

Neuropsychology in Epilepsy-Surgery

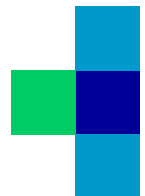
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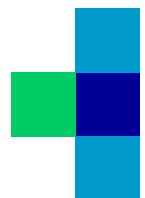


Neuropsychology in Epilepsy-Surgery

Basic principle: comprehensive neuropsychological test inventory examining a wide array of relevant cognitive functions. Results are only interpretable in the context of the whole profile.

Profile of specific dysfunctions contrasting with normal functions: which cortical area may be functionally impaired?

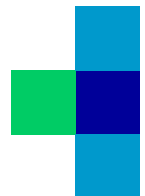
- Focus - localization
- Assessment of risk
- Evaluation
 - Searching for optimal treatment decisions
- Scientific research
 - Unique insight into functional anatomy



Neuropsychology in Epilepsy-Surgery

Focus – localization

- Are the cognitive deficits consistent to a known structural lesions / epileptic focus?
- Do the specific cognitive deficits refer to other or additional brain areas of dysfunction.
- Hints pointing toward an atypical hemispheric dominance?



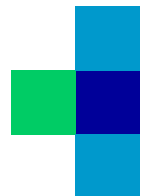
Neuropsychology in Epilepsy-Surgery

Assessment of risk

In surgical treatment of epilepsy, the **goal** is to treat the patient not only symptomatically, but also to save his **cognitive abilities**.

With respect to risk the questions are:

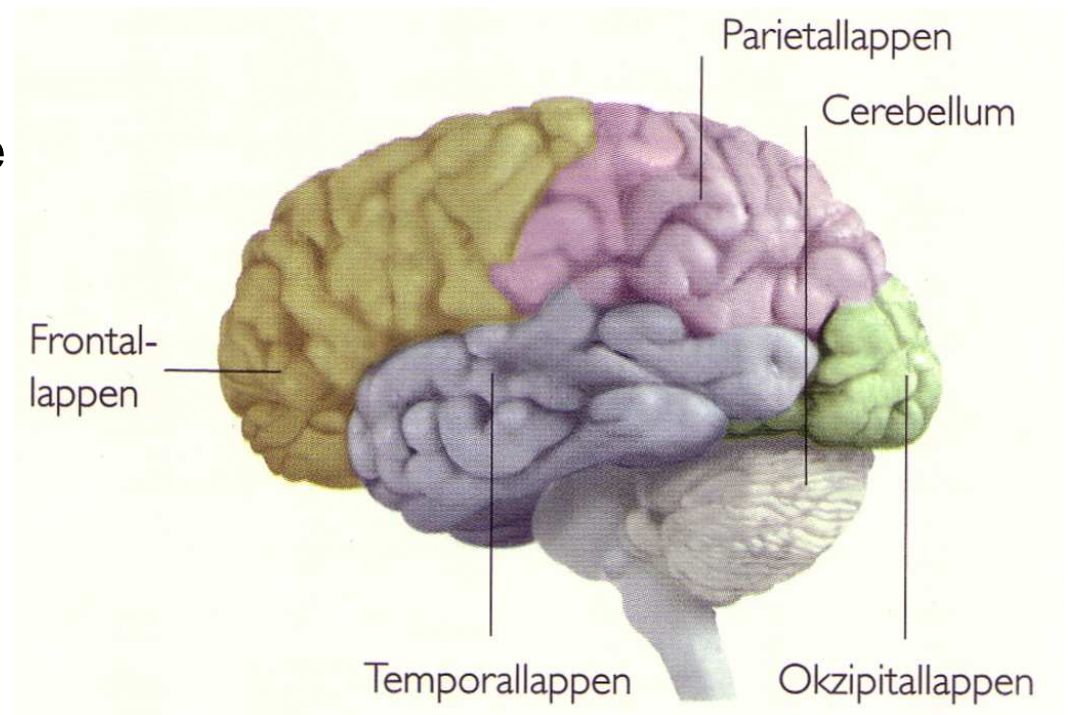
- What may the consequences of the surgical intervention in this patient be?
- What resources are available to compensate possible deficits



Neuropsychology in Epilepsy-Surgery

- Temporal lobe functions: language and memory

Assessment of language functions and hippocampal integrity to sustain memory are the critical issues in surgical treatment of temporal lobe epilepsy

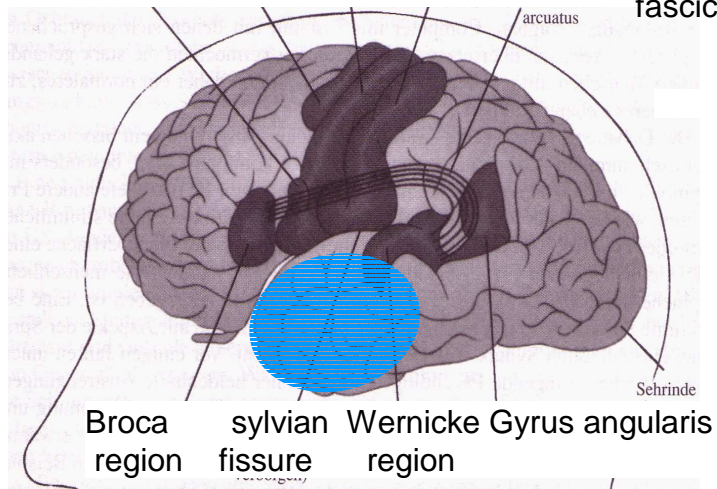


Temporal lobe functions: I. language

motor cortex suppl.mtor c. primary motor c.

sensomotoric c.

fasciculus arcuatus

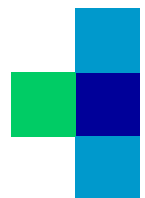


Essential language areas may be situated within the borders of the typical anterior temporal resections

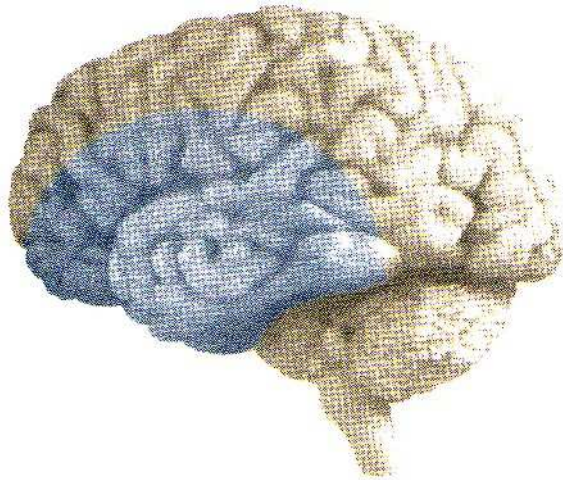
(Baxendale 2002)

Typical language disorders in LTLE

- Anomia
- reduced verbal fluency

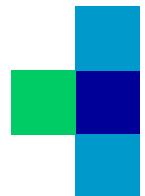


Temporal lobe functions: I. language



left TLE: often functional reorganization
ipsilateral and **contralateral**

I. Ipsilateral reorganization of language:
widespread distribution of naming and
reading areas (Devinsky 1993; Schwartz 1998,
Billingsley 2001)

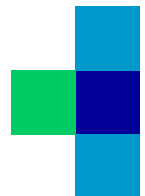


Temporal lobe functions: I. language

Object naming tests: standard part of neuropsychological test batteries - **Boston Naming Test (BNT)**

Preoperatively naming deficits point toward left neocortical dysfunction.

Postoperative naming deficits are frequent in LTLE patients with neocortical resection. Naming problems occur in 40% of left TLE patients postsurgical (Davies et al. 1998)

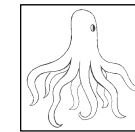


Temporal lobe functions: I. language

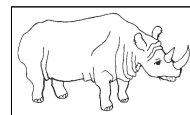
Predictors for postoperative naming deficits in TLE patients

Epilepsy onset < 14 y
age at surgery < 30 y
naming deficits preoperative
lesionectomy
right TLE

No decline



octopus or jellyfish?

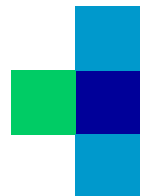


rhino or hippo?

Epilepsy onset > 14 y
age at surgery > 30 y
intact naming preoperative
anterior temporal lobectomy
left TLE

Decline

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Temporal lobe functions: I. language

Onset of epilepsy, temporal speech organization and postoperative language deficits

late onset of epilepsy or IPI



localized naming organization
in the medial /posterior TL



intact language development



negative impact with increasing
extend of neocortical resection

early onset of epilepsy or IPI



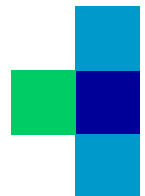
diffuse temporal / extratemporal
organization



slight language deficit



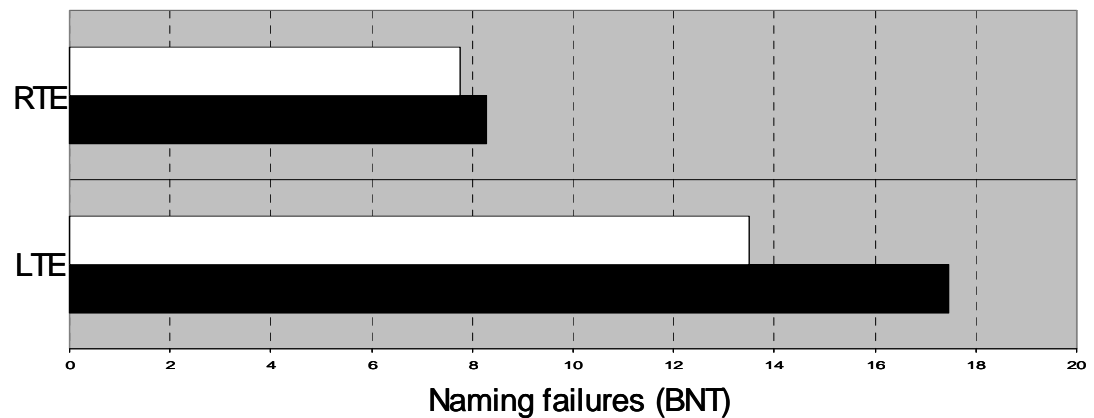
relatively low impact of
TL surgery



Temporal lobe functions: I. language

Naming, auditory perception, semantic processing and speech production in mTLE

Pre- and postoperative
naming errors
(Boston Naming Test)

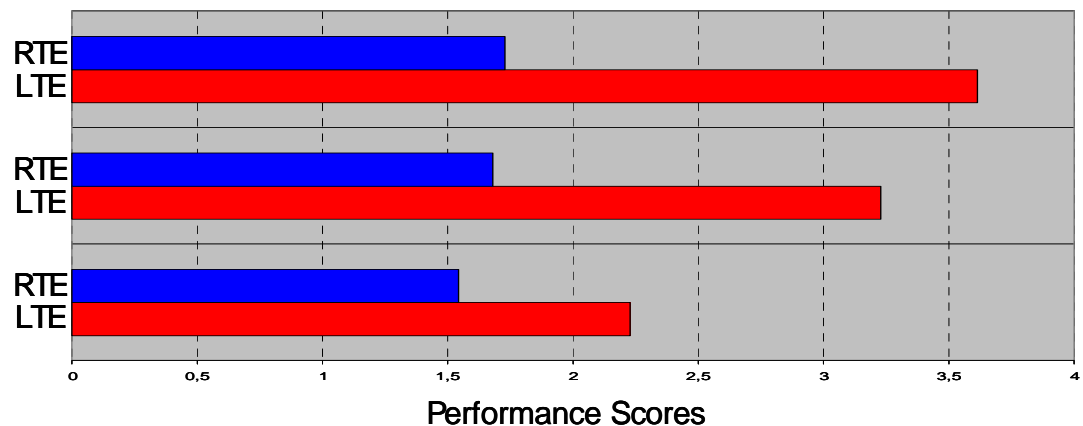


Postoperative language:

AUD: auditory perception

SEM: semantic processing

SP: speech production



Temporal lobe functions: I. language

II: contralateral reorganisation

Increased atypical language lateralization in TLE

normal subjects*: 94% left hemisphere dominant
6% atypical dominance

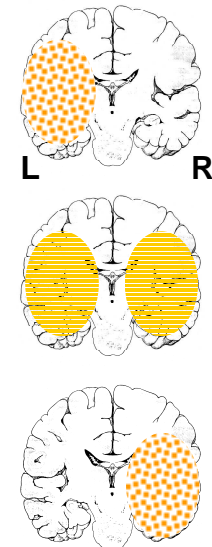
TLE*: 76% left hemisphere dominant

16% bilateral language representation

9% right hemisphere dominant

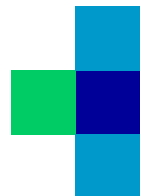
*right handed

(Springer 1999)



Temporal lobe functions: I. language

- The brain is able to reorganize functions - to contralateral homologous regions.
- Different pattern of bilateral involvement, - as dissociation between expressive and receptive language skills - could be demonstrated.
- Relocation takes place only in a part of left TLE.
influencing factors:
 - lesion onset
 - severity of hemispheric damage
 - individual differences in brain plasticity potential



Temporal lobe functions: I. language

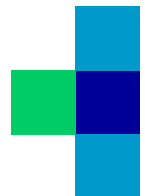
- Expectation:

Reorganization of language particular likely, when epileptic lesions are located in the vicinity of the classical language-related areas - rather than in more remote brain regions like the hippocampus.

- But:

The hippocampus seems to play an important role in the determination of language dominance

(Knecht 2004, Weber et al. 2006)

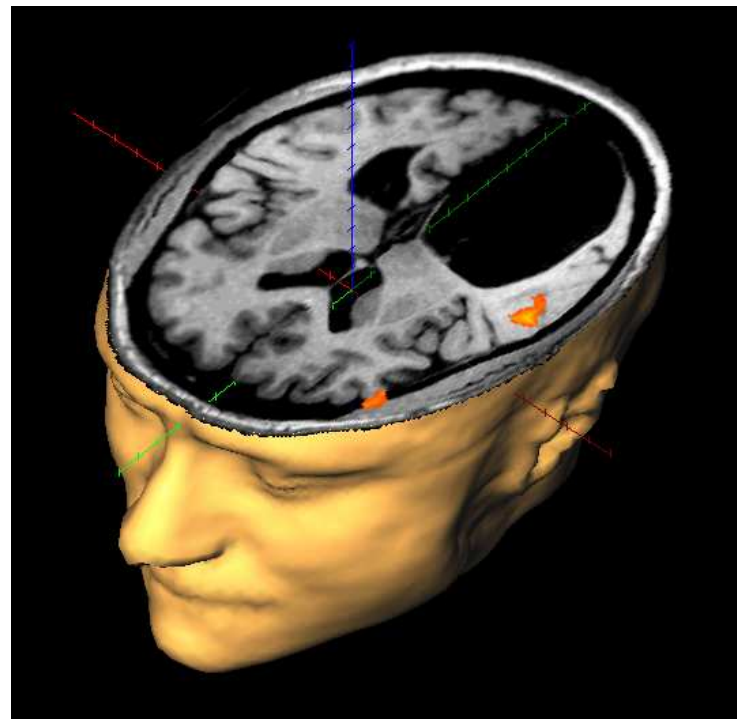
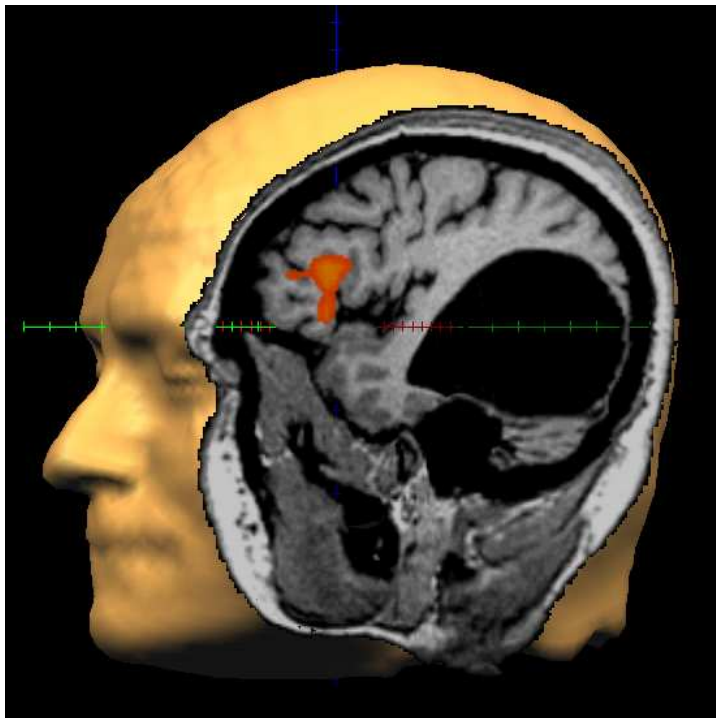


Temporal lobe functions: I. language

Patient: 48 y, female, porencephalic cyst left

fMRI: Word fluency
Broca activation

fMRI encoding word pairs:
Wernicke activation left



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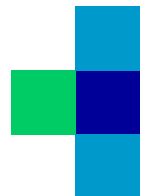
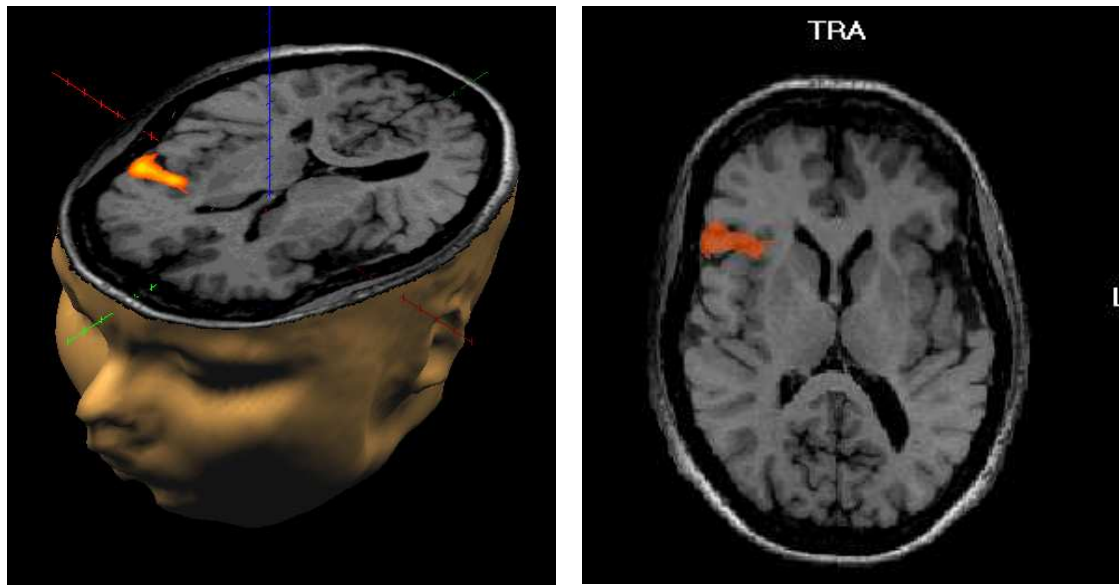


Temporal lobe functions: I. language

Patient EC 42 y, female, left HS
seizures onset 14y

neuropsychology: Language- and memory functions normal

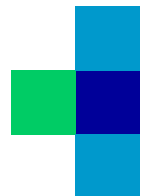
Word fluency: right frontal (Broca) activation



Temporal lobe functions: I. language

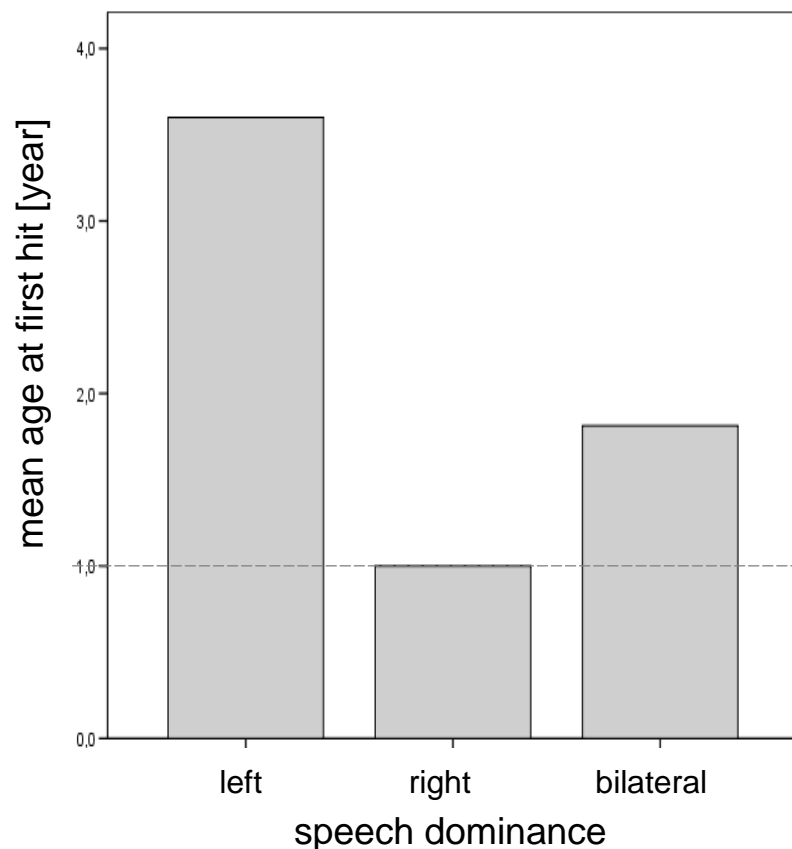
Language representation and mTLE

- 26% of left sided HS is associated with atypical language dominance (Erlanger collective)
- HS seems to be a critical prerequisite for interhemispheric language reorganization



Temporal lobe functions: I. language

Hippocampal sclerosis and speech dominance: Age at IPI



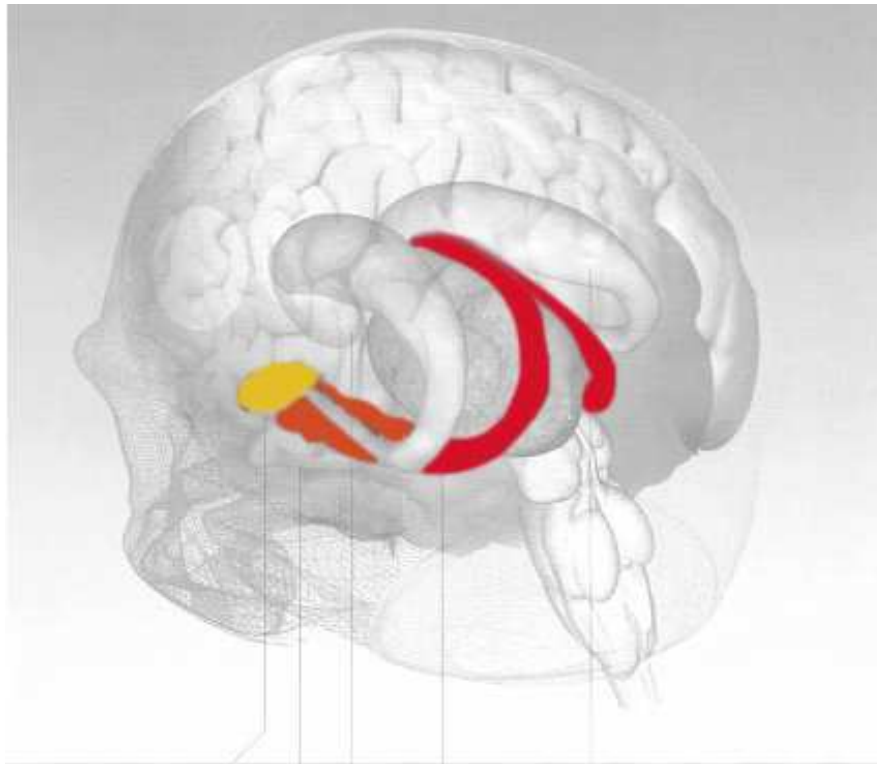
Functional reorganization as a consequence of age at IPI (initial precipitating injury)

Atypical language dominance in TLE is associated with an early age of brain injury / seizure onset.

N= 33 leftsided TLE



Temporal lobe functions: II. memory

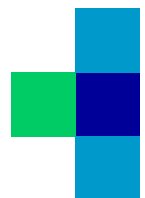


Hippocampal formation

- Anatomical substrate for **memory**
- Crucial role in **generation of seizures** in mesial temporal lobe epilepsy

Mesial temporal lobe epilepsy is associated with loss of hippocampal neurons and deficits in declarative memory functions in variable scale.

Surgical resection strategies are a successful treatment, but bear the risk of postoperative memory decline



Temporal lobe functions: II. memory

The hippocampus is implicated in the formation of all aspects of conscious memories:

- episodic memory:
conscious recollection of events and their relation
- semantic memory for facts and concepts
- spatial memory, involving spatial location and recognition



DIE ZEIT

Neuer Planet gefunden?

Vielleicht kein Planet - aber es wurde ein sehr interessanter Himmelskörper in unserem Sonnensystem entdeckt, der größer als Pluto ist

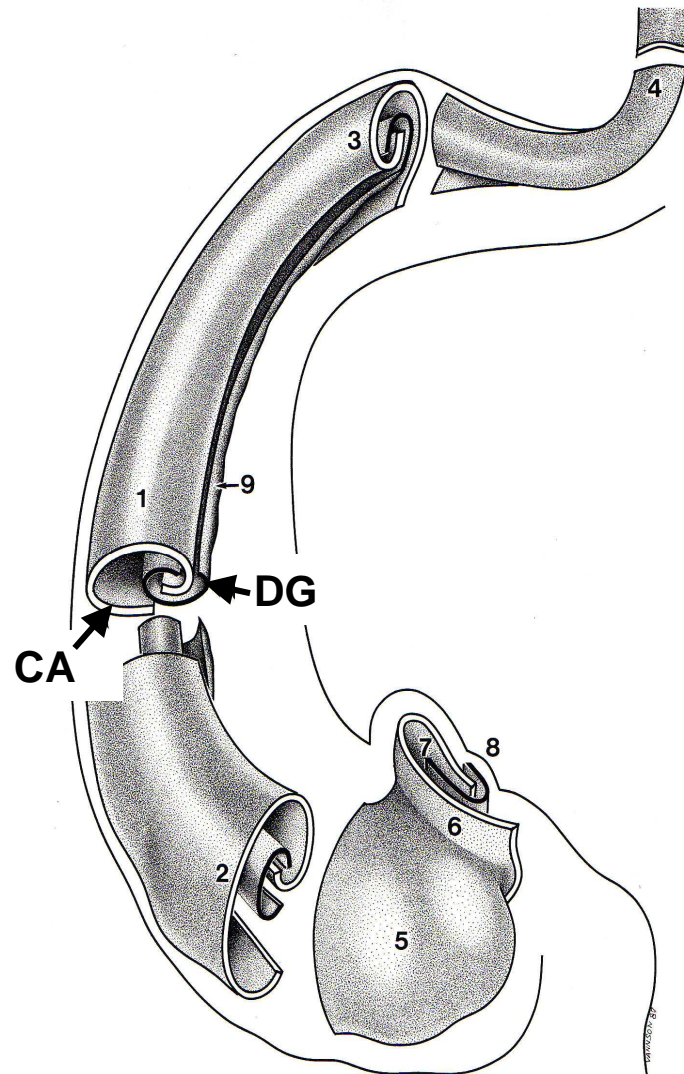
Von Gero von Randow

Zehnter Planet des Sonnensystems entdeckt - müssen jetzt die Schulbücher umgeschrieben werden? Wohl kaum. Allerdings stimmt es, dass gestern Abend die Entdeckung eines interessanten großen Himmelskörpers im Sonnensystem bekannt gegeben werden konnte. Das vermutlich

Pythagoras: $c^2 = a^2 + b^2$



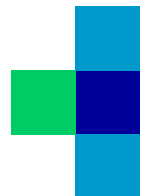
Temporal lobe functions: II. memory



Internal structure of the hippocampus.

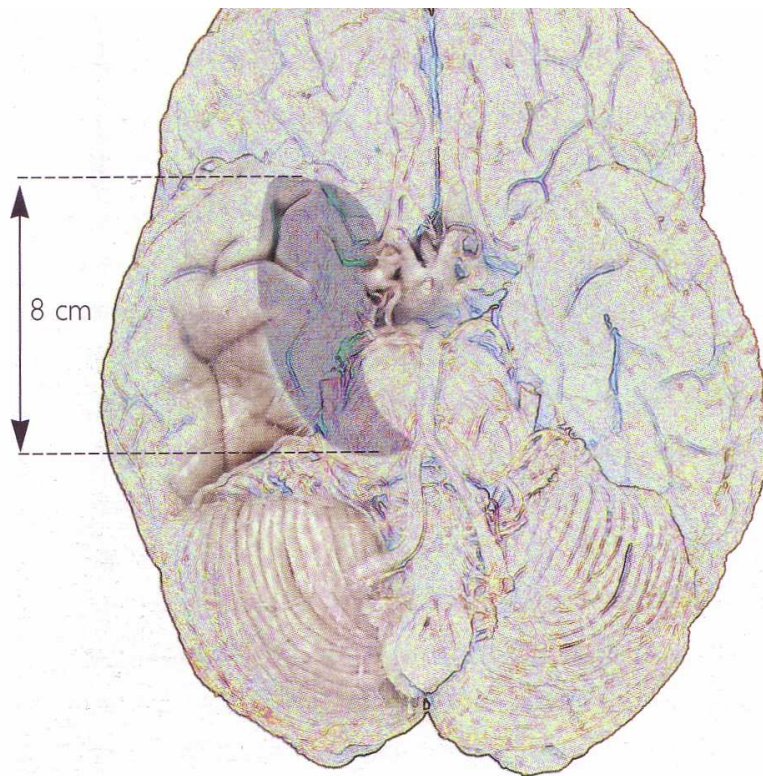
allocortical structure: bilaminar,
2 interlocking, U-shaped laminae,
cornu Ammonis (CA) and dentate gyrus (DG)

- 1 hippocampal body;
- 2 hippocampal head;
- 3 hippocampal tail;
- 4 terminal segment of the tail



Temporal lobe functions: II. memory

Amnesia and medial Temporal-Lobe

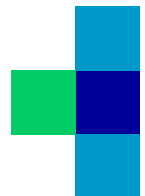


H.M.:

1953 at Montreal: male patient 27y, severe, not refractory epileptic seizures. Resection of medial structures of both temporal lobes:

- 2/3 of the Hippocampus
- most parts of the Amygdala
- parts of bordering areas

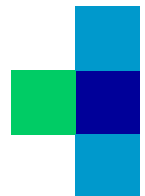
HM became seizure-free postop.



Temporal lobe functions: II. memory

Postsurgical HM was not handicapped in:

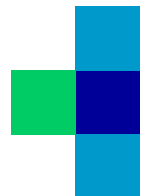
- Intelligence
- Perception
- Language functions
- Knowledge and skills
- Procedural memory (implicit memory, priming)



Temporal lobe functions: II. memory

BUT: anterograde memory functions were totally erased

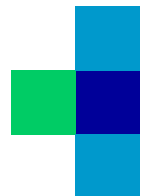
- Resection deleted memory for new information → anterograde Amnesia
- HM suffered also from retrograde Amnesia for ca. 2 – 10 years before surgery



Temporal lobe functions: II. memory

Case HM provided evidence ...

- ... that the hippocampus is implicated in the formation of all aspects of conscious (declarative) memories: episodic memory, semantic memory, figural and spatial memory
- ... for the consolidation hypothesis: for a limited period of time after encoding, the medial TL is responsible for memory.
- Engrams for long-term memories are stored in networks outside the hippocampus

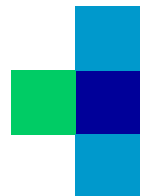


Temporal lobe functions: II. memory

Hippocampal formation:

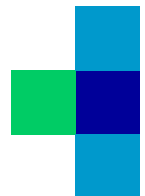
→ left MTL: specialized for verbal memory

→ right MTL: specialized for nonverbal memory



Temporal lobe functions: II. memory

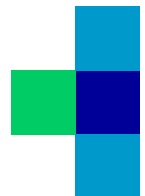
- **Left TLE:** verbal learning and memory frequently affected
 - further impairment is very likely when left mesial structures are surgically resected.
- **Right TLE:** characteristically nonverbal memory deficits are found preoperatively
 - surgery does not cause significant additional loss systematical



Temporal lobe functions: II. memory

Memory Tests

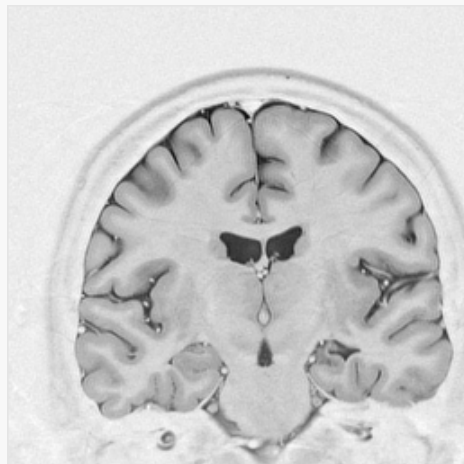
- Verbal Tests: Verbal learning of wordlists, word pairs
Example: Auditory verbal learning test (AVLT)
Wechsler Memory Scale (WMS-R)
- Figural Tests: Learning of figural or topographic information
Example: Rey-Complex-Figure Test (RCF)
Wechsler Memory Scale (WMS-R)
Visual Object and Space Perception (VOSP)



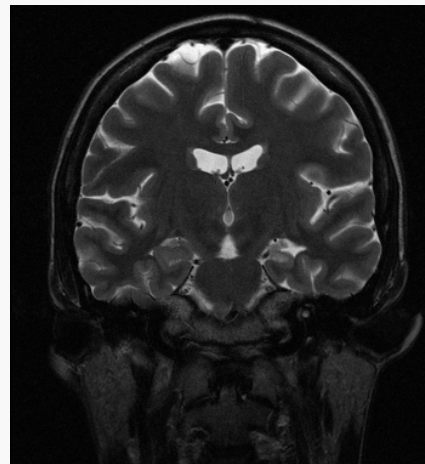
Temporal lobe functions: II. memory

MRI

hippocampal sclerosis, left

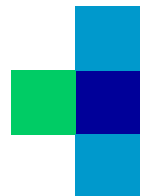


IR T1



T2

Cognitive
consequences ?

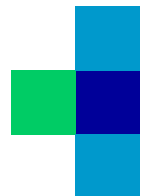
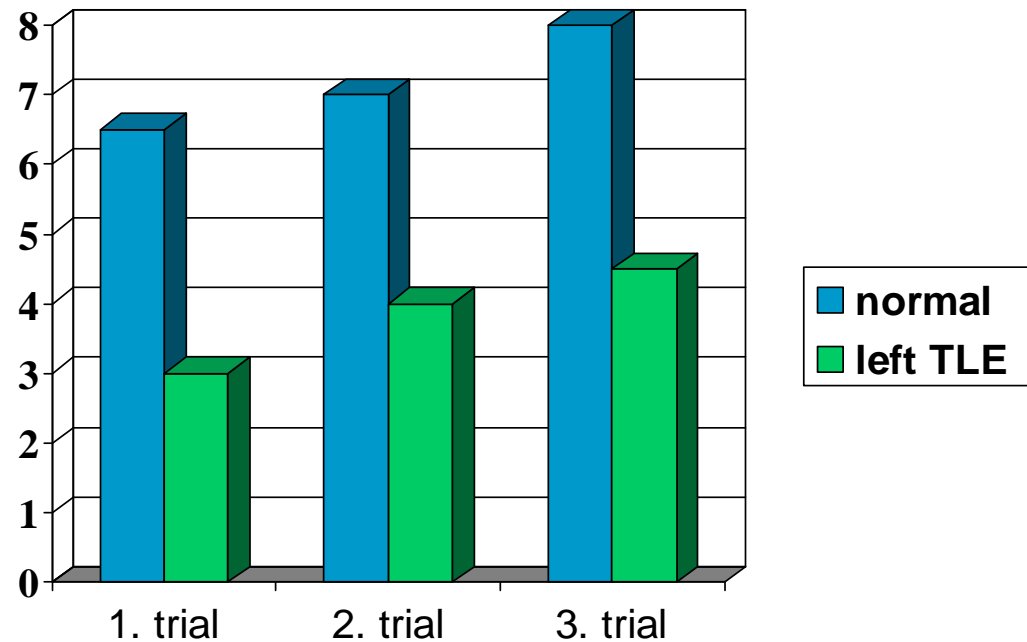


Temporal lobe functions: II. memory

Impaired verbal learning in a patient with HS left

Test: Learning of 8 word-pairs

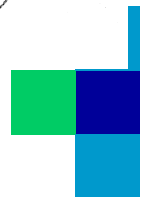
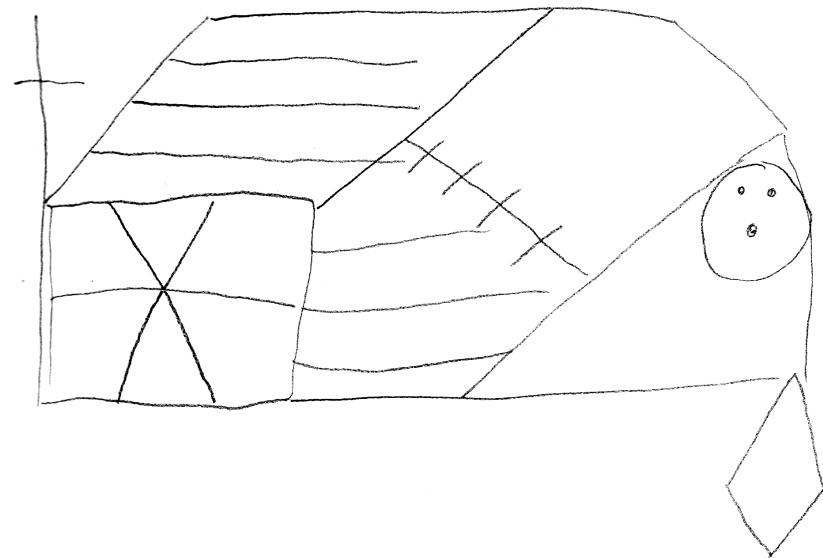
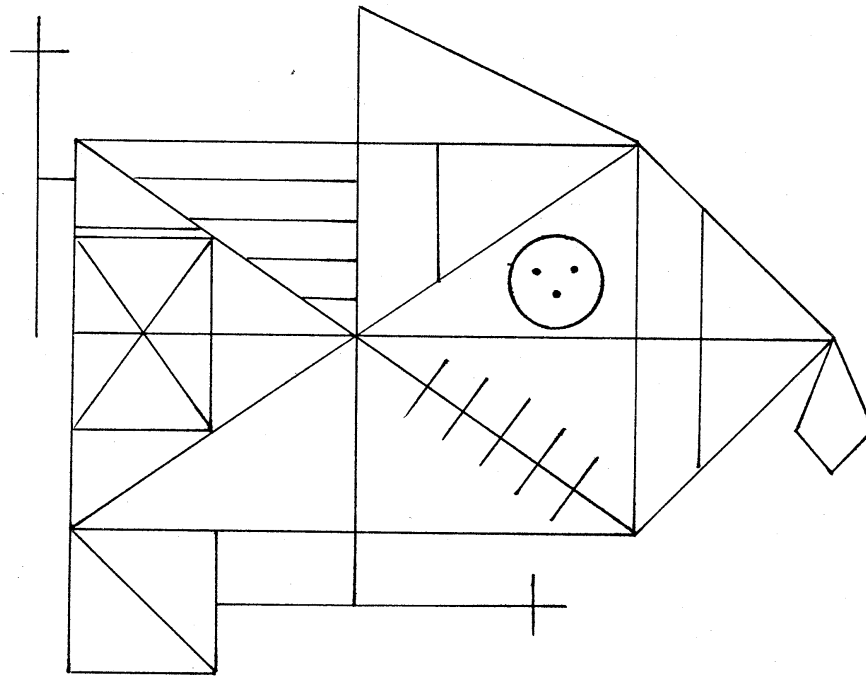
- 4 semantically related (metal – iron)
- 4 semantically non-related (lettuce – pen)



Temporal lobe functions: II. memory

Cognitive consequences of right TLE: Figural memory Deficits

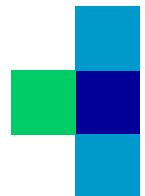
Test: recall of REY-figure



Temporal lobe functions: II. memory

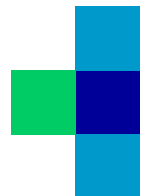
But even in clear evidence for HS in MRI, memory functions may be sustained in the neuropsychological examination:

- 1.) In cases, where the epileptogenic lesion is acquired within the first years of live, plasticity processes may cause that the right TL becomes responsible for verbal memory functions
- 2.) There are specific types of HS who leave the functions widely intact



Temporal lobe functions: II. memory

- Verbal memory shift to the right TL even in left sided speech dominance
- Critical period for interhemispheric reorganization of episodic memory: mainly restricted to the first 5 years.

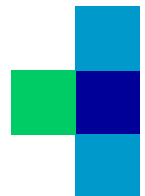


Temporal lobe functions: II. memory

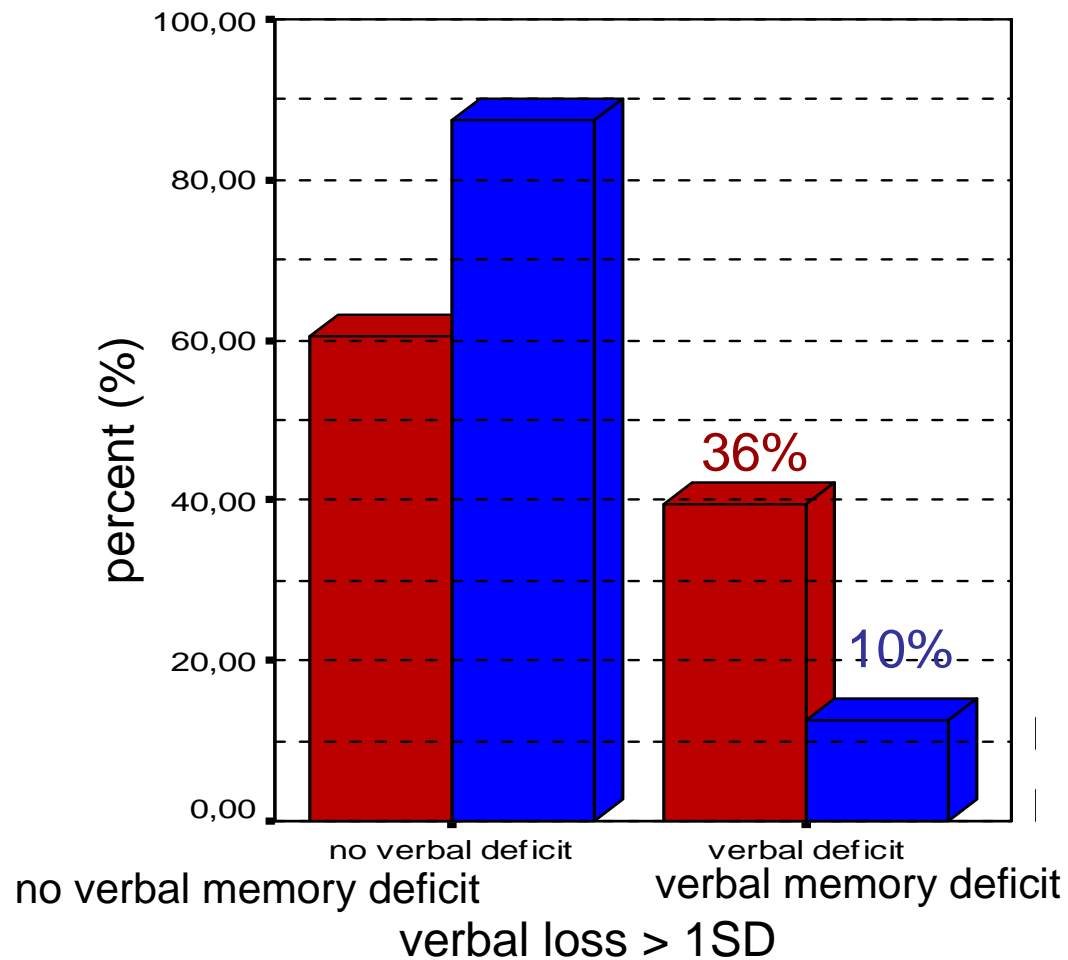
Risk of verbal memory loss

- Global amnestic syndromes: related to bilateral hippocampal dysfunction - a rare consequence in today's epilepsy surgery
- Verbal memory deficits in patients after dominant hemisphere resections:

Chelune (1993, 1995):	45%
Philips (1995):	79%
Engmann (2001):	non significant change
Gleissner (2002):	51%
Bengner (2002):	27%
ZEE	36%



Temporal lobe functions: II. memory



Verbal memory deficit
after surgery

side of surgery

left

right

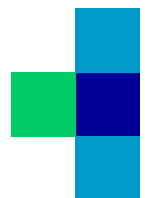
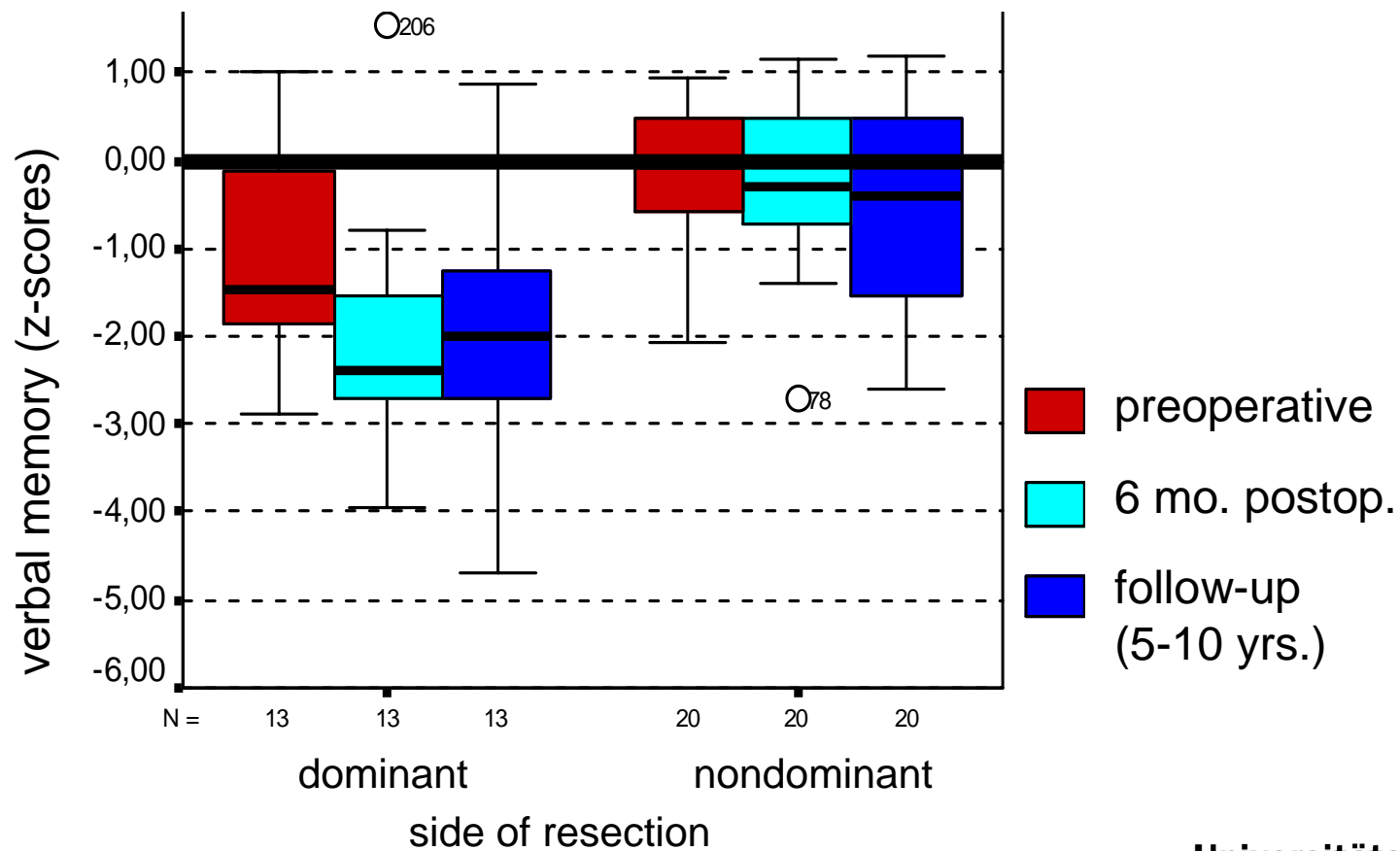
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Temporal lobe functions: II. memory

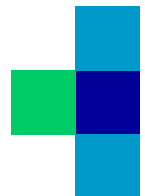
Left Temporal Lobe Epilepsy: Verbal memory in follow up investigations



Temporal lobe functions: II. memory

The loss in verbal memory following surgical treatment show considerable variations

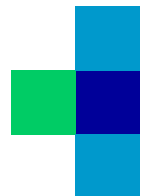
Main intention:
Identifying patients
who are most at risk



Temporal lobe functions: II. memory

Predictors for verbal memory loss

- Left TL resections
- High preoperative verbal memory performance
(Chelune 1995, Davis 1998, Gleissner 2002)
- Normal imaging findings for the ipsilateral hippocampus
(Rausch 1993, Trennery 1996)
- Insufficient functional integrity of the contralateral TL
(Chelune 1995, Helmstaedter 1999, Jokeit 1999, Gleissner 2002)
- Older age at surgery, late onset of epilepsy
(Hermann 1995, Davis 1998, Gleissner 2002)



Temporal lobe functions: II. memory

Two important aspects

1. Functional reserve capacity of the contralateral TL

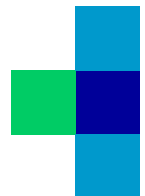
Insufficient functional integrity of the contralateral TL

(Chelune 1995, Helmstaedter 1999, Jokeit 1999, Gleissner 2002 TL 2002)

2. Functional adequacy of the ipsilateral TL

High preoperative functional integrity (high preop. verbal memory) of the ipsilateral TL

(Chelune 1995, Davis 1998, Gleissner 2002)



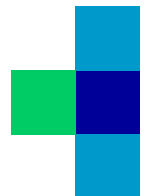
Temporal lobe functions: II. memory

1. Functional reserve capacity contralateral

Memory deficits are dependent on the functional reserve of the contralateral temporal lobe:

The functional integrity of the contralateral TL is important for avoiding **global amnesia**

For **verbal memory** function, the model of „contralateral reserve capacity“ refers to **processes of plasticity** and compensation (> Wada Test)



Temporal lobe functions: II. memory

2. Functional adequacy of the ipsilateral TL

The functional adequacy of the tissue to be resected determines the extent of memory loss

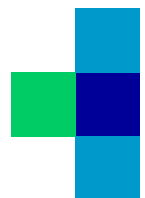
Evidence from memory assessment:

Neuropsychological studies

(Rausch 1987, Chelune et al. 1991, 1992; McSweeney et al. 1993; Bauer 1994, Helmstaedter 1999)

Intracarotid Amobarbital Procedure (IAP)

(Kneebone 1995)



Temporal lobe functions: II. memory

2. Functional adequacy of the ipsilateral TL

Evidence from anatomical data

MR Imaging and MR volumetry

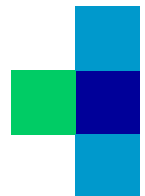
Left TLE patients without indicators of hippocampal atrophy suffered significant memory loss after surgery

Trennery et al. (1991,1993), Chelune (1995), Martin et al. (2001)

MR spectroscopy data

There is an accumulating evidence suggesting that ¹H MRS-derived NAA is an indicator of brain function

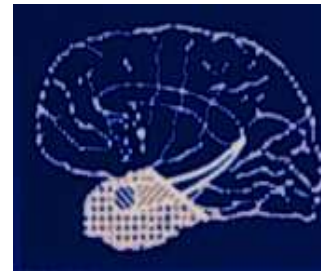
Sawrie et al. (2001), Pauli et al. (2000)



Temporal lobe functions: II. memory

Consequences of different surgical modalities on verbal memory

Standard resection (SR)
2/3 anterior temporal lobectomy



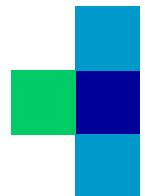
SAH
Selective Amygdala-
Hippocampectomy



Tailored resections



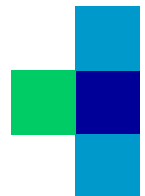
Verbal memory loss
significantly higher in SR



Temporal lobe functions: II. memory

Risk factors for verbal memory deficits

- surgery in the dominant hemisphere
- ipsilateral functional adequacy
(high preoperative verbal memory, superior left hemispheric memory in IAP, normal hippocampal MRI/MRS)
- low reserve capacity contralateral
(inferior right hemispheric memory in IAP, older age at onset)
- greater extent of resection
- older age at surgery



Frontal lobe epilepsy

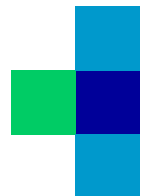
Frontal lobes: biggest and most complex part of the cortex.

Frontal lobe functions are manifold and vary in dependence of the affected subregions.

Higher order control function

Multiple diversity of neuronal connection with other brain areas
frontal lobe dysfunction often only identifiable in the whole cognitive profile

FLE often comes along with bilateral EEG changes - accordingly neuropsychological tests results difficult to lateralize.



Frontal lobe epilepsy

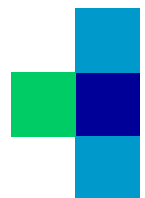
Tests known to be sensitive for frontal lobe dysfunction (Milner 1984).

Cognitive flexibility:

- word fluency, design fluency (J. Gotman)
- capacity to react under appropriate consideration of environmental stimuli and to adopt in a flexible way to changing demands (Wisconsin Card Sorting Test)
- capability to inhibit strong habitual reactions (Stroop Test).

Disorders in executive functions:

- Motor co-ordination, Sequencing
- Attention, switching of attention, interference avoidance,
- Working memory
- Anticipation, planning of operations



END



**Universitätsklinikum
Erlangen**

