



MESIAL

TEMPORAL LOBE EPILEPSY

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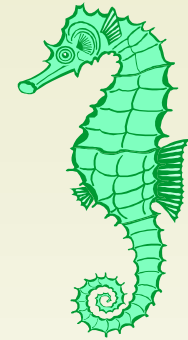
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Epilepsy Surgery Project (EPODES)

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TEMPORAL LOBE EPILEPSY

TLE are heterogeneous disorders sharing the same topographical seizure onset with diverse etiology, 30-35% all epilepsies, 2/3rd mesial, 1/3 lateral

ICEES (1989)

1. Localisation related epilepsies and syndromes
 - TLE
 1. Amygdalo-hippocampal (mediobasal limbic or rhinencephalic) seizures – MTLE
 2. Lateral temporal seizures
 - FLE
 - PLE
 - OLE

New proposal ILAE (2001)

- Symptomatic or probably symptomatic focal epilepsies
 1. Limbic epilepsies
 - **MTLE-HS**
 - MTLE defined by specific etiologies
 - Other types defined by location and etiology
 2. Neocortical epilepsies

Special Article

Report of the ILAE Classification Core Group

Jerome Engel, Jr., Chair

Reed Neurological Research Center, David Geffen School of Medicine at UCLA, Los Angeles, CA, U.S.A.

TABLE 2. Epilepsy syndromes by age of onset and related conditions

Neonatal period
Benign familial neonatal seizures (BFNS)
Early myoclonic encephalopathy (EME)
Ohtahara syndrome
Infancy
Migrating partial seizures of infancy
West syndrome
Myoclonic epilepsy in infancy (MEI)
Benign infantile seizures
Dravet syndrome
Myoclonic encephalopathy in nonprogressive disorders
Childhood
Early onset benign childhood occipital epilepsy (Panayiotopoulos type)
Epilepsy with myoclonic atstatic seizures
Benign childhood epilepsy with centrotemporal spikes (BCECTS)
Late onset childhood occipital epilepsy (Gastaut type)
Epilepsy with myoclonic absences
Lennox-Gastaut syndrome (LGS)
Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS) including Landau-Kleffner syndrome (LKS)
Childhood absence epilepsy (CAE)
Adolescence
Juvenile absence epilepsy (JAE)
Juvenile myoclonic epilepsy (JME)
Progressive myoclonus epilepsies (PME)

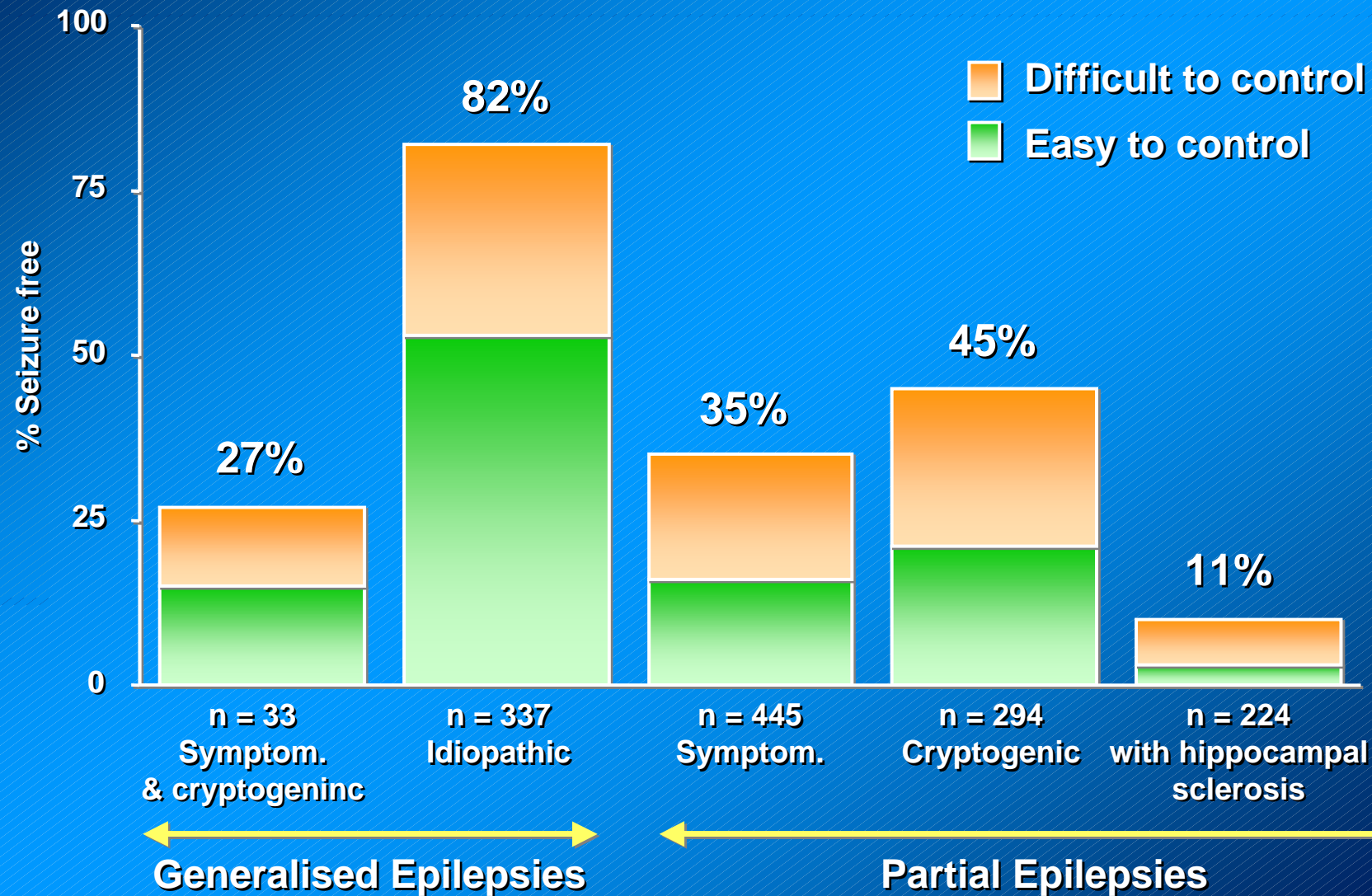
Progressive myoclonus epilepsies (PME)
Less Specific Age Relationship
Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE)
Familial temporal lobe epilepsies
Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS)
Rasmussen syndrome
Gelastic seizures with hypothalamic hamartoma
Special epilepsy conditions
Symptomatic focal epilepsies not otherwise specified
Epilepsy with generalized tonic-clonic seizures only
Reflex epilepsies
Febrile seizures plus (FS+)
Familial focal epilepsy with variable foci
Conditions with epileptic seizures that do not require a diagnosis of epilepsy
Benign neonatal seizures (BNS)
Febrile seizures (FS)

Types of MTLE

1. MTLE with hippocampal sclerosis (HS)
(%70 Wolf HK, 1993; our series % 80)
2. Structural lesions in or adjacent mesio temporal areas
 1. Tumor: ganglioglioma, DNET, astrocytoma,...
 2. Vascular: cavernoma, AVM ..
 3. Malformations of cortical development
 4. Trauma
 5. Infections

Response to medical treatment

Semah et al. 1998, 2200 pts



Definition

— Temporal lobe epilepsy which consists of seizures originating from mesial temporal structures associated with **Hippocampal Sclerosis.**

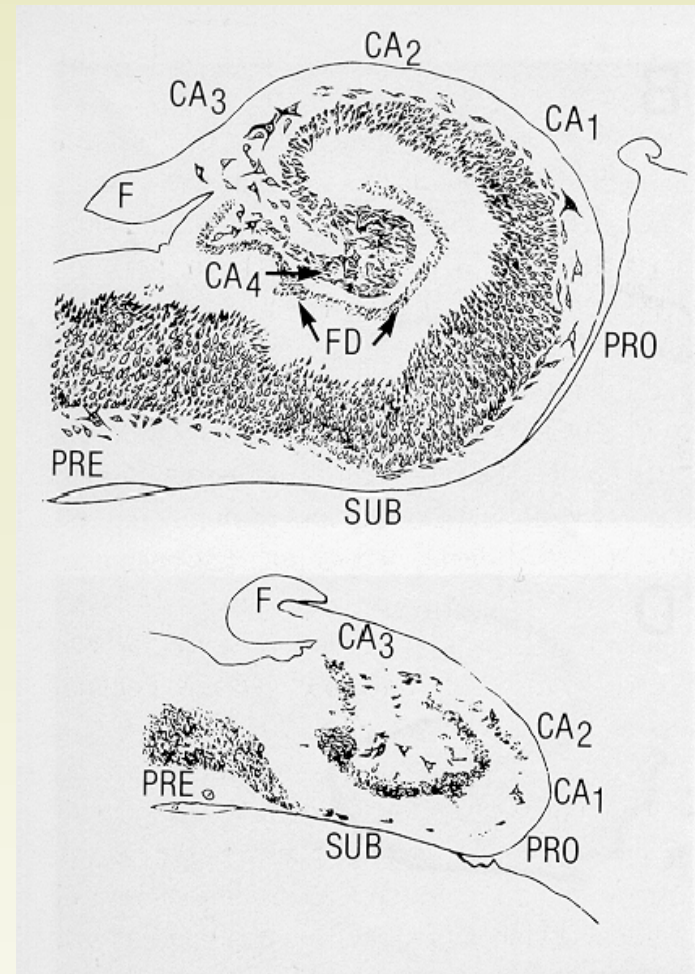
It has been elaborated in terms of:

- *clinical signs and symptoms,*
- *neuropsychological and psychiatric aspects,*
- *electrophysiological characteristics,*
- *morphological and functional imaging findings,*
- *etiological and pathophysiological mechanisms,*
- *clinical course and*
- *response to both AEDs and surgical therapy*

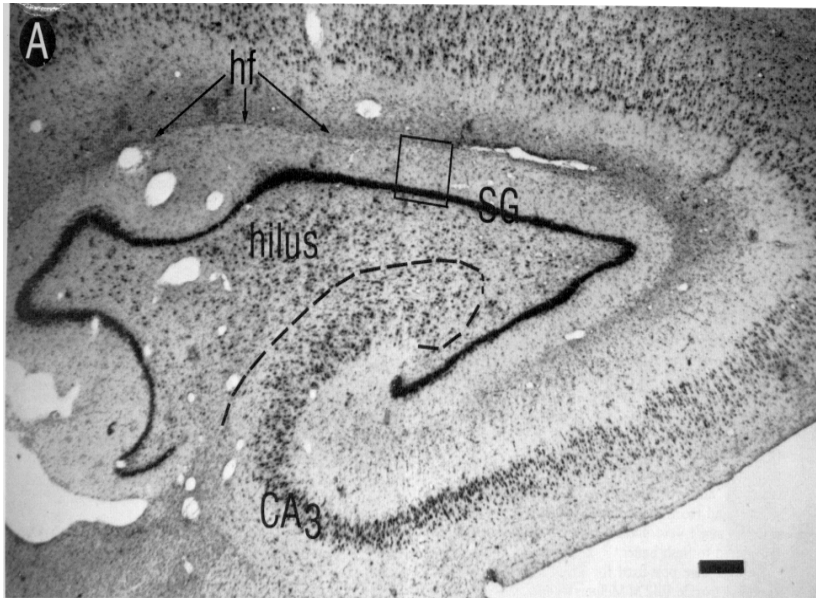
It is considered as a syndrome with several subtypes.

History *(Gloor 1991)*

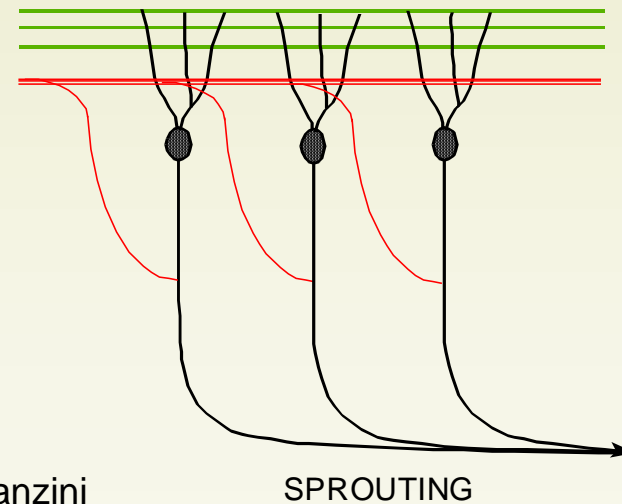
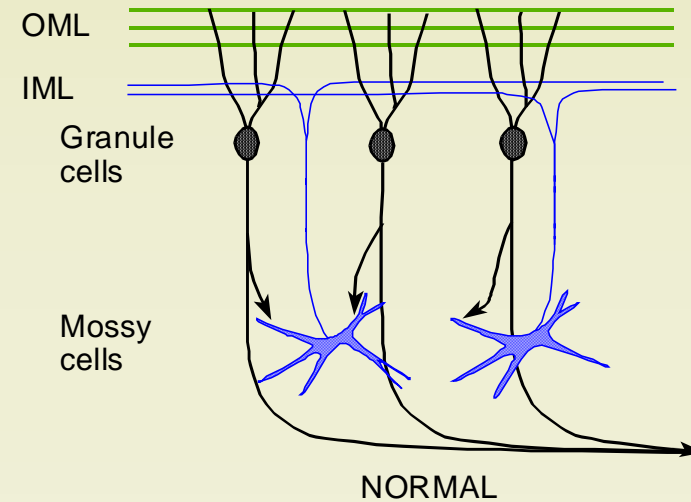
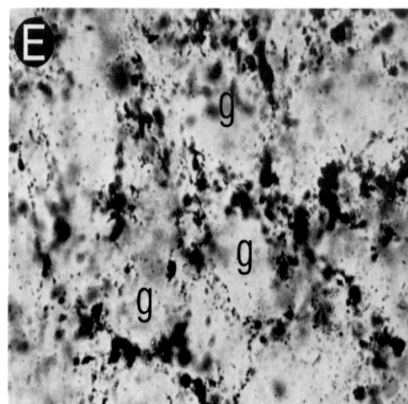
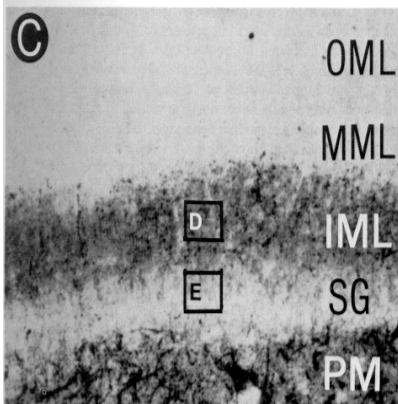
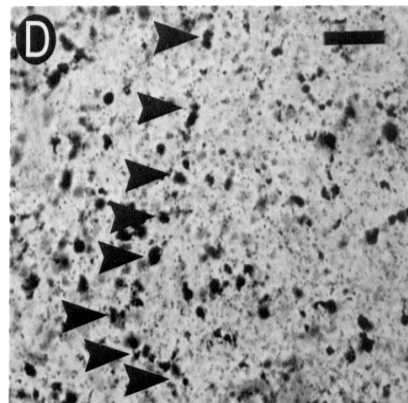
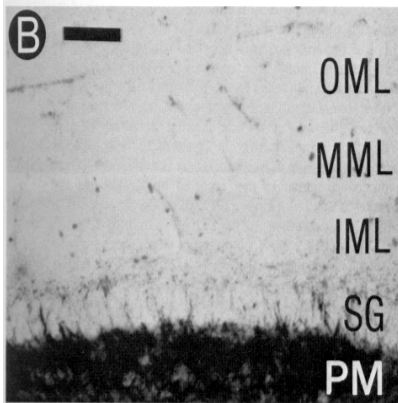
- 1825 sclerotic atrophy Bouchet and Cazauvieilh
- 1868 Meynert confirmed presence of hippocampal changes
- 1880 Sommer documented the microscopic examination
- 1899 Bratz argued hippocampal atrophy not always the result of epilepsy, illustrated mic. findings with woodcut
- 1936 Stauder established association between TLE&HS
- 1953 Earle described “incisural sclerosis” PCA ischaemia birth cause CPS (MNI)
- 1954 Meyer hypoxic ischaemic episode related not birth but early childhood (Maudsley H.)
- 1964 Falconer et al introduced MTS



From Bratz 1886



....HS is found frequently in TLE and is considered expression of an underlying process responsible for a progression towards a more severe clinical picture.....



From G. Avanzini

SPROUTING

DEFINITION OF HIPPOCAMPAL SCLEROSIS

Minimal criteria:

- CA1 and endfolium neuronal loss
- Gliosis with relative sparing of transitional cortex, measured at the mid-body of the antero-posterior axis.
- Circuitry reorganization namely mossy fiber sprouting

Additional findings :

- 1) Dentate dispersion (50%);
- 2) Reorganization outside dentate gyrus, namely CA1
- 3) Extrahippocampal pathology, namely temporal white matter

Etiological factors

- Febrile seizures (Complex FS)
- Trauma
- Infections
- Anoxia/hypoxia
- Preexisting abnormality
- Immunological factors
- Genetic predisposition (GEFS+)

HS: cause of or consequence of seizures ?

1. Complex febrile seizures and/or initial precipitating injury → HS

- Retrospective studies from surgical series support strong association between FS and TLE (*Saltık 2003(85%), Abu Halil 1993, O'Brien 1996, Mathern 1995*)
- MRI evidence of HS after CFS in children (*VanLandingham 1998, Schulz 2001*)
- Analysis of patients with MTLE-HS: $n=266$, 64% FS, 41% CFS (*unpublished*)
- It can be followed by generalized seizures in adulthood (*Jackson 1999, Briellmann 2001*)
- Twin study implicating HS to be an acquired postnatal lesion related to IPI rather than genetic predisposition (*Jackson 1998*)

2. Pre-existing abnormalities → FS → CFS → HS

- Prospective studies failed to show FS lead to TLE (*Nelson & Ellenberg 1976, 1978*)
- Estimated risk for developing epilepsy after CFS 1/75.000 children /year
- HS with cortical dysplasia → more severe HS & more FS (*Fauser 2006*)
- MRI suggest subtle, pre-existing hippocampal malformation (*Fernandez 1998*)

Epidemiology and incidence

- It is the more common epileptic syndrome
- Exact incidence & prevalence is not known
- Probably accounts for 20% of pts w epilepsy, 65% of pts w MTLE
- In surgical series majority of patients (49-70%) have HS
(*Falconer 1964, Babb 1987*)
- Incidental detection on MRI images (*Moore KR et al. AJNR 99*)
2/207 patients
- Autopsy series: *Meencke 1991; 30.5%, Spielmeyer 1927; 80%*
 - *Bilateral :Meencke 1991; 56%, Sano 1953; 14%*
- The youngest pathologically confirmed surgical pt: 2yrs (*Kanos 2000*)

Clinical features

- Frequent history of IPI (initial precipitating injury-at a critical age)
 - Frequent family history of seizures
 - Seizure onset at first decade (6-14 yrs)
 - **Latent period:** time between IPI and habitual seizures
 - **Silent period:** Initial seizures may respond well to AED therapy
 - Progressive (?); behavioral, memory deficit, increased EEG spikes
 - Prognosis: Usually intractable after certain period of time
- 11-20- 45% benign course** (*Semah 1998, Ozkara 20004, Stephen 2001*)

Controlled trial of surgery revealed; surgery is superior to prolonged medical therapy (*Wiebe 2001*)

Seizure semiology

- Aura → arrest → automatisms w/wo alteration in consciousness (and amnesia)
- **Aura:** often in isolation and frequent
 - Abdominal, non-specific, fear & anxiety, experiential, vegetative, olfactory and gustatory hallucinations rare
- **CPS:** Staring, oro-alimentary, gestural automatisms, unilateral dystonic posturing contralateral to the focus, head deviation, autonomic manifestation
- **Postictal state:** amnesia for the event, a period of confusion
- Seizures usually triggered by menstruation, infections, sleep deprivation, stress
- Generalized tonic clonic seizures are not frequent

Electro-clinical patterns *(Chassoux 2003)*

- **Mesial:** no evidence of early spread beyond TL
- **Anterior mesio-lateral:** early ant. spread involving ant. lat. temp cortex , insulo-fronto opercular areas
- **Widespread mesio lateral:** involving both ant and post lat temp and perisylvian areas
- **Bitemporal:** early contralateral temp spread

Ictal lateralizing signs

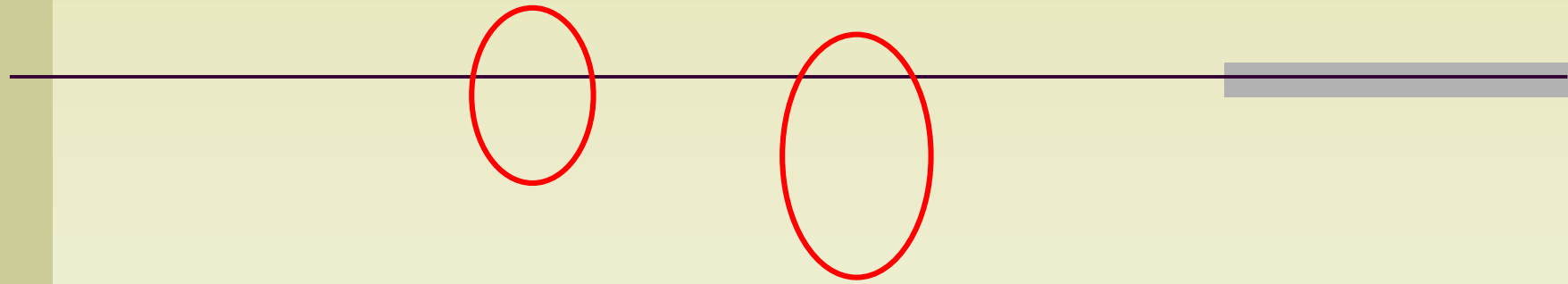
- Dystonic posture of arm → contralateral %20-30
- Early head deviation → ipsilateral
- Late head deviation → contralateral
- Arm automatisms → ipsilateral
- Aphasia, prolonged recovery → dominant
- Speech, quick recovery → nondominant
- Spitting, vomiting, urinary urge → nondominant

Left MTS

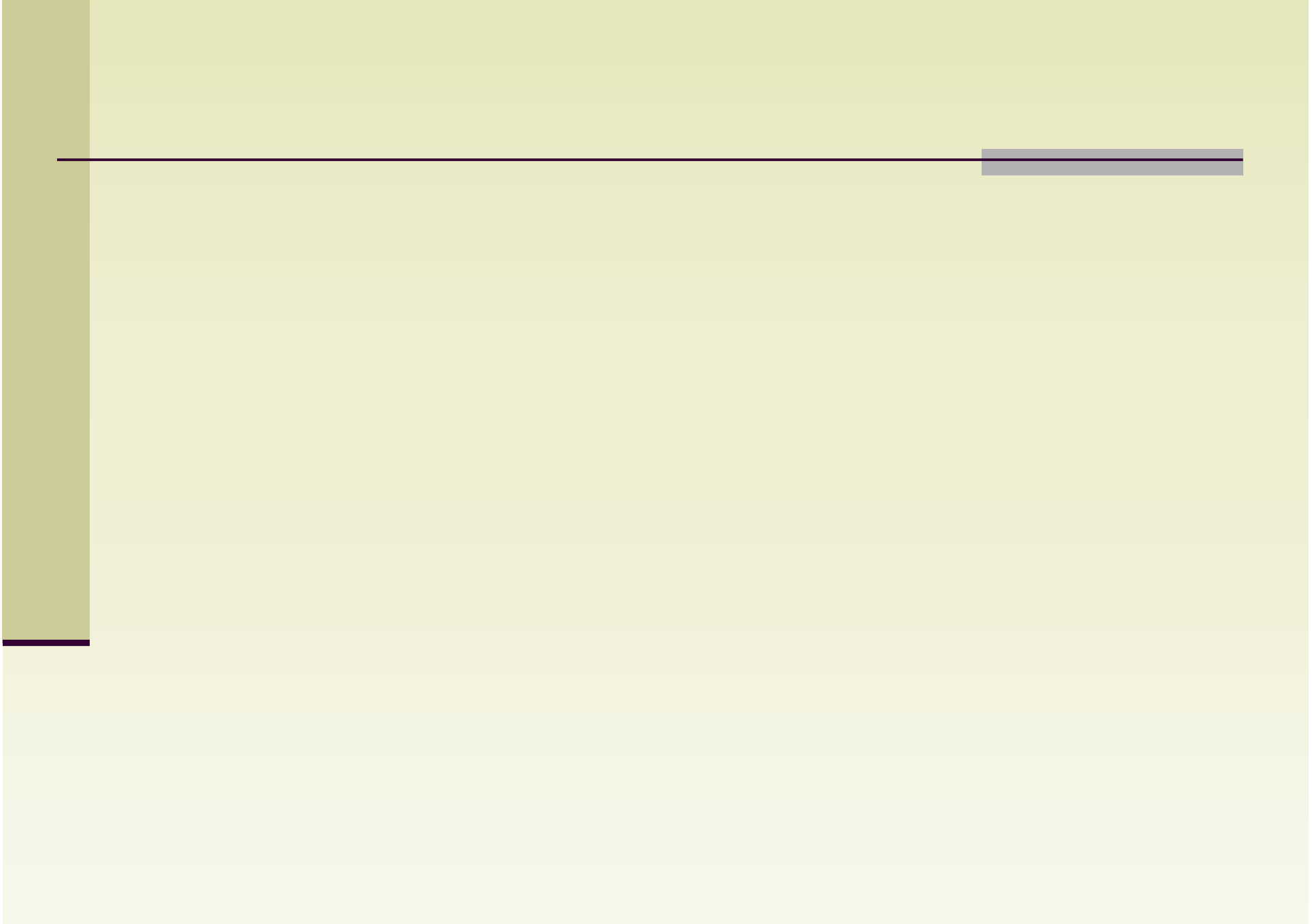


Right MTS

Interictal EEG: Focal slow, rhythmic sharp waves or sharp slow wave complexes
Isolated or as short trains, uni or bilateral, max at basal ant temp electrodes.



Activated by relaxation or early stages of slow wave sleep



(Right MTLE-HS) in TLE total seizure duration correlates with glial density in CA2, CA3 and presence of excitatory post synaptic potentials (*Spencer 1997*)



Propagation

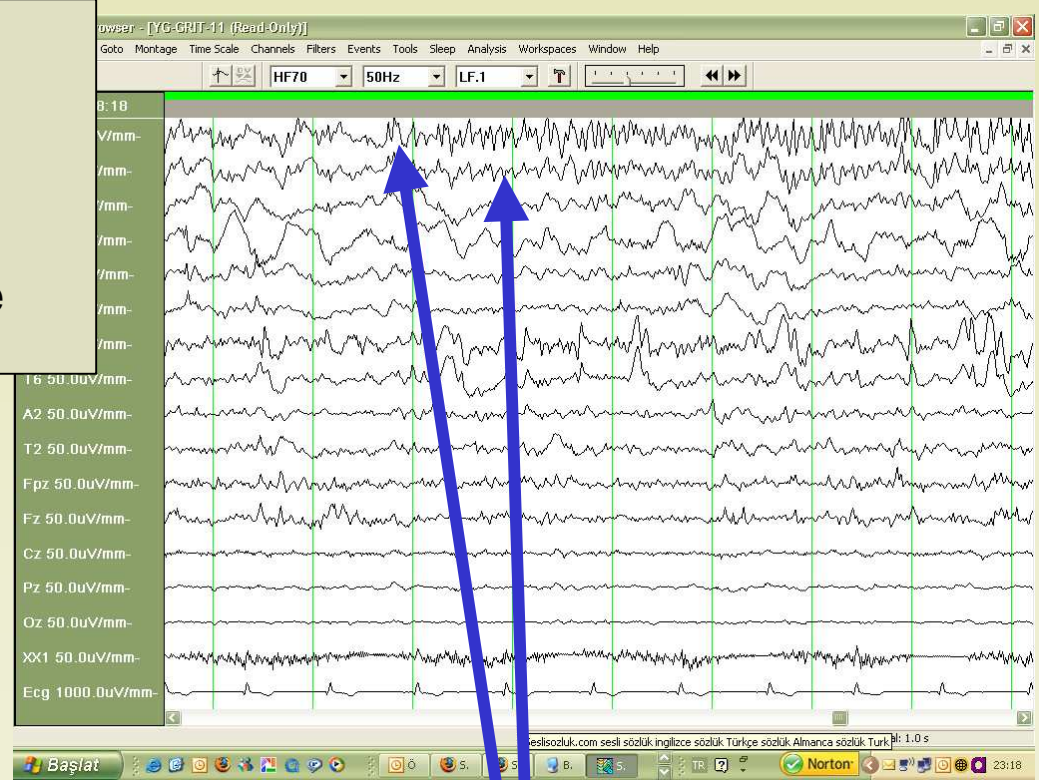
- Long delay of propagation; correlates neuron loss at CA4 (*Spencer 1992*)
- Seizure spread is slow compared to other brain areas
- 60 % ipsilateral temporal neocortex, 30 % first contralateral hippocampus; 10% at the same time contralateral hippocampus and ipsilateral temporal neocortex (*Spencer 1987*)

Intracranial recordings

- Low frequency high amplitude hypersynchronous spikes prior to superimposed faster rhythm, correlates cell loss at CA1 (more common)
- Low voltage higher frequency discharge (*Spencer 1995, Velasco 2000*)

Intracranial recordings

Low frequency high amplitude hypersynchronous spikes prior to superimposed faster rhythm, correlates cell loss at CA1 (more common)
Low voltage higher frequency discharge (Spencer 1995, Velasco 2000)



MRI findings:

T1W: Volume loss
correlated with low neuron density

T2W : hyperintensity,
nonvisualisation of internal structures

DUAL PATHOLOGY



Focal cortical dysplasia Type 2a & HS



Interictal FDG-PET

sensitivity ~70% in TLE, hypometabolism ant. TL, thalamus, basal ganglia, frontal cortex, insula (NETWORK)

Our study: 75% concordant with MRI

Ictal SPECT

highly sensitive; interictal 0.44, postictal 0.75, ictal 0.97 (*Devous 1998*)

(^1H) MRS : NAA/Cr decrease marker for neuronal loss

Correlation between H-1 MRS and memory before and after surgery in mesial temporal lobe epilepsy with hippocampal Sclerosis. *Hanoğlu L, et al. 2004*

Correlation between MRS and abnormal side

Right side scores of RTLE and left side scores of LTLE correlates with verbal memory

MRS is not predictive for memory outcome

Neuropsychological findings

- Material specific memory impairment
- May be clinically progressive
- Verbal memory impairment correlates with cell loss in dominant CA3
- *Our data: n:128; 81 pts showed memory dysfunctions concordant with the MRI, 37 pts had bilateral abnormalities and 10 pts were normal*
- **Memory in patients with drug-responsive mesial temporal lobe epilepsy and hippocampal sclerosis:** Özkara Ç. et al. *Epilepsia, 2004*
- *may be directly related to the underlying pathology i.e.HS*
- *may be permanent*
- *Progressive deterioration in cognitive functions: may result from drug resistant , frequent seizures*

Psychiatric findings

Interictal behavioral disorders especially depression is frequently seen

(Quinske 2000, Glosser 2000)

Depression in patients with MTLE-HS (n:86); Akbaş B., Özmen M, Özkara Ç, Eşkazan E, Özyurt E (2001 BA).

- *depressive symptoms were present in 58%*
- *anxiety 51.7 %*
- *more pronounced with right sided lesions*

Surgery & Outcome

Predictors of good outcome

- Unilateral Hc atrophy,
- unilateral temporal hypometabolism,
- CA1 cell loss,
- asymmetric memory,
- an early risk factor,
- presence of MTS
- no secondary generalization

Surgical approach:

- Selective amygdalahippocampectomy,
- Anterior Temporal Lobectomy

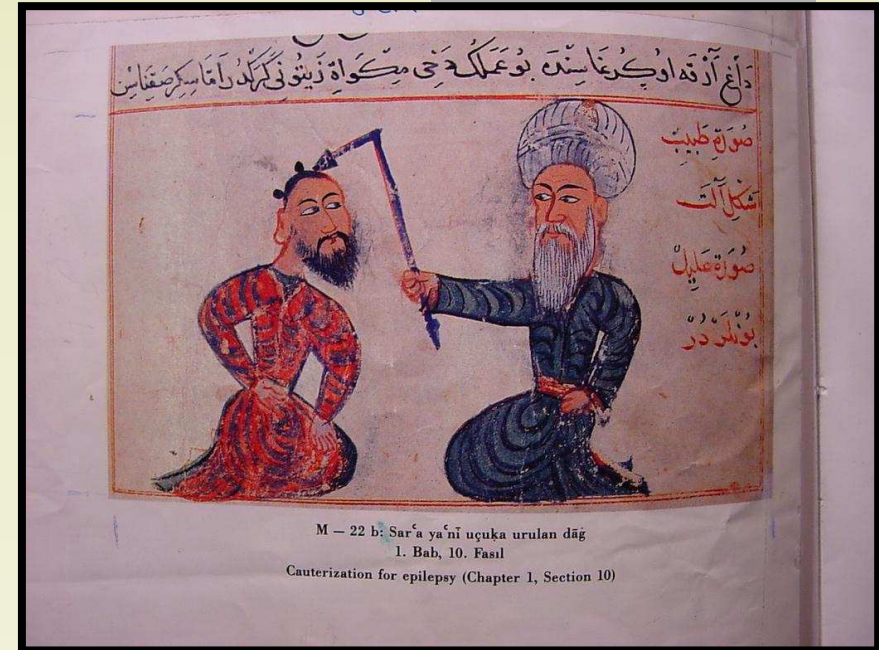
Seizure freedom: 70-90%

Long term relaps: 15% (Spencer 1996)

SF dropped from: 69% at 12 months

50% at 60 months

(Berkovic 1995)



Cerrahiyyetül Haniyye
by Şerafettin Sabuncuoğlu
15th century
Ottoman Empire
Cauterization for epilepsy

SURGICAL OUTCOME OF PATIENTS WITH MTLE-HS

Özkara Ç et al. *Epilepsia* (in press)

- N:165
- Male/female: 83/82, Right/left: 81/84
- Mean age at surgery (year): 25.9±8.3 (8-57)
- Mean follow-up (year): 5 ± 2.7 (1-11)
- At the last available follow-up: 72.1% Engel I
- At the end of first year: 77.1% Engel I
- Long term relaps rate : 25%
- Cure: 42.7% → seizure free for at least 2 years and no AEDs

***No good physician quavers
incantations when the malady he is
treating needs the knife”***

Sophokles Ajax:582