidates for epilepsy surgery at our centre. In this case we usually recommend awaiting future improvement of imaging techniques. We do not implant vagal-nerve-stimulators in patients with non-lesional MRI with focal epilepsy since this prevents future high-field MRI.

**Intra-operative approach**

One of the major targets in epilepsy surgery is to resect not just the lesion but also a rim—about 8–10 mm—of the surrounding epileptogenic cortex area. However, a so-called ‘extended’ lesionectomy in the insular cortex is mostly limited to a few millimetres. This is clearly different compared to epilepsy surgery in other areas.

For circumscribed insular lesions and most tempo-insular lesions (especially with involvement of temporomesial structures) the transsylvian approach was appropriate. We used the transcortical approach with frontal and multilobular involvement of the insular lesion, in some cases in combination with a transsylvian approach.

Increasing use of tools like neuronavigation or continuous intra-operative electrophysiological monitoring contributes to the prevention of surgical morbidity (Neuhold et al., 2007). 50% of the patients were operated with intra-operative electrophysiological monitoring, especially with frontal or central involvement. Additionally, we increasingly use neuronavigation, which is very helpful for deep-seated and not well-defined lesions.

In the future, further developments of imaging techniques like DTI and functional MRI and their fusion with neuronavigation will contribute to identify eloquent areas and important fibre bundles.

**Functional outcome**

In our series, permanent morbidity was 8% (one patient with slightly aggravated hemiparesis and one with hemihypesthesia) and temporary morbidity was observed in 8% of the patients. Furthermore, two hemianopias (8%) occurred as calculated deficits. Taken together, postoperative deficits were mild and well tolerated by the affected patients.

There is no data available concerning functional outcome in a larger group after surgery for insular lesions. After resection for tumours of the insula an immediate postoperative (not necessarily permanent) morbidity between 20% (94 patients with 101 resections; Simon et al., in press) and 45.5% (Duffau et al., 2002) is reported. Neuhold et al. (2007) report that, in their series of
72 patients harbouring insular gliomas of different extent and histopathological grade, 18.1% transient mild or moderate paresis and 9.7% permanent impairment postoperatively. One has to keep in mind that the surgical strategy for tumour-resections is different from resections for epileptogenic lesions, especially because of the larger size and infiltrating character of most tumours.

Depending on the location of the epileptogenic lesion patients have to be informed in detail about possible deficits after the operation. They should be able to balance the chance for seizure relief and the limitations due to calculated deficits.

## Follow up and seizure control

The mean follow up in this study was 37.5 months and all patients had at least a 12 month follow up period.

Of the patients, 62.5% became completely seizure-free (ILAE I, LAO) and more than three quarters achieved a satisfactory seizure situation (ILAE1-3). In the largest series reported thus far (Duffau et al., 2002), 9 of 11 patients with low-grade gliomas and medically intractable epilepsy achieved good seizure outcome (81.1% Engel Class I). As in our study, satisfactory seizure outcome was possible even with subtotal resection in six of seven patients.

We recently analysed our experience with microsurgical resections for insular gliomas (Simon et al., in press). Preoperative seizures (mostly not drug-resistant) occurred in 83 patients (82%). One-year epileptological follow up was available for 56 patients, of which 43 (78%) were seizure-free or had only occasional, non-disabling seizures (according to Engel Class I).

In comparison with other studies, concerning seizure outcome after epilepsy surgery for non-insular lesions (Table 7), our results are better for frontal resections (Jeha et al., 2007; Elsharkawy et al., 2008) but similar to those after temporal resections (Clusmann et al., 2002; Salanova et al., 2002) and similar to ‘posterior’ resections (Dalmagro et al., 2005; Binder et al., 2008). The meta-analysis of Tellez-Zenteno et al. (2005) revealed a long-term rate of seizure freedom of 66% after temporal lobe resections and 46% after parietal and occipital resections. The rate of complete seizure relief after frontal lobe resections in this review was only 27%. However, most of the studies contributing to this meta-analysis were performed before availability of high-field MRI (≥1.5 Tesla). Therefore, these data are certainly outdated and may not mirror the long term perspective of modern, image-guided epilepsy surgery.

We conclude that in selected patients, epilepsy surgery for insular lesions is acceptably safe. Although the extent of the perilesional resection is restricted and the number of subtotal resections is substantial, the rate of satisfactory seizure outcome is surprisingly high. Surgical therapy for insular lesions is therefore a promising option and should be considered. Our study can contribute to an understanding of insular epilepsies and the critical evaluation of the surgical treatment option.

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## References


