

# Practical Issues with Memory in Epilepsy

Zhiyi Sha MD, PhD

Assistant Professor of Neurology

University of Minnesota

I have suffered epilepsy for over 20 years. I just turned 40. I have noticed how bad my memory has become. My memory used to be as sharp as a tack before I had seizures.

Table 2  
Areas affected by epilepsy<sup>a</sup>

Having epilepsy affects my...	Number	Mean	5 or 6 (%)
<i>School</i>			
Performance in school	238	4.0	54
<i>Cognitive functions</i>			
Ability to remember things	961	3.8	46
Ability to concentrate	955	3.8	46
Mental and emotional well-being	957	3.6	41
Ability to think clearly	954	3.5	40
<i>Lifestyle</i>			
Ability to drive a car	768	3.0	36
Job performance	379	2.6	17
<i>Relationships</i>			
Relationships with others	960	3.1	32
Relationship with spouse or partner	675	2.8	28
Relationship with my children	535	2.7	26
Sex life	707	2.4	21
Level of concern about having children	492	3.3	39
Overall quality of life	972	3.5	39

\* Fisher et al. : Epilepsy Research 41 (2000) 39–51

**Table 1. Ranking of cognitive deficits in focal epilepsies**

Functional domain	Affected (<1 SD)	Severely affected (<2 SD)	N of patients
Verbal learning and memory	68%	56%	3,193
Speech <sup>a</sup>	66%	43%	2,285
Figural learning and memory	64%	54%	2,964
Motor performance	63%	40%	2,334
Attention <sup>b</sup>	55%	36%	3,112
Visuoconstruction	47%	31%	1,980
Intelligence ('crystallized')	29%	17%	1,992
Speech-dominant hemisphere	atypical: 36%		428

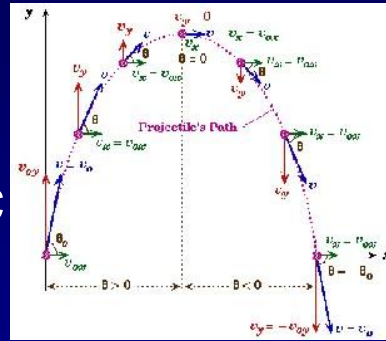
<sup>a</sup>Including: naming, speech comprehension, verbal fluency (phonetic, semantic).

<sup>b</sup>Including: reaction times, cancellation tasks, inhibition tasks, trail making tests.

# Classifications of Memory

- Declarative or Explicit

- Semantic
- Episodic
- Autobiographic



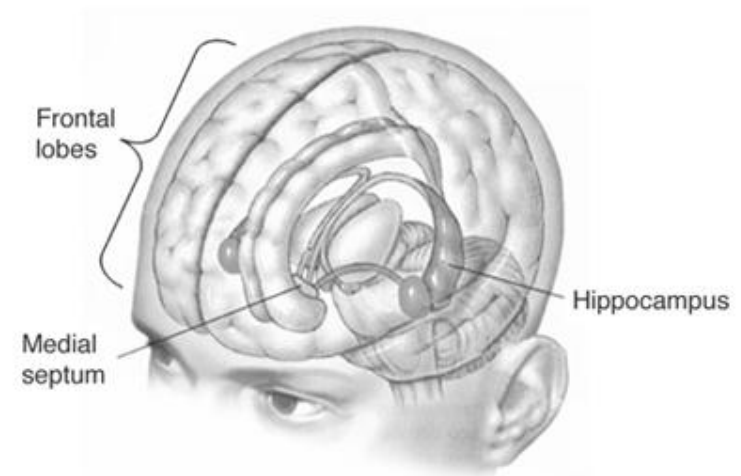
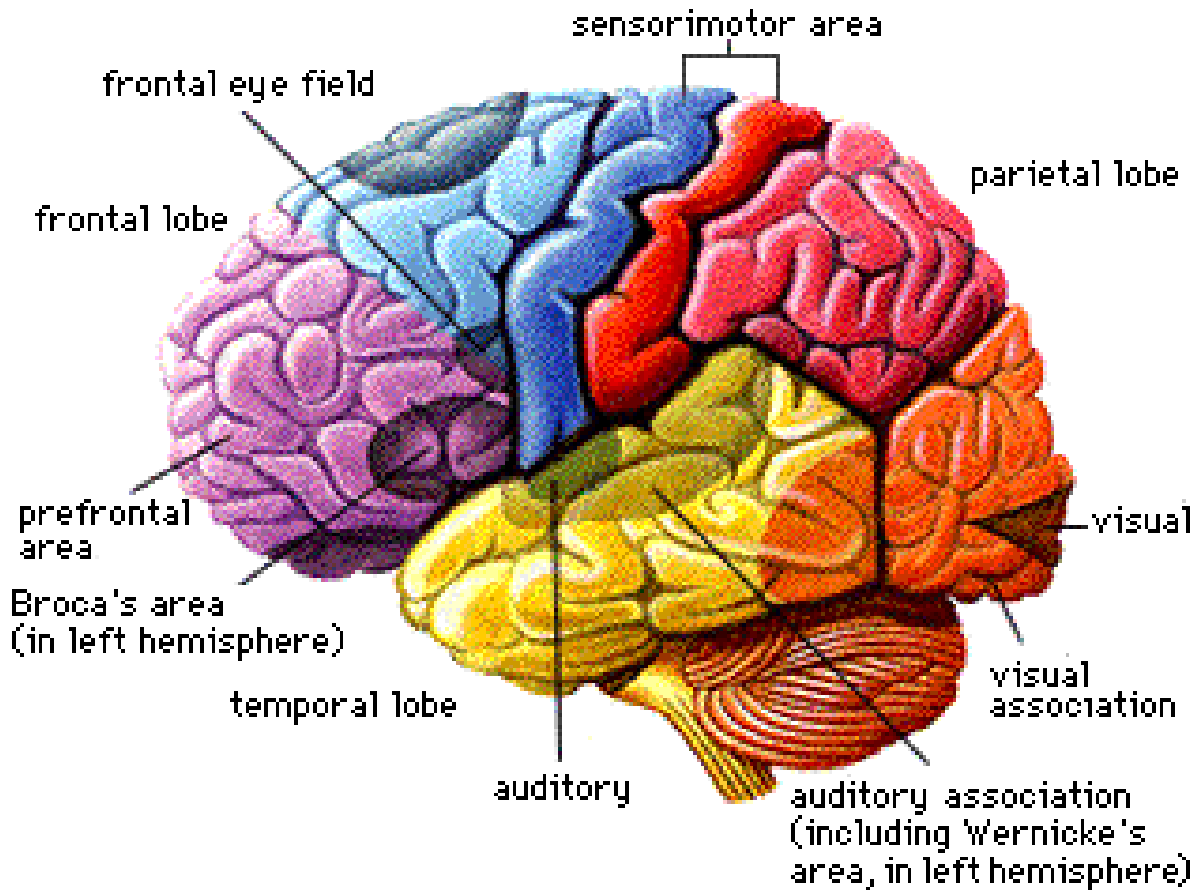
- Immediate
- Short term
- Long term

- Procedural or Implicit



# Memory Processes

- Encoding or registration
- Storage
- Retrieval, recall or recollection



# Factors Affecting Memory In Epilepsy

- Underlying disease
- Seizure activity
- Anticonvulsant medications
- Age
- Genetic background
- Psychological well-being
- Epilepsy surgery

**Morphological factors**  
(largely irreversible)

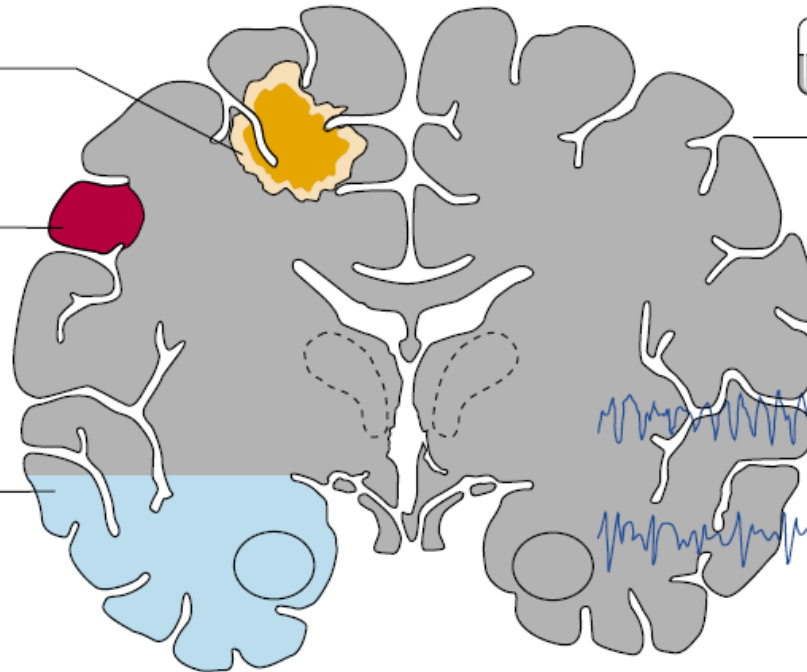
**Clinical and demographic features**  
Age at onset  
Lateralisation or topography of epileptogenic area  
Duration of epilepsy  
Sex

**Functional factors**  
(largely reversible)

Potentially progressive lesions  
(eg, tumour, encephalitis,  
paraneoplastic lesions)

Broadly stationary lesions  
(eg, HS, FCD,  
post-traumatic lesions)

Epilepsy surgery



Antiepileptic drugs

Psychiatric  
comorbidity

Seizures

Interictal epileptic  
discharges?

*Morphological and functional factors influencing cognition in the chronic epilepsy syndromes discussed in the text. FCD=focal cortical dysplasia; HS=hippocampal sclerosis.*

# Temporal Lobe Epilepsy

- Most common form of epilepsy
- Disabling, irreversible behavioral disturbances
- Most intractable to medications, seizure free less than 10%
- Most have hippocampal sclerosis
- Great candidate for surgical treatment

# Temporal Lobe Epilepsy

- Mostly affect declarative memory
- Procedural memory unaffected
- Memory lateralization

Dominant hemisphere

Significant verbal  
episodic memory deficit

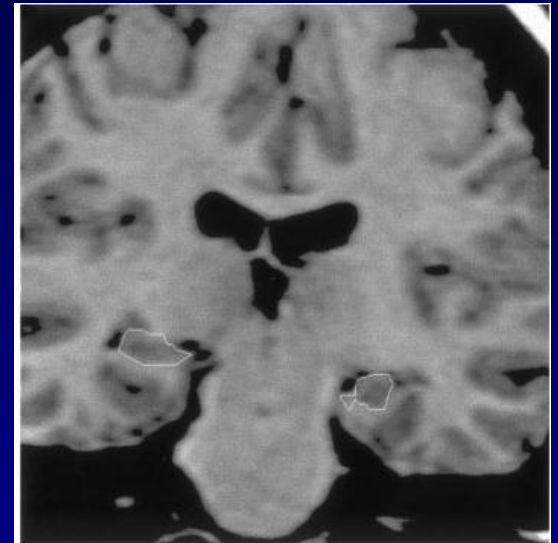
- Non-dominant hemisphere

Less consistent visual-spatial  
memory deficit

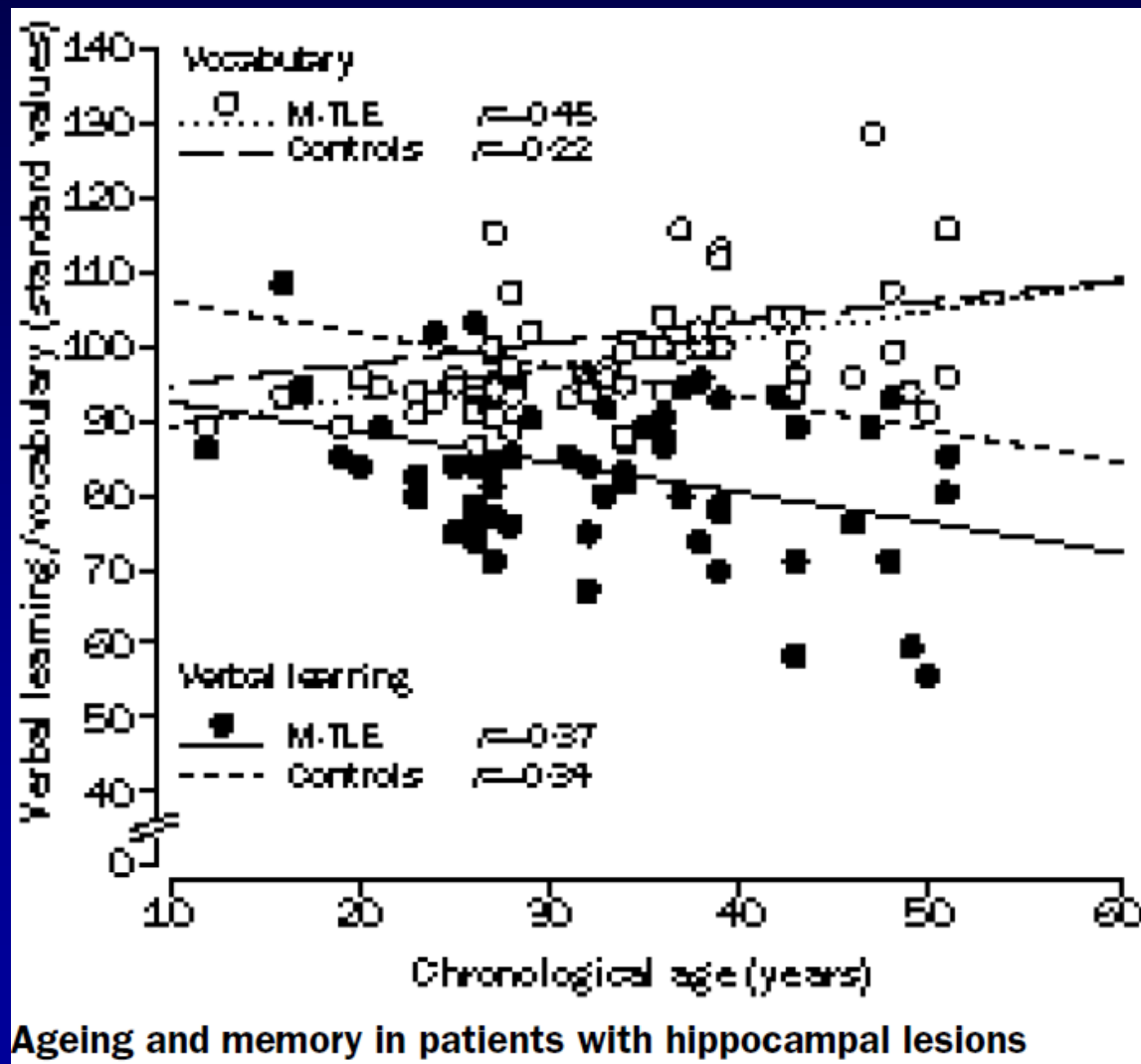
- Lateral temporal lobe: learning new material.  
Mesial temporal lobe: long term memory

# Hippocampal Sclerosis is a Progressive Disorder

- 12 patients with HS followed for 2.5 to 5.2 years
- MRI repeated at the end of follow up
- 10% volume loss of hippocampus in patients with continued seizures
- Progressive hippocampal atrophy only occurred in people with continued seizures.



# Memory deficit in epilepsy vs. Dementia



# Antiepileptic Drugs (AEDs)

---

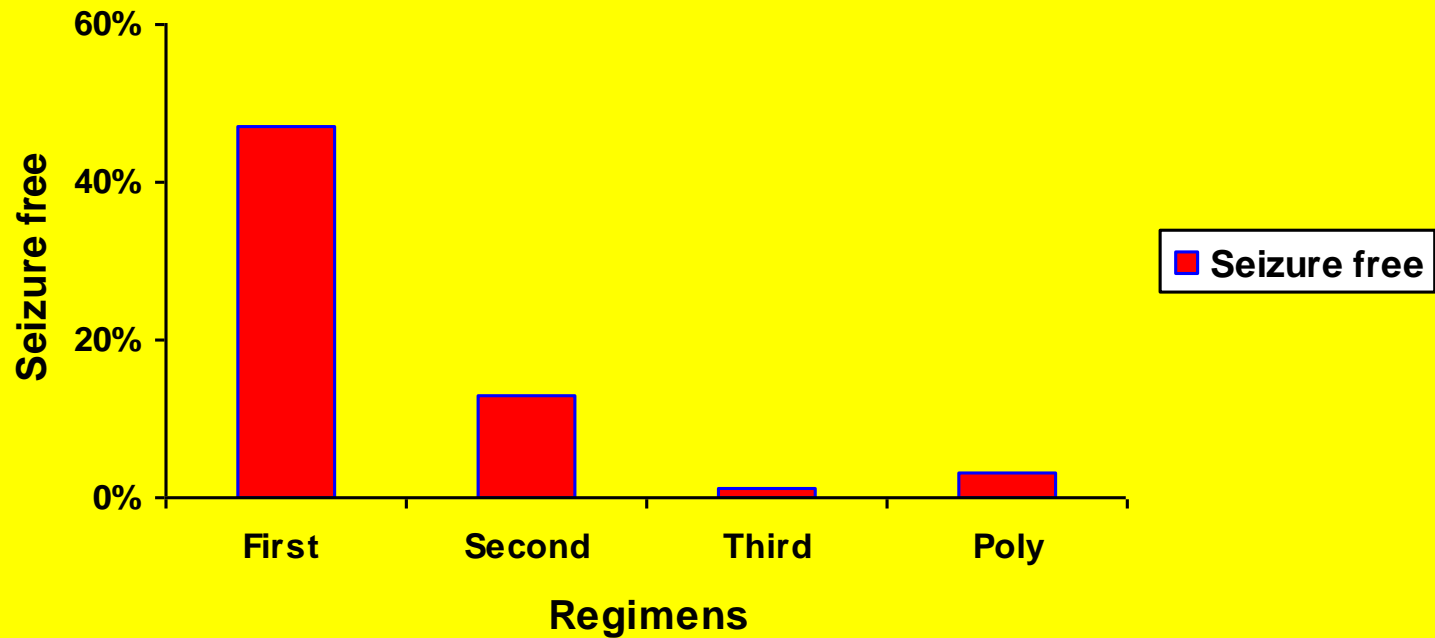
Older:

- Phenobarbital
- Phenytoin
- Carbamazepine
- Valproic Acid
- Ethosuximide

Newer:

- Lamotrigine
- Oxcarbazepine
- Zonisamide
- Felbamate
- Topiramate
- Levetiracetam
- Gabapentin
- Tiagabine
- Pregabalin
- Lacosamide

## Success of Antiepileptic Drug Regimens



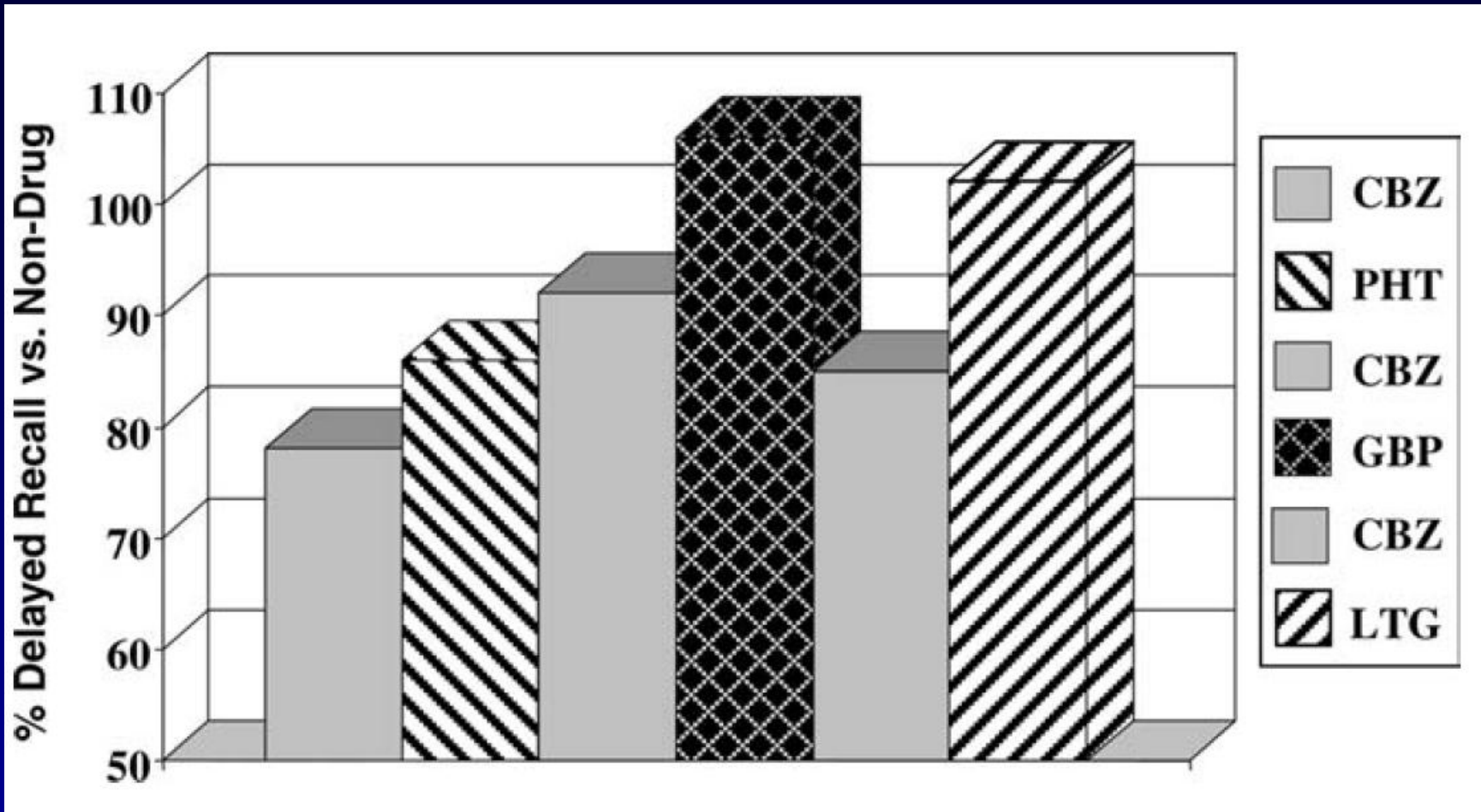


Fig. 1. Medical College of Georgia (MCG) stories: delayed recall, healthy volunteer studies [9,11,12]. CBZ, carbamazepine; PHT, phenytoin; GBP, gabapentin; LTG, lamotrigine.

# Newer AEDs and Memory

- Lamotrigine
- Gabapentin
- Topiramate
- Zonisamide
- Lacosamide?
- Levetiracetam?

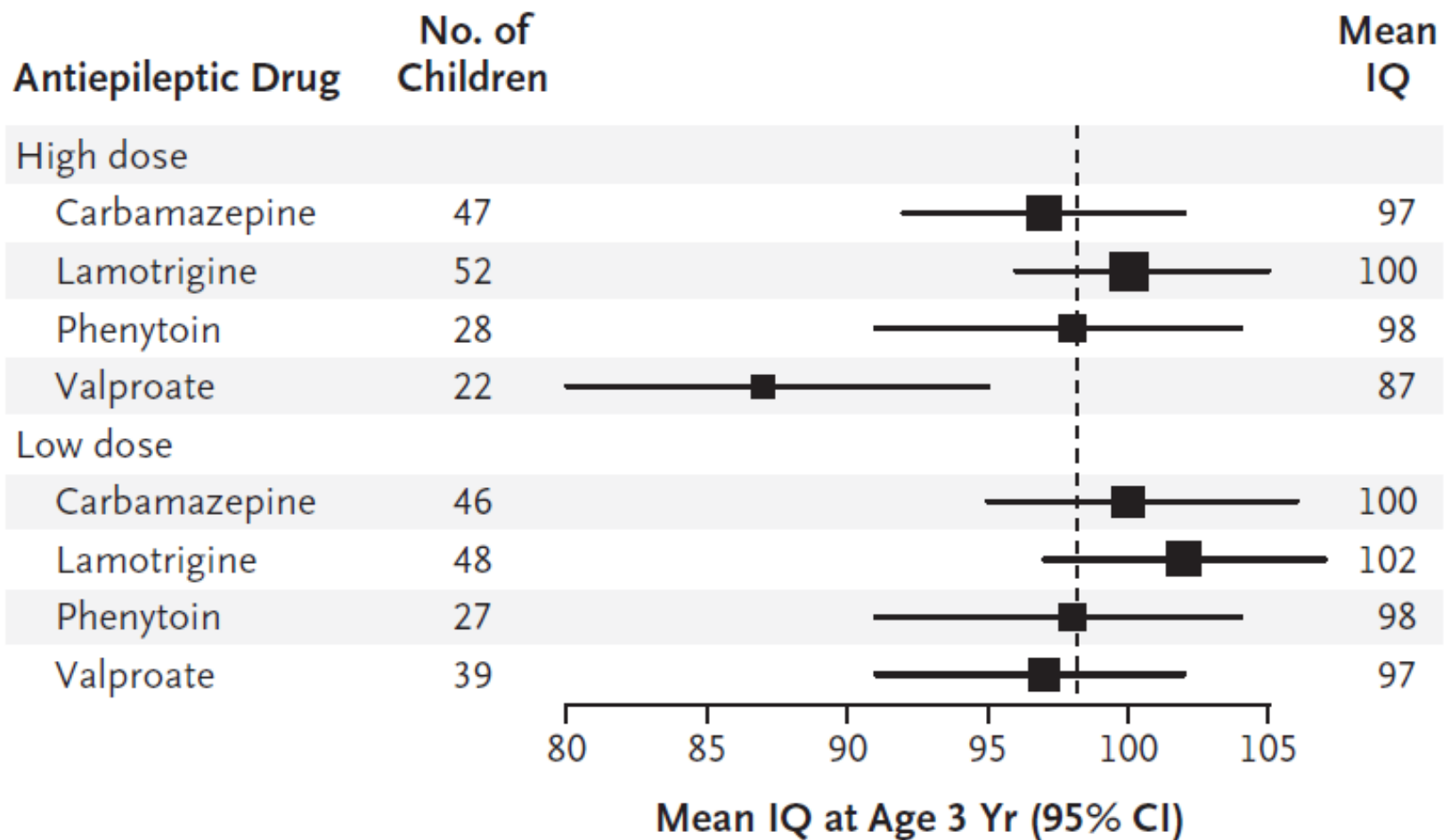
# Neurodevelopmental Effects of Antiepileptic Drugs (NEAD Study)

- Prospective, observational, multicenter study in the U.S and U.K.
- Pregnant women with epilepsy taking single AED between 199 to 2004
- Primary analysis: IQ at 6 years of age
- AED monotherapy
  - Carbamazepine
  - Lamotrigene
  - Phenytoin
  - Valproate

**Table 2.** IQ Scores of Children at 3 Years of Age According to In Utero Exposure to Antiepileptic Drugs.\*

Variable	Carbamazepine (N=73)	Lamotrigine (N=84)	Phenytoin (N=48)	Valproate (N=53)
Mean IQ (95% CI)†	98 (95–102)	101 (98–104)	99 (94–104)	92 (88–97)
Mean difference in IQ from valproate group (95% CI)‡	6 (0.6–12.0)	9 (3.1–14.6)	7 (0.2–14.0)	
P value§	0.04	0.009	0.04	

\* Meador, et al. N Engl J Med 2009;360:1597-605.



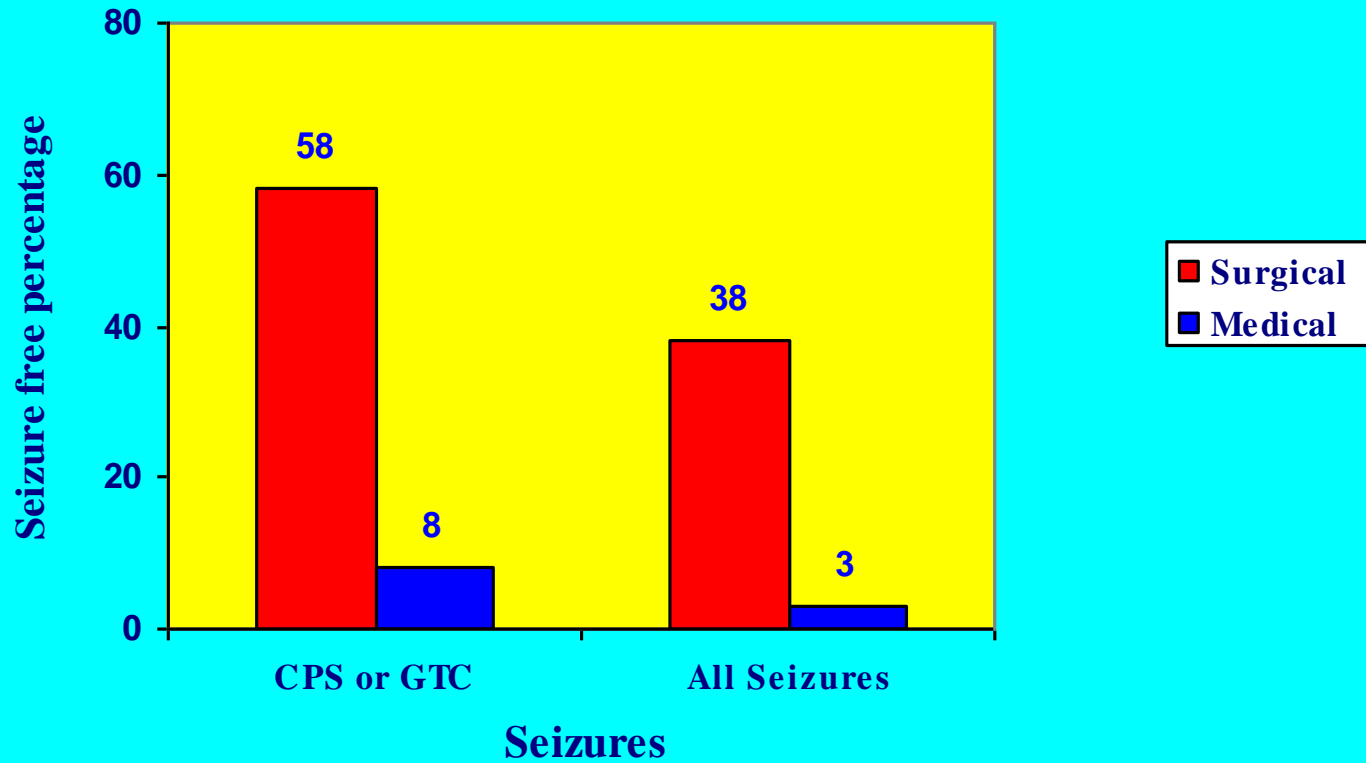
**Figure 1.** IQ Scores of Children Who Were Exposed to Antiepileptic Drugs In Utero, According to Drug and Dose.

\* Meador, et al. N Engl J Med 2009;360:1597-605.

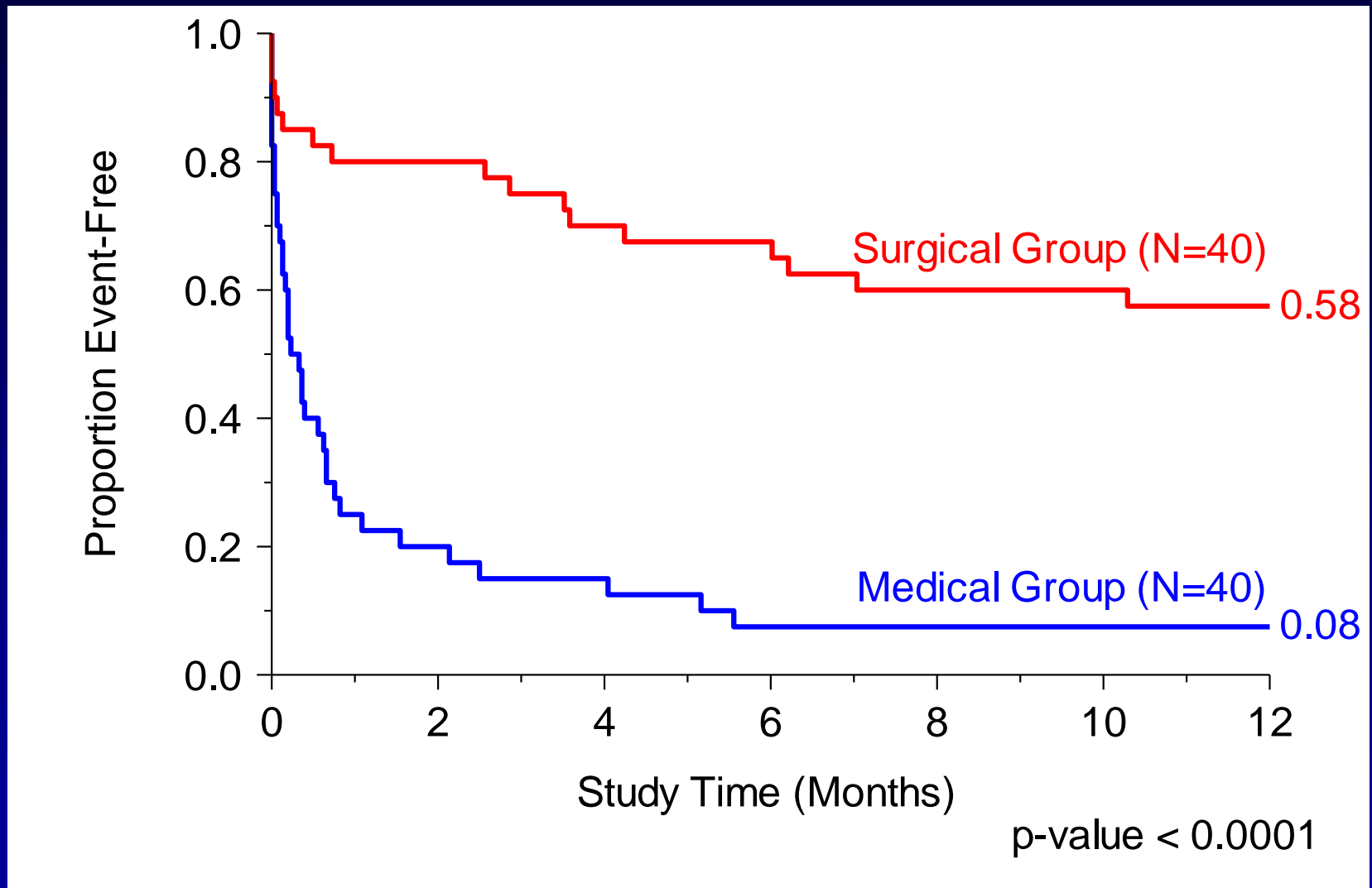
# Epilepsy Surgery

- Temporal lobectomy
- Lesionectomy
- Multiple Subpial Transections (MST)
- Callosotomy
- Hemispherectomy

## Seizure Free at 12 Months

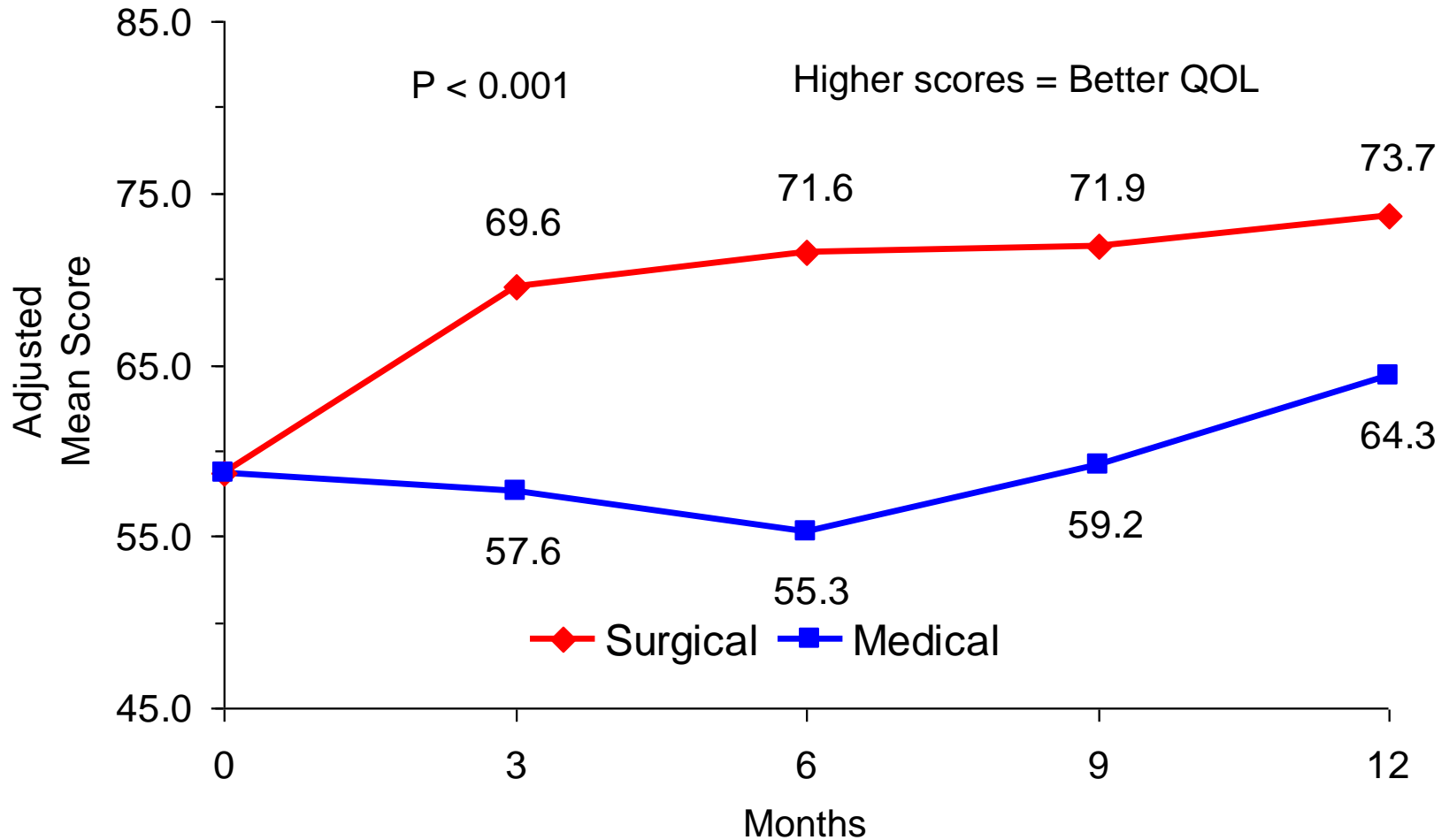


# Free from Complex Partial & Generalized Seizures



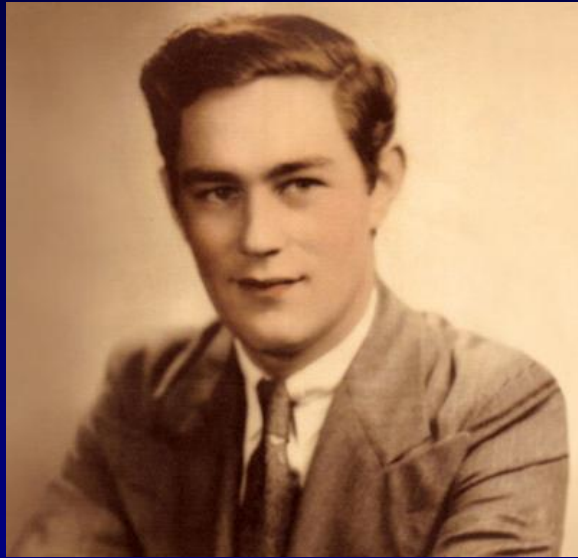
\* Wiebe S, et.al. *New Engl J Med.* 2001;345:311-318  
University of Western Ontario & London Health Sciences Centre, Ontario, CANADA

# Quality of Life (QOLIE-89)



\* **Wiebe S, et.al. *New Engl J Med.* 2001;345:311-318**  
**University of Western Ontario & London Health Sciences Centre, Ontario, CANADA**

# Patient H.M (1926 – 2008)



- Severe intractable epilepsy
- Surgery in 1953, Bilateral temporal lobectomy
- Severe anterograde declarative memory amnesia
- Retrograde memory amnesia: complete 1-2 yrs, partial 11 yrs.
- Working memory and procedural memory intact.

# Predictors for Post-ATL Cognitive Decline

- ATL on language dominant hemisphere
- Higher pre-op cognitive performance
- No hippocampal sclerosis
- Older age at surgery
- Older age of seizure onset
- Poor post-op seizure control

\* Helmstaedter. Epilepsy & Behavior 2004; 5: S45-S55

# Self-reported Memory Deficits

- Poorly correlated with objective findings
- Underestimate memory problems: limited awareness
- Overestimate memory problems
  - Depression 8% - 48%
  - Anxiety 19% - 45%
  - Medication adverse effects: AEDs and Pcyhotropic
  - Psychogenic

## Report from AAN

In general, neuropsychological assessment is most useful in patients with more subtle deficits. It is also useful for detecting deficits in patients with particularly high premorbid intelligence levels”” in which bedside-type clinical testing may be insensitive to mild alterations. Neuropsychological testing has an important role in patients undergoing epilepsy surgery and can provide useful rehabilitative guidance in patients recovering from TBI and stroke and prognostic information for patients with HIV.

**Table** Tests commonly used to assess the major domains of neuropsychological function

Neuropsychological domain	Neuropsychological test
Attention	Digit span
	Letter cancellation
	Trails A test
Language	Boston Naming Test
	Boston Diagnostic Aphasia Examination
	Western Aphasia Battery
	Verbal fluency
Memory	Wechsler Memory Scale
	Rey Auditory Verbal Learning Test
	California Verbal Learning Test
Visuospatial skills	Rey-Osterrieth Complex Figure
	Block design subtest of WAIS-R
Executive function	Wisconsin Card Sort Test
	Stroop Test
	Trails B test
Intelligence	WAIS-R
	Wechsler Intelligence Scale for Children
	New Adult Reading Test
Motor speed	Finger Tapping
	Grooved Pegboard
Educational achievement	Wide Range Achievement Test