Quest for the „best“ – approaches to mesial temporal lobe structures

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Department of Neurosurgery, University of Bonn, Germany
Domains related to surgery for MTLE

Patient and epileptic disorder

Operation

Psychiatric „Depression“

Seizure Control

Neurological and Cognitive Outcome

psychosocial development
familial and social integration
perspective: school and job
AEDs
Extent of resection
AH or ATL
Neuropsychological concepts
Criteria „what to resect“

- **Main goal:** enough resection for complete seizure relief
  - i.e. total removal or disconnection of the „epileptogenic zone“
- **but preserve as much (cognitive) function as possible**

**Structures, which should be resected for MTLE:**

- **Hippocampus (length of resection ?)**
- **Amygdala**
- **Parahippocampus (with entorhinal cortex and subiculum)**
  - + temporal pole ? + lateral temporal neocortex ?

- **Critical choice of technique and approach ?**
Extent of mesial Resection has an impact...

- more HC resected in 43 ATL and resection of entorhinal cortex
  ➔ better seizure control (Columbia and Campinas)
    (Bonilha L. et al, Epilepsia 48:571-578, 2007)

- larger resection in 204 SAH (Parahippocampus !)
  ➔ better seizure control (Zürich)
    (Siegel AM. et al., Epilepsy Res. 6:56-65, 1990)

- more resection in all compartments
  ➔ better seizure control (Cleveland)

- total HC resection better than anterior HC resection (Seattle)
Extent of mesial Resection has no impact...

- most failures due to wrong diagnosis, but not dependent on the extent of resection (Montreal)
  

- the length of hippocampal resection is not important per se, but tailoring to intraoperative electrocorticography (Seattle)
  

⇒ data from literature equivocal!
Differential Benefits?

Pole resection + AH

Especially **figural** memory worse after **right** sided operation

**Probably dependent on approach, not hippocampus?**

Trans-sylvian AH

Especially **verbal** memory worse after **left** sided operation

Neuropsychological and Seizure Outcome depending on Hippocampal Resection Length - an ongoing randomized prospective trial

3 participating centers
(J.Schramm – Bonn, J.Zentner - Freiburg, T.Lehmann - Berlin)

randomisation for length of mesial resection (2.5 vs. 3.5 cm)

250 – 350 patients are planned, ATL and SAH allowed

all have pre and postop neuropsychological exam and pre-and postop volumetric MRI

214 cases enrolled, 398 volumetric MRIs

Results not available yet
ATL or SAH ...

- equal seizure control with ATL and SAH for MTLE (Montreal)
  

- no differences for MTLE (Bonn)
  

- ATL better than SAH in children (Bonn)
  

- most important: Resection of Amygdala
  

→ at least very similar seizure control rates
Hypothesis

Standard or limited resection strategies for TLE

Anterior temporal lobectomy (ATL)
Amygdalohippocampectomy (AH)
Lesionectomy/corticectomy (LX)

lead to different results?

→ seizure control
→ cognitive outcome
→ QOL

Goldstein, Polkey 1993; Gleissner et al. 2002
Change of Resection Strategy

Standard ATL

Differentiated limited Resections

Change of Paradigm

Standard ATL ➔ differentiated limited Resections
## Extent of resection and seizure outcome

<table>
<thead>
<tr>
<th>Procedure</th>
<th>N (官司)</th>
<th>N (%)</th>
<th>N (官司)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATL</td>
<td>98</td>
<td>78 (80)</td>
<td>20 (20)</td>
</tr>
<tr>
<td>AH</td>
<td>138</td>
<td>115 (83)</td>
<td>23 (17)</td>
</tr>
<tr>
<td>LX w AH</td>
<td>27</td>
<td>20 (74)</td>
<td>7 (16)</td>
</tr>
<tr>
<td>LX w/o AH</td>
<td>58</td>
<td>50 (86)</td>
<td>8 (14)</td>
</tr>
<tr>
<td>All</td>
<td>321</td>
<td>263 (82)</td>
<td>58 (18)</td>
</tr>
</tbody>
</table>

Differences not significant

Simplified concept of cognitive function I

Lat: short-term or working memory
immediate recall
verbal learning

Mes: long-term retrieval/consolidation
delayed free recall

Tests: VLMT, AVLT

Results after different left-sided resections

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>short-term</th>
<th>long-term</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATL N=22</td>
<td>immediate recall ↓</td>
<td>delayed recall ↓</td>
</tr>
<tr>
<td>AH N=21</td>
<td>„stable“</td>
<td>delayed recall ↓</td>
</tr>
<tr>
<td>Lat. Lx N=16</td>
<td>stable</td>
<td>stable</td>
</tr>
</tbody>
</table>

⇒ Different **qualitative** effects on verbal memory

## Verbal performance postop

<table>
<thead>
<tr>
<th>Verbal</th>
<th>improved</th>
<th>stable</th>
<th>deteriorated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>ATL</td>
<td>83</td>
<td>18 (22)</td>
<td>29 (35)</td>
</tr>
<tr>
<td>AH</td>
<td>126</td>
<td>21 (17)</td>
<td>66 (52)</td>
</tr>
<tr>
<td>Lx w AH</td>
<td>24</td>
<td>8 (33)</td>
<td>9 (38)</td>
</tr>
<tr>
<td>Lx w/o AH</td>
<td>52</td>
<td>8 (15)</td>
<td>28 (54)</td>
</tr>
</tbody>
</table>

*p < 0.05 compared to other resection types

Simplified concept of cognitive function II

Right: Figural / visual memory

no differentiation
mesial and lateral

Test: serial design list learning

Attention: side unspecific

Test: symbol counting time
score of a maze test

Lamberti 1999, Gleissner et al. 1998
## Attention and visual performance postop

<table>
<thead>
<tr>
<th>Attention</th>
<th>improved</th>
<th>stable</th>
<th>deteriorated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>ATL</td>
<td>83</td>
<td>27 (33)*</td>
<td>45 (54)</td>
</tr>
<tr>
<td>AH</td>
<td>126</td>
<td>56 (44)</td>
<td>61 (49)</td>
</tr>
<tr>
<td>Lx w AH</td>
<td>24</td>
<td>10 (42)</td>
<td>13 (54)</td>
</tr>
<tr>
<td>Lx w/o AH</td>
<td>52</td>
<td>25 (48)</td>
<td>23 (44)</td>
</tr>
</tbody>
</table>

*p < 0.05 compared to other resection types

### Visual Performance

<table>
<thead>
<tr>
<th></th>
<th>all</th>
<th>N (%)</th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>all</td>
<td>285</td>
<td>81 (28)</td>
<td>120 (42)</td>
<td>84 (30)</td>
</tr>
</tbody>
</table>

With no significant differences between resection types

QOL
Challenge: extent of resection!

Too extended

- too much cognitive deterioration ➔ less QOL ?!

"just right"

- good seizure control
- no unnecessary cognitive impairment
- better QOL ?!

Not extended enough

- insufficient seizure control ➔ less QOL ?!
## QOL after Surgery for MTLE (128 of 140)

<table>
<thead>
<tr>
<th>ILAE</th>
<th>[% of best values]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
</tr>
<tr>
<td>83 in 1</td>
<td>83</td>
</tr>
<tr>
<td>13 in 2</td>
<td>79</td>
</tr>
<tr>
<td>14 in 3</td>
<td>79</td>
</tr>
<tr>
<td>11 in 4</td>
<td>69</td>
</tr>
<tr>
<td>6 in 5</td>
<td>57</td>
</tr>
<tr>
<td>1 in 6</td>
<td>47</td>
</tr>
</tbody>
</table>

von Lehe M et al. Epilepsy Behav. 2006
Postop Changes in QOL-Trends (N=128)

Relative Change in QoL Score

Seizure outcome [ILAE Classification]

von Lehe M et al. Epilepsy Behav. 2006
Collateral Damage
Early postoperative MR: Resection
Early postop MR: „collateral damage“

9 mm „affected brain“

22 mm „affected brain“
MR lesion and verbal memory

Helmstaedter et al. JNNP: 75:323-326, 2004
Correlation: „Collateral Damage“ and Memory

<table>
<thead>
<tr>
<th>Verbal memory and lateral temporal function</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Learning</td>
<td>p = 0.03</td>
</tr>
<tr>
<td>Immediate recall</td>
<td>p = 0.05</td>
</tr>
<tr>
<td>➔ Stronger than effects of side!</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Verbal memory and mesial functions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No effect of (col)lateral damage</td>
<td></td>
</tr>
<tr>
<td>Deterioration of delayed recall with:</td>
<td></td>
</tr>
<tr>
<td>OP left</td>
<td>p = 0.05</td>
</tr>
<tr>
<td>Preoperative performance</td>
<td>p = 0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Figural memory deterioration</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>collateral damage and right sided surgery</td>
<td></td>
</tr>
<tr>
<td>(F=5.9, p = 0.02)</td>
<td></td>
</tr>
</tbody>
</table>

Helmstaedter et al. JNNP: 75:323-326, 2004
Early MR signal changes are not only "edema"

correlate with defects in the later course

approx. 50% of the "affected brain" transforms into a "persisting lesion" (r=0.41, p < 0.05)
Complications
Complications of mesio-temporal resections

• Symptomatic postop hemorrhage 3.8% (Clusmann et al. 2004)

• Infection 1-2%

• “Manipulation hemiplegia” (1-2%, but typical after manipulation, injury or spasm of the Arteria choroidea anterior)
  – Hemiparesis, Hemianopia

• Vasospasm (esp. after transsylvian AH) (Schaller et al. 2004)

• Death (below 1%)
Ischemic complications

Especially after mesio-temporal resections, formerly „manipulation hemiplegia“

12 choroidal infarctions (2.8%) with 422 temporomesial surgeries

often hemianopia and moderate hemiparesis
Ischemic complications after SAH
Differentiated limited Resections for MTLE

- Promising selectivity, but success strongly depending on the correctness of the diagnosis!
- Surgery technically difficult
  - Collateral Damage
  - mesial Structures, Choroidal Arteries
  - Extent of Resection?
- Chances
  - Seizure Control!
  - Preservation of cognitive abilities!
  - Quality of Life?
- Which approach to choose for SAH?
Different approaches to AH
Different approaches for SAH from Duvernoy and Yaşargil
Approaches to mesial temporal structures

- Transsylvian¹

- Transcortical²

- Subtemporal³


Transsylvanian approach (right)
Incision into the temporal stem at the Limen
Amygdala and temporal horn of ventricle
Hippocampal Fissure, Arachnoid, PCA
Posterior Disconnection
Hippocampal en-bloc Resection
Transsylvian or transcortical AH?

Randomized prospective trial 1999-2001

140 adult patients operated with either a transsylvian or transcortical approach for amygdalohippocampectomy

Results:

**Verbal Memory** - significant losses in all domains after left sided surgery (p<0.001)

**Figural memory** - overall unchanged

**Attention** - improved significantly (p=0.005)

Lutz, Clusmann et al. Epilepsia, 2004
Transsylvian or transcortical AH?

Cognitive results mainly not dependent on approach.

Executive functions mainly unchanged, except for postoperative improvements in verbal fluency after transcortical AH only (p=0.003), other factors like seizure control, verbal IQ, drugs etc. not significant as covariates

➔ Improvement of frontal lobe function?

Lutz, Clusmann et al. Epilepsia, 2004
Verbal Fluency pre - postop

Lutz et al. Epilepsia, 2004
Benefit of basal / subtemporal approach?

- Improved verbal memory, preservation of temporobasal language areas, elevated glucose metabolism ipsilaterally extratemporal and temporal
  

- Potential complications: venous injury, retraction

- Anterior T3-approach as alternative?
Usefulness of Optic-Tract Fiber-Tracking for mesial temporal surgery

Thudium M, Campos A, Urbach H, Clusmann H
Objective: avoiding visual field defects

- Mesial temporal surgery (Selective Amygdalohippocampectomy) - High risk of visual field defects (ca 50% !)

- Possible solution: Navigated DTI fiber tracking of Meyer’s loop, basal temporal approach
transsylvian approach
subtemporal/basal approach
Method: DTI Fiber Tracking

- T1, T2, FLAIR, DTI Sequences
- Segmentation of Ventricle + Hippocampus
- DTI-Fiber Tracking, 2 ROIs: Roof of Temporal Horn, Calcarine Sulcus

Retraction and Corticotomy
Entry into Ventricle
Intraoperative aspect with HUD

- Intraoperative Visualisation: Navigation + Microscope HUD
- Basal approach: subtemporal, basal transcortical
Later: Discrepancy Reality vs. Navigation!
En-bloc Mobilization und Resection
Dissection of vessels in hippocampal fissure
Hemostasis
Results

- n=10 Patients underwent selective Amygdalohippocampectomy, n=2 transcortical T3, n=8 subtemporal trans-fusiform gyrus
- 8/10: no postoperative visual field defect
- 2/10 deficits:
  n=1 transcortical: minimal scotoma,
  n=1 subtemporal: incomplete quadrantanopia (retraction?, infarction?, not approach-related?)
Discussion

- Significant visual field deficits (quadrantanopia) reported in 37%\(^1\) and 53%\(^2\) of cases, minor deficits 78%\(^3\) ➞ our series: only 10% relevant deficits
- Consistent with previous fiber dissection studies: Entry into temporal horn from a basal direction spares optic tract fibers\(^4,5\)
- Interindividual variation of Meyer’s loop\(^1,2,4,5\): DTI-Fiber-tracking allows tailored approaches + intra-op guidance
Discussion - References


Usefulness of basal approaches

- DTI fiber tracking is useful for preoperative approach planning and intraoperative visualization
- Basal temporal approaches might prove to be superior to other approaches regarding post-OP visual field deficits and cognitive outcomes
- Larger prospective series are needed
Different Age Groups

Children

Elderly
Better seizure control in younger patients

Plasticity in young and adult Patients

Verbal Memory: Learning Capacity after left TL Resection

<table>
<thead>
<tr>
<th></th>
<th>preop</th>
<th>postop 3</th>
<th>postop 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td>46</td>
<td>38*</td>
<td>45</td>
</tr>
<tr>
<td>Adults</td>
<td>44</td>
<td>30*</td>
<td>33*</td>
</tr>
</tbody>
</table>

*P<0.05 vs preop

Gleissner U et al. Brain 128: 2822-29, 2005
Gratifying cognitive outcomes in children

Resection on right:
- significant improvements regarding verbal memory (p=0.008) and attention (p=0.038)
- type of procedure without effects

Resection on left:
- significant improvements regarding visual memory (p=0.015) and attention (p=0.031)
- some deterioration especially after left AH

⇒ no significant differences between procedures
⇒ Overall: better results compared to adult series

Clusmann H et al. Neurosurgery 54 : 847-860, 2004
Seizure outcome in 83 Children

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>satisfactory</th>
<th>unsatisfactory</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATL</td>
<td>33</td>
<td>31 (94%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>AH</td>
<td>25</td>
<td>19 (76%)</td>
<td>6 (24%)</td>
</tr>
<tr>
<td>Lx</td>
<td>25</td>
<td>22 (88%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>all</td>
<td>83</td>
<td>72 (87%)</td>
<td>11 (13%)</td>
</tr>
</tbody>
</table>

Outcome [Engel 1987] vs Outcome (Engel 1993)

Clusmann H et al. Neurosurgery 54: 847-860, 2004
Multifactorial Analysis - N=89 Kids

- Predictive Factors (Logistic Regression):
  - Side: „left“ worse (p=0.017)
  - Procedure: „selAH“ worse (p=0.021)

→ SAH „too selective “ for childhood-M?TLE ?

- Excluded Factors:
  - Gender, Histology, Med. History, Febrile Seizures, Seizure Type and – Frequency, MR-Diagnosis

Clusmann H et al. Neurosurgery 54 : 847-860, 2004
Hippocampal sclerosis and atrophy + ???
<table>
<thead>
<tr>
<th>Seizure Control Old vs Young [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engel I</td>
</tr>
<tr>
<td>Age ≥ 50</td>
</tr>
<tr>
<td>Old n=52</td>
</tr>
<tr>
<td>Age &lt; 50</td>
</tr>
<tr>
<td>Young n=451</td>
</tr>
<tr>
<td>p value Fisher’s test = 0.17</td>
</tr>
</tbody>
</table>

Grivas et al. Epilepsia, 2006
Only minor changes after surgery observed, but...

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal Memory</td>
<td>29.4%</td>
<td>50.0%</td>
<td>5.9%</td>
<td>14.7%</td>
</tr>
<tr>
<td>Visual Memory</td>
<td>35.3%</td>
<td>47.1%</td>
<td>5.9%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Attention</td>
<td>8.8%</td>
<td>29.4%</td>
<td>20.6%</td>
<td>35.3%</td>
</tr>
</tbody>
</table>

**Neuropsychological Score:**

0 (far below average) – 5 (far above average)

Grivas et al. Epilepsia, 2006
Conclusion

complete seizure control

and

preservation of cognitive and higher function

Neuropsychological profile and individual expectations

influence choice of surgical strategy

Consider all potential factors

⇒ Surgical decision makes a difference!
Task List for MTLE Surgery

• do not wait too long and encourage operating on children
• carefully choose the adequate surgical approach and use the chances of limited resections
• „superselective“ resections in the future?
• improve surg. techniques to diminish collateral damage and approach related morbidity
• critically evaluate the potential of radiosurgery ?? and hippocampal DBS
• Multimodal analysis of outcome incl. QOL
hdcw

iueh
hdcw

iueh
MRI early after right AH
Ischemic complications after SAH
Pseudohypoxic Brain Swelling

17 cases, multiple institutions
variable severity of symptoms
4 fatal cases (24%), 4 complete recovery (24%)
CT / MR – hypointensity of basal ganglia and thalamus
probably due to intra/postoperative CSF-loss
For example via suction drains

Van Roost et al, Neurosurgery, 2003
Pseudohypoxic Brain Swelling
**Modified Engel’s Classification**

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>no seizures, except auras</td>
<td>satisfactory</td>
</tr>
<tr>
<td>II</td>
<td>rare seizures (≤ 2 / yr)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>improvement in seizure frequency &gt; 75%</td>
<td>unsatisfactory</td>
</tr>
<tr>
<td>IV</td>
<td>improvement in seizure frequency &lt; 75% or worsening</td>
<td></td>
</tr>
</tbody>
</table>

ILAE classification of postop seizure control

Class 1 (completely seizure free, no auras)

Class 2 (only auras)

Class 3 (1-3 seizure days / year, ± auras)

Class 4 (4 seizure days / year to 50% reduction)

Class 5 (< 50% reduction)

Class 6 (increase)

on a yearly basis, lao = last available outcome