



Accelerated long-term forgetting and autobiographical amnesia

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*Everyone needs his memories: they keep
the wolf of insignificance from the door*

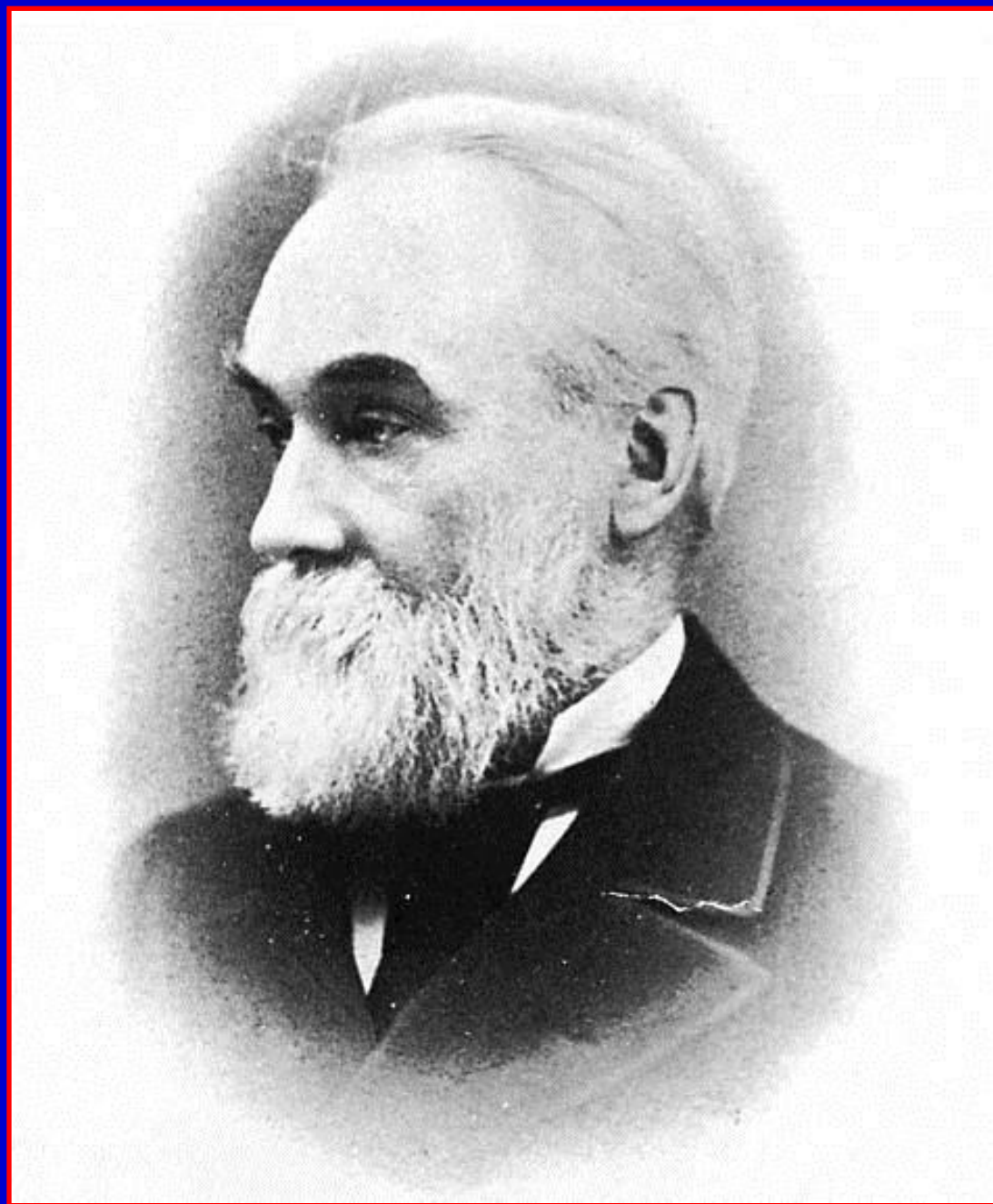
Saul Bellow

ALF & AbA

- Transient epileptic amnesia
- What is autobiographical memory?
- ‘focal autobiographical amnesia’
- Accelerated long term forgetting
- Time course of memory and loci of impairment
- Conclusions & future directions

ALF & AbA

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“(4.) A fourth occasion is perhaps worth record. I was attending a young patient whom his mother had brought me with some history of lung symptoms. I wished to examine the chest, and asked him to undress on a couch. I thought he looked ill, but have no recollection of any intention to recommend him to take to his bed at once, or of any diagnosis. Whilst he was undressing I felt the onset of a *petit mal*. I remember taking out my stethoscope and turning away a little to avoid conversation. The next thing I recollect is that I was sitting at a writing-table in the same room, speaking to another person, and as my consciousness became more complete, recollected my patient, but saw he was not in the room. I was interested to ascertain what had happened, and had an opportunity an hour later of seeing him in bed, with the note of a diagnosis I had made of ‘pneumonia of the left base.’ I gathered indirectly from conversation that I had made a physical examination, written these words, and advised him to take to bed at once. I re-examined him with some curiosity, and found that my conscious diagnosis was the same as my unconscious,—or perhaps I should say, unremembered—a diagnosis had been. I was a good deal surprised, but not so unpleasantly as I should have thought probable.”

Transient Epileptic Amnesia

previous reports

- **The case of Dr Z**
 - Hughlings Jackson, Brain, 1889/1898
- **Isolated reports of 'amnesic seizures'**
 - Epileptic amnesic attacks, Pritchard, 1985
 - Epileptic transient amnesia, Stracciari, 1990
 - Ictal amnesia, Rowan, 1991
 - Epileptic amnesic syndrome, Galassi, 1988/1992
 - Pure amnesic seizures, Palmini, 1992
- **Epilepsy mimicking TGA**
 - Hodges, Brain, 1990
- **Transient epileptic amnesia defined**
 - Kapur, JNNP, 1993
- **TEA: 10 current cases + 21 reviewed**
 - Zeman et al 1998

time

The Impairment of **Memory** in **Epilepsy**

Mr P.M.

- 58 year old man
- 28 episodes of transient amnesia over 18 months
- All on waking
- Circa 20 minutes
- Amnesia for brother's death
- Lamotrigine abolished
- Returned with olfactory hallucinations when treatment omitted
- Lamotrigine abolished

time

The Impairment of Memory in Epilepsy

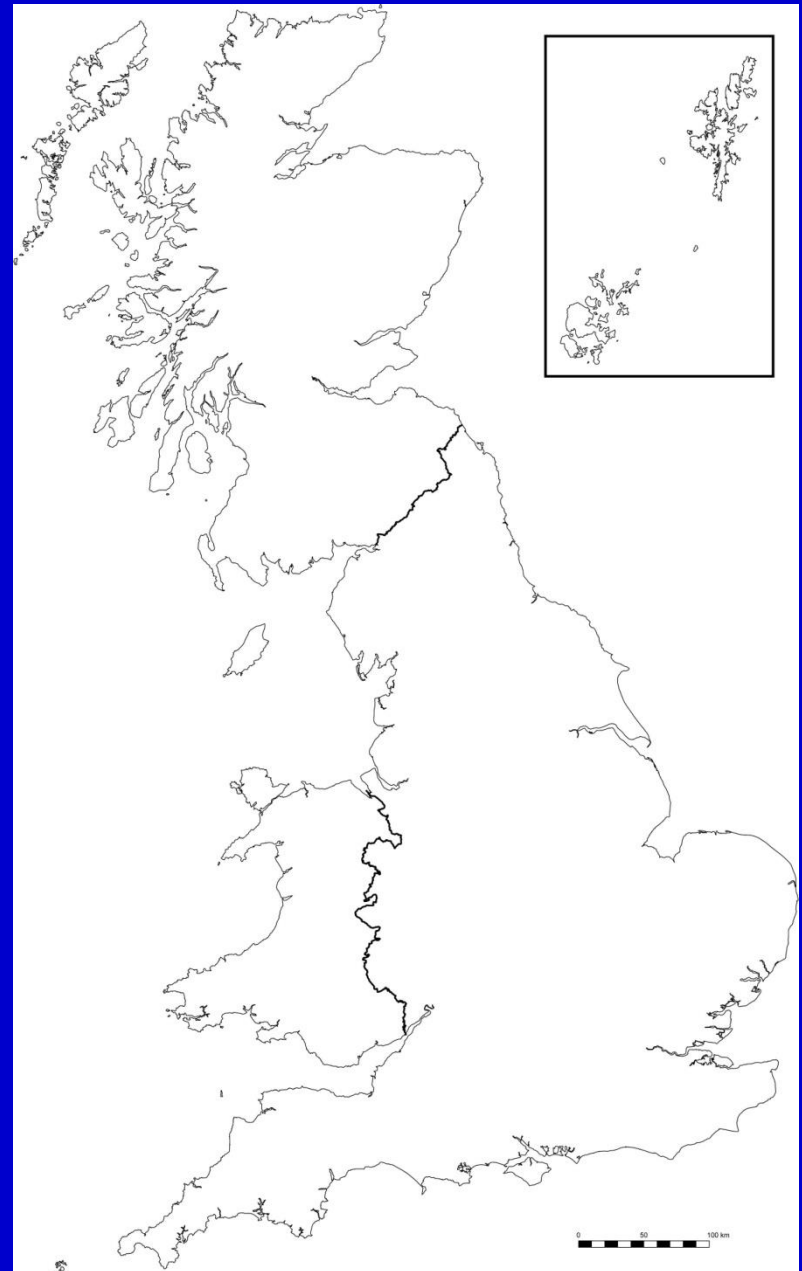
Diagnostic criteria

Recurrent, witnessed episodes
of transient amnesia

Other cognitive functions intact

Evidence of epilepsy

- i. other clinical features of epilepsy
- ii. response to anticonvulsant medication
- iii. epileptiform abnormalities on EEG



time

The Impairment of Memory in Epilepsy

Methods

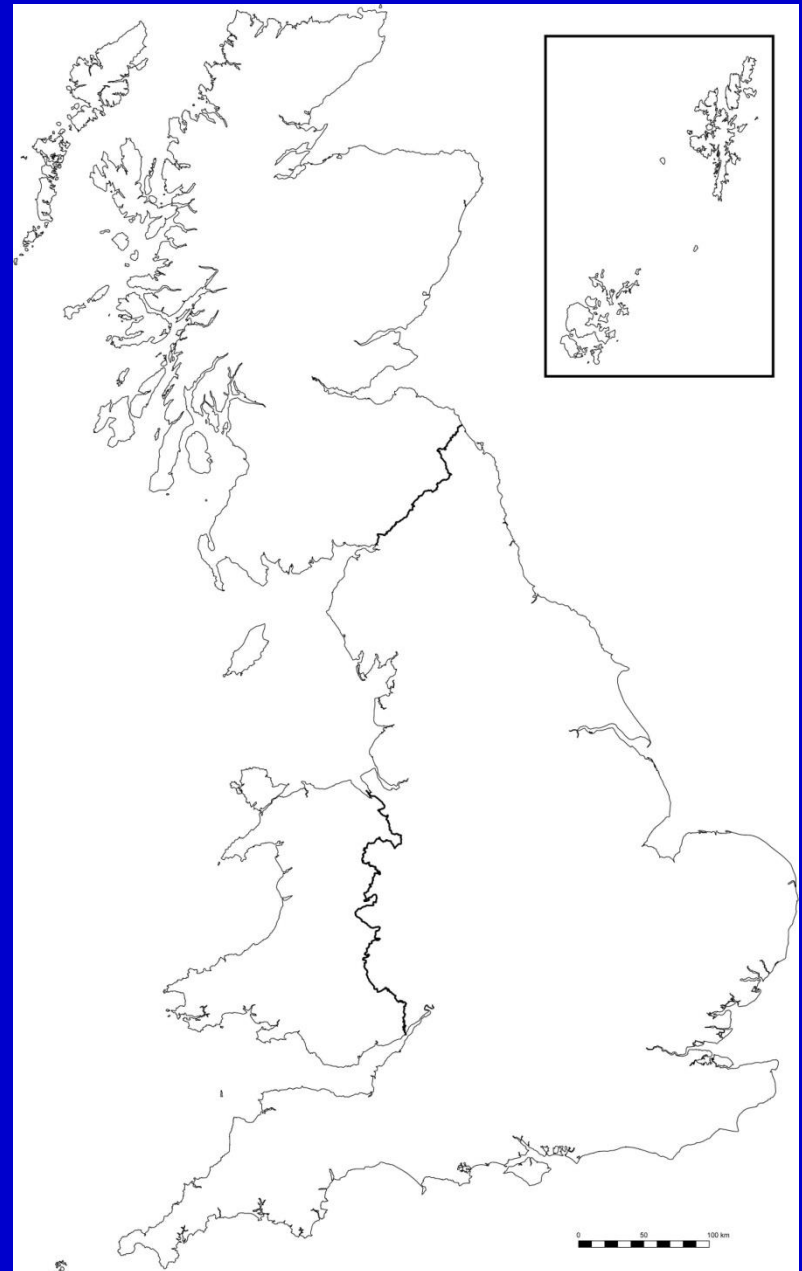
UK-wide recruitment

History and examination

Neuropsychology

EEG

Structural MRI



time

The Impairment of Memory in Epilepsy

Demographics

50 patients

sex ratio

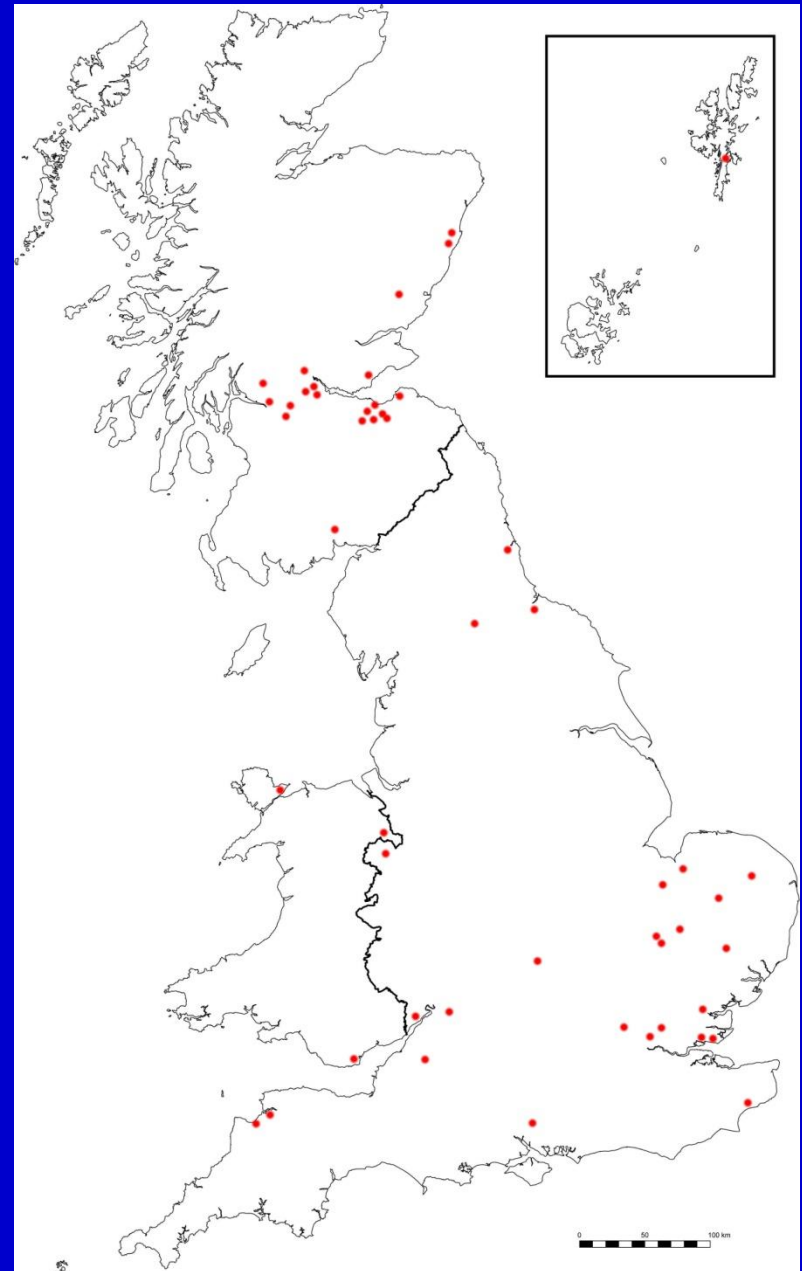
male = 34 (68%)

female = 16 (32%)

age seen

range = 46 to 84 years

mean = 68.3 years



Clinical Features of TEA

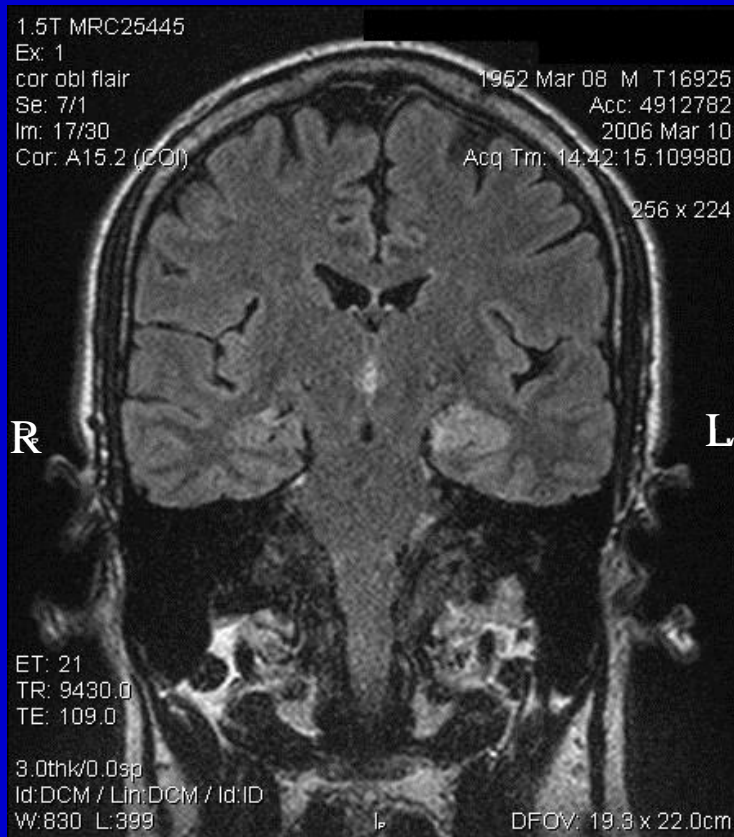
Butler et al *Annals of Neurology* 2007;61:587-598

- Onset in later life
- Male predominance
- Attacks 30-60 minutes
- Attacks one/month
- Attacks on waking common
- Amnesia can be sole feature
- +/- olfactory hallucinations, automatisms, brief unresponsiveness
- Partial recall common
- Excellent treatment response
- Diagnosis usually delayed
- Interictal memory complaints usual
 - 2/3 Autobiographical amnesia
 - 1/2 Accelerated forgetting
 - 1/3 Topographical amnesia

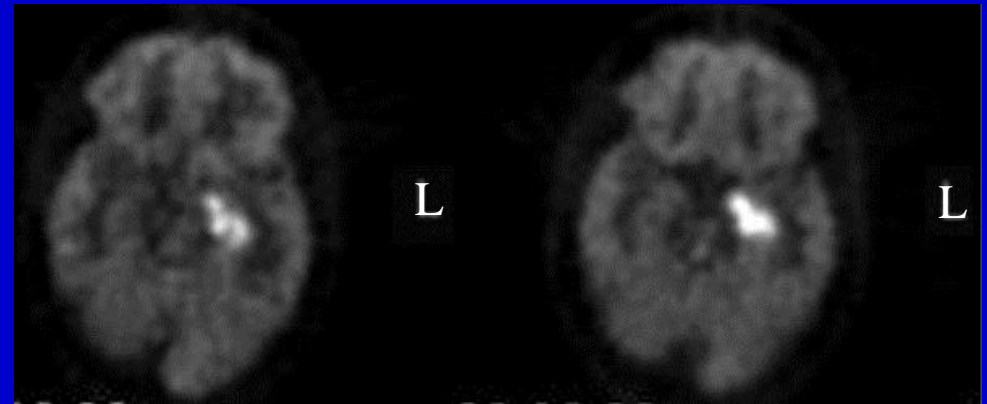
Transient Epileptic Amnesia

Butler & Zeman *Nature Clin Pract Neurol* 2008

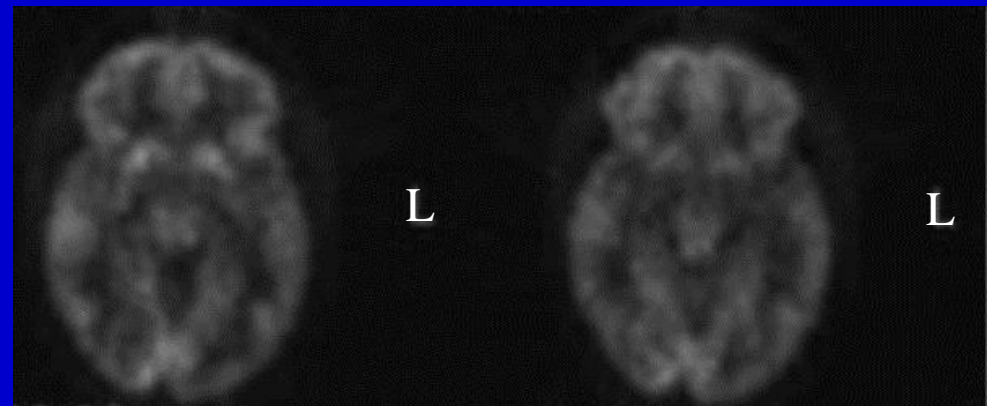
Peri-ictal MRI

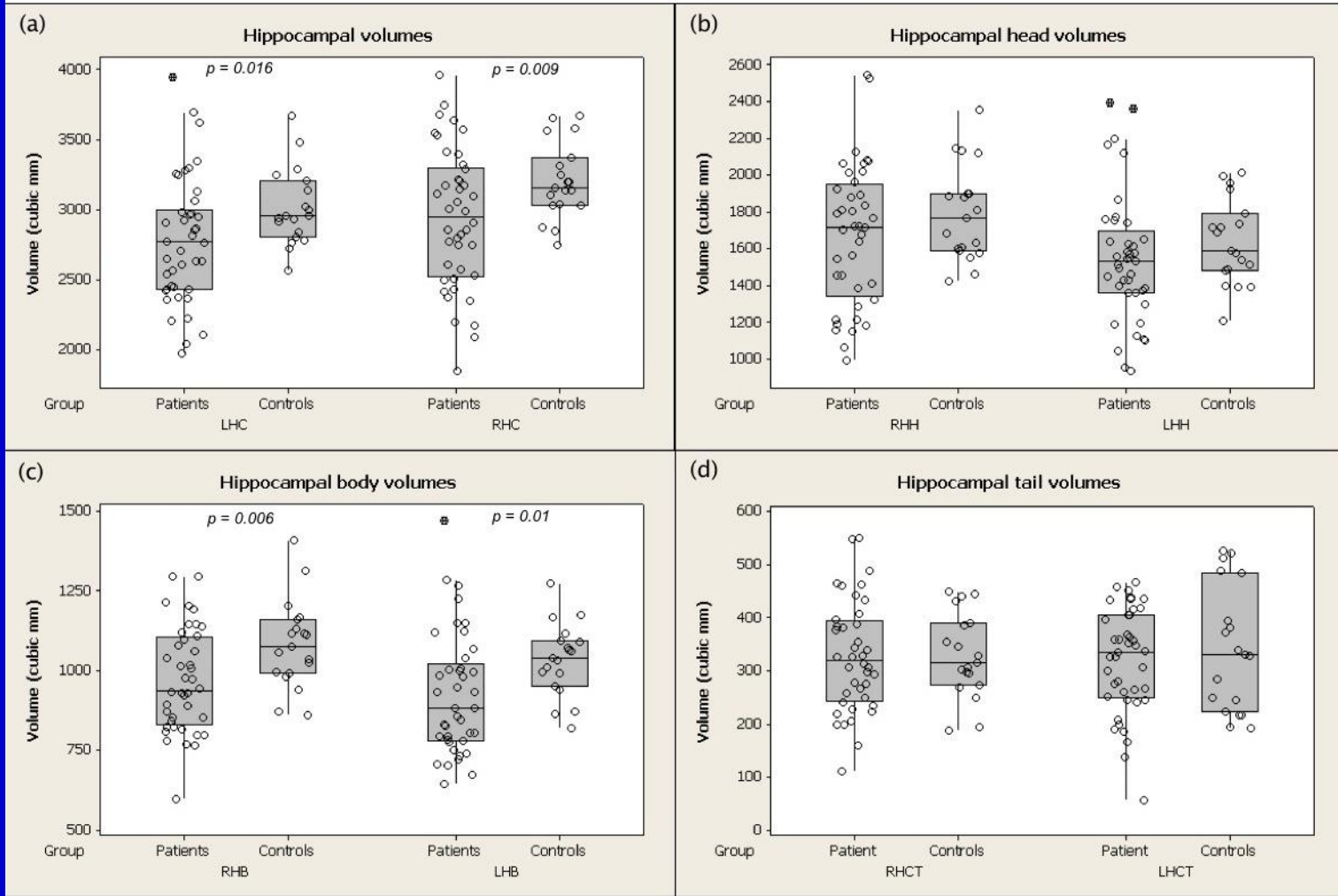


Peri-ictal FDG-PET



One month later





Butler et al Brain 2009: 132; 357–368

Transient Epileptic Amnesia

– Clinical

- epilepsy causing intermittent transient memory disturbance

– Cognitive

- Transient disruption
 - memory encoding/early consolidation and/or
 - memory retrieval

– Neurobiological

- Medial temporal
 - EEG, imaging
- Ictal or post-ictal

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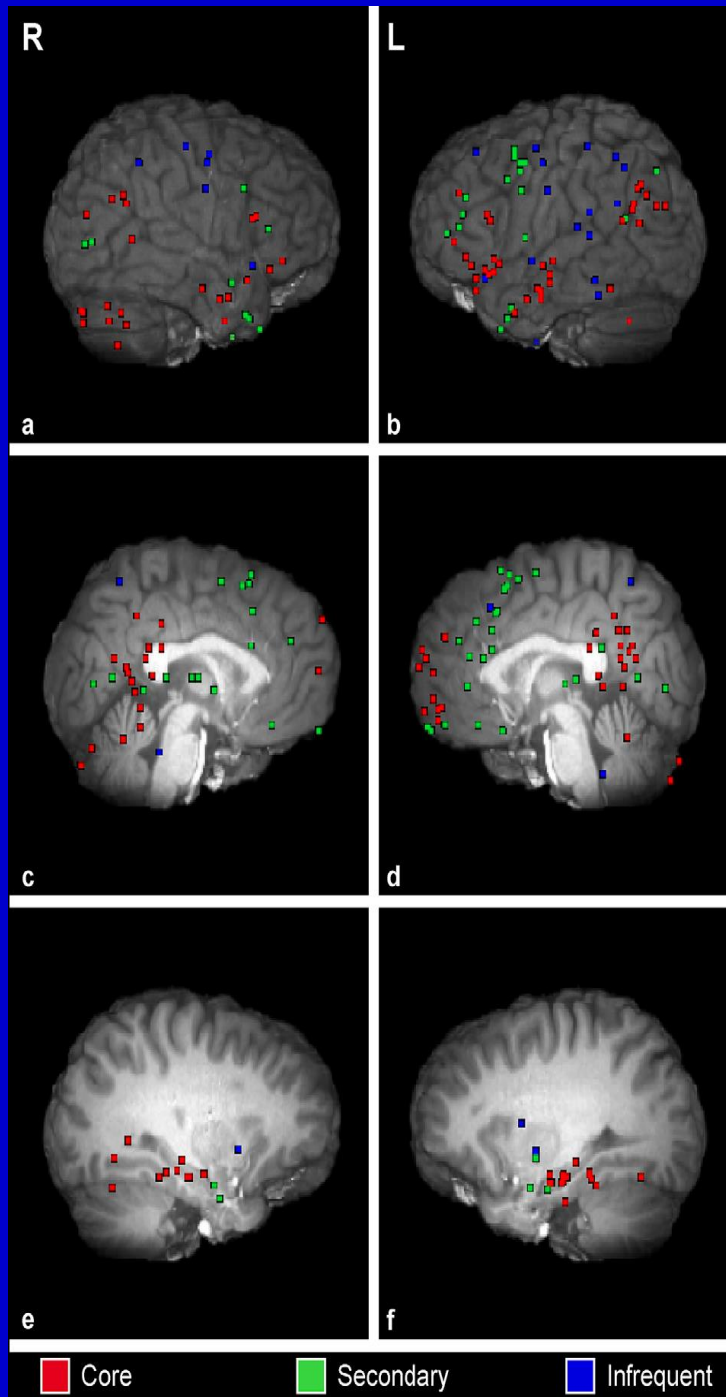
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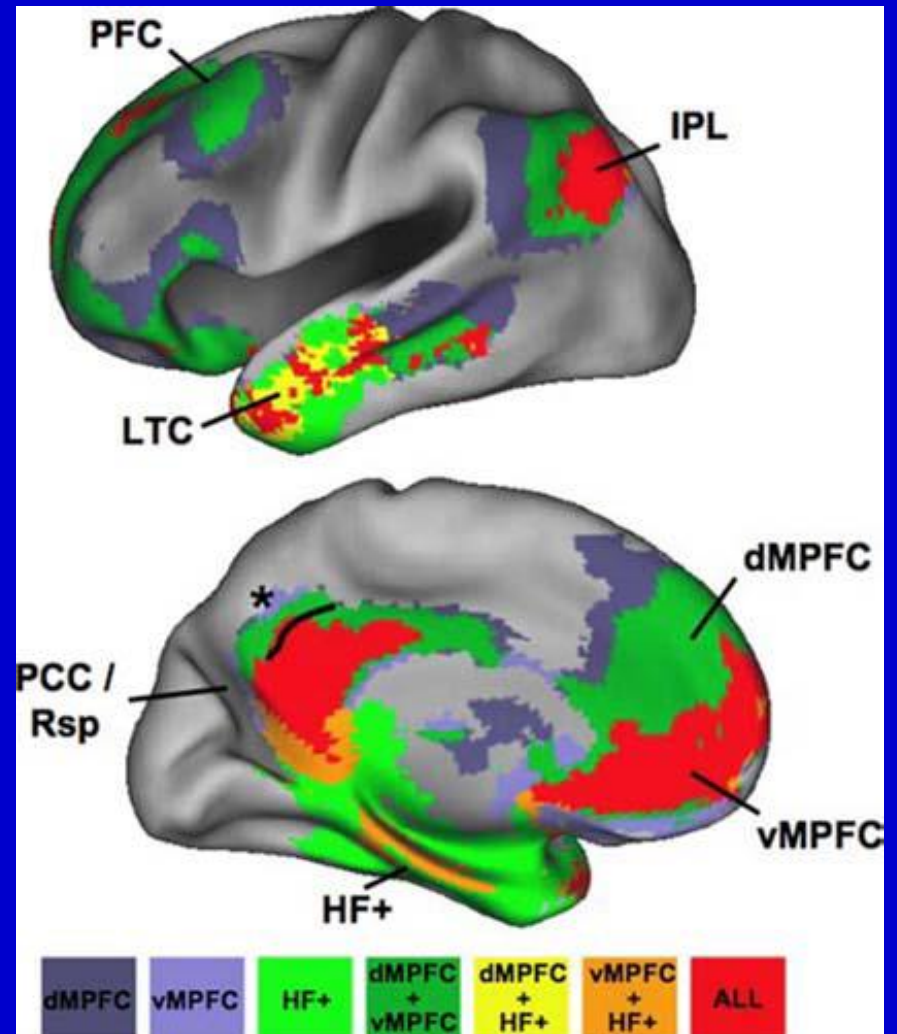
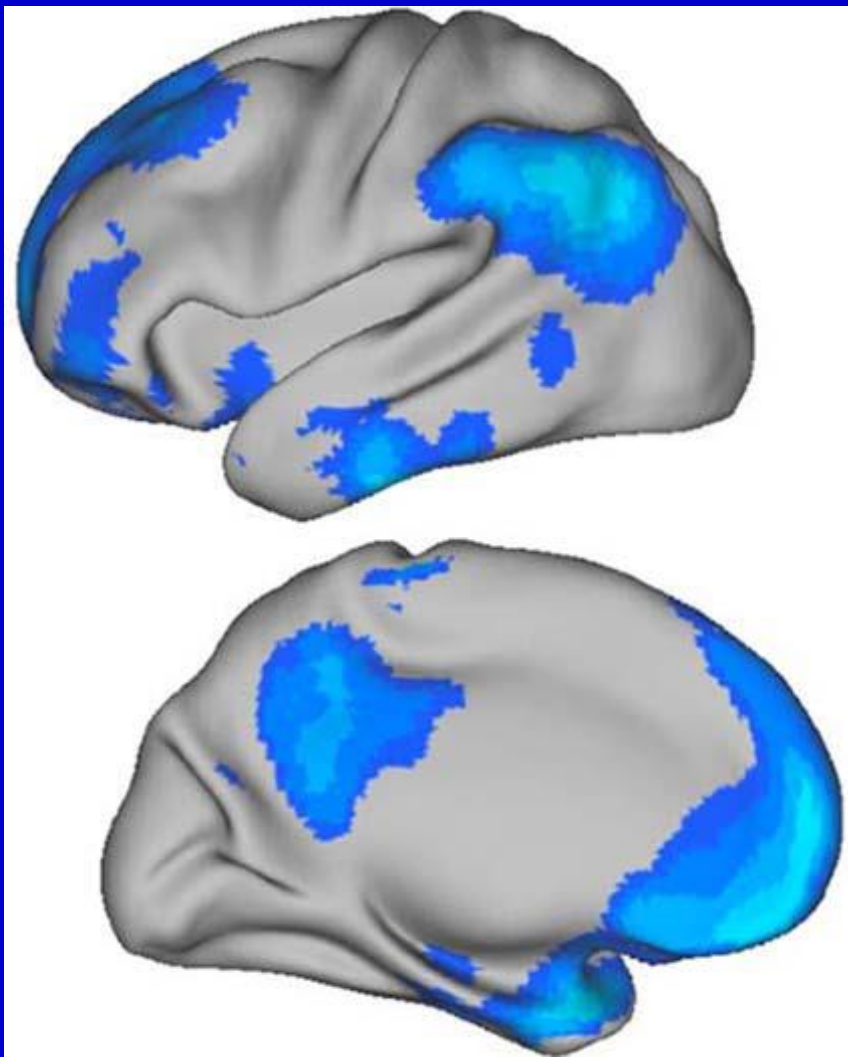
Autobiographical Memory

- your memory for your past
 - Self-referential – ‘all about you’
 - Includes facts and episodes
 - Involves
 - Memory search and retrieval
 - Temporality or narrative
 - Incorporates
 - Semantics
 - Imagery
 - Emotion

Klein, 2004; Kihlstrom , 2009; Svoboda, 2006; Piolino, 2009; Rubin, 2012

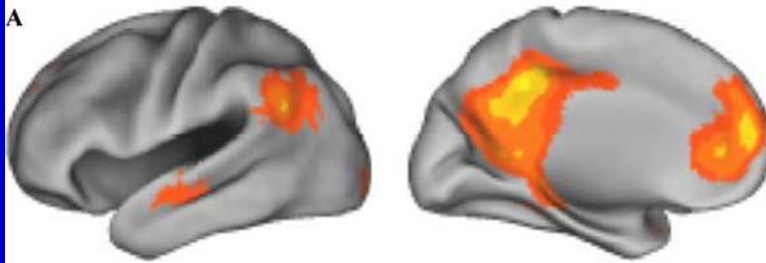


Svoboda et al
Neuropsychologia
2006;44: 2189–08.

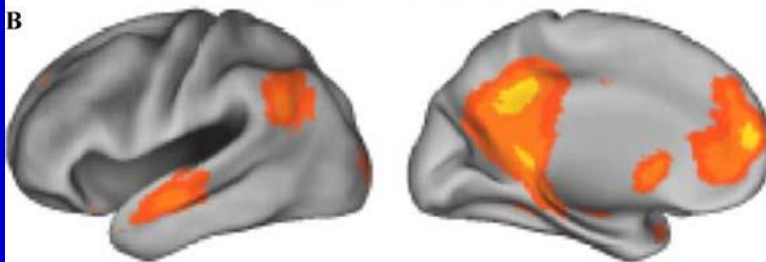


Buckner et al ANYAS
2008 1124:1-38

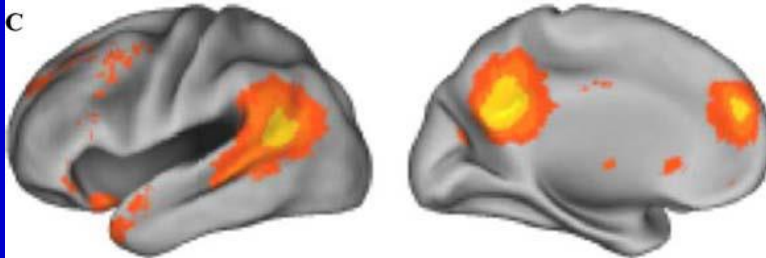
AUTOBIOGRAPHICAL MEMORY



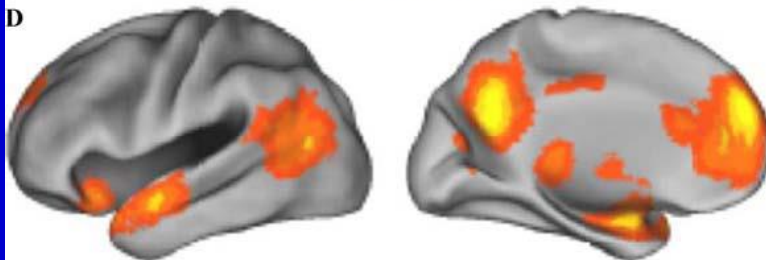
ENVISIONING THE FUTURE



THEORY OF MIND



MORAL DECISION MAKING



Buckner et al ANYAS
2008 1124:1-38

Autobiographical Memory

- Crucial for *human* cognition
 - Mirror self recognition
 - Theory of mind
 - Mental time travel ~ auto-noesis
- Facilitates
 - Self-knowledge and social emotions
 - Interpersonal relationships
 - Imagination, future thinking, problem solving

Kihlstrom 2009; Tulving 1985, 2002; Conway 2000

Autobiographical Memory

– Assessment

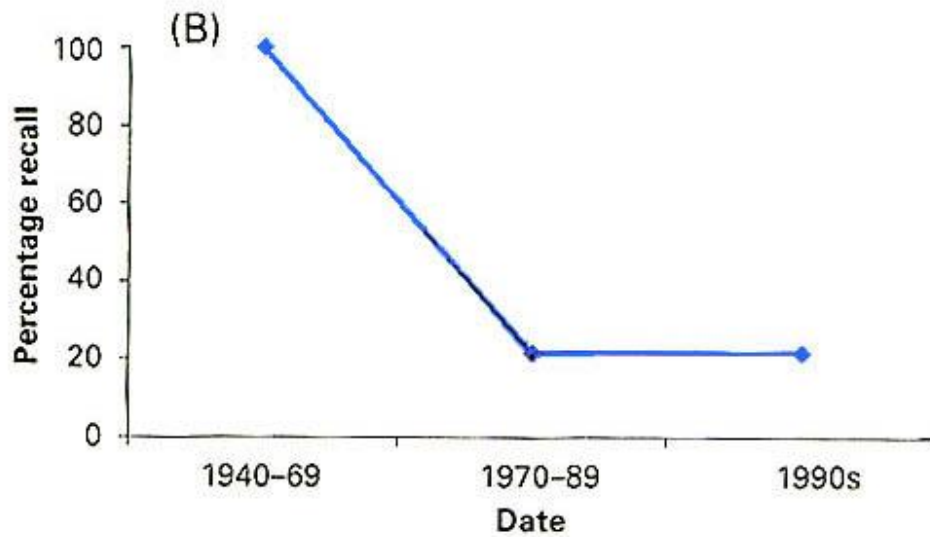
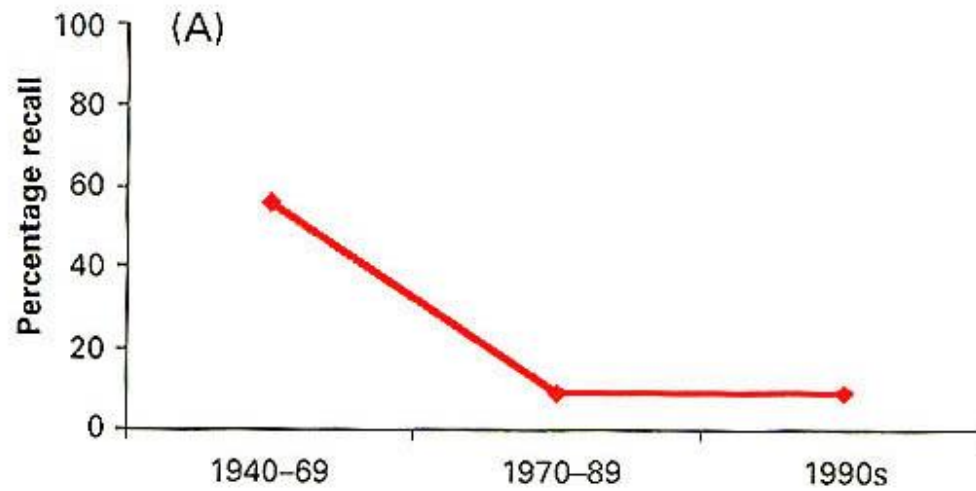
- Lack of experimental control
- Approaches:
 - Free recall
 - Crovitz & Schiffmann (1974) cue word technique
 - Kopelman (1989/90) Autobiographical Memory Interview
 - Ditschel (1992) Autobiographical fluency
 - Levine (2002) Autobiographical Interview
 - Piolino (2006) TEMPau task
 - Autobiographical memory recognition tests
 - Prospective assessment eg diary, SenseCam

Autobiographical Memory

- A vulnerable system
 - ...travel through subjective time, allowing individuals to re-experience specific past events...the last feature of ... memory to become fully operational in development and the first ... to go in ageing and most amnesias (Piolino et al, 2009)

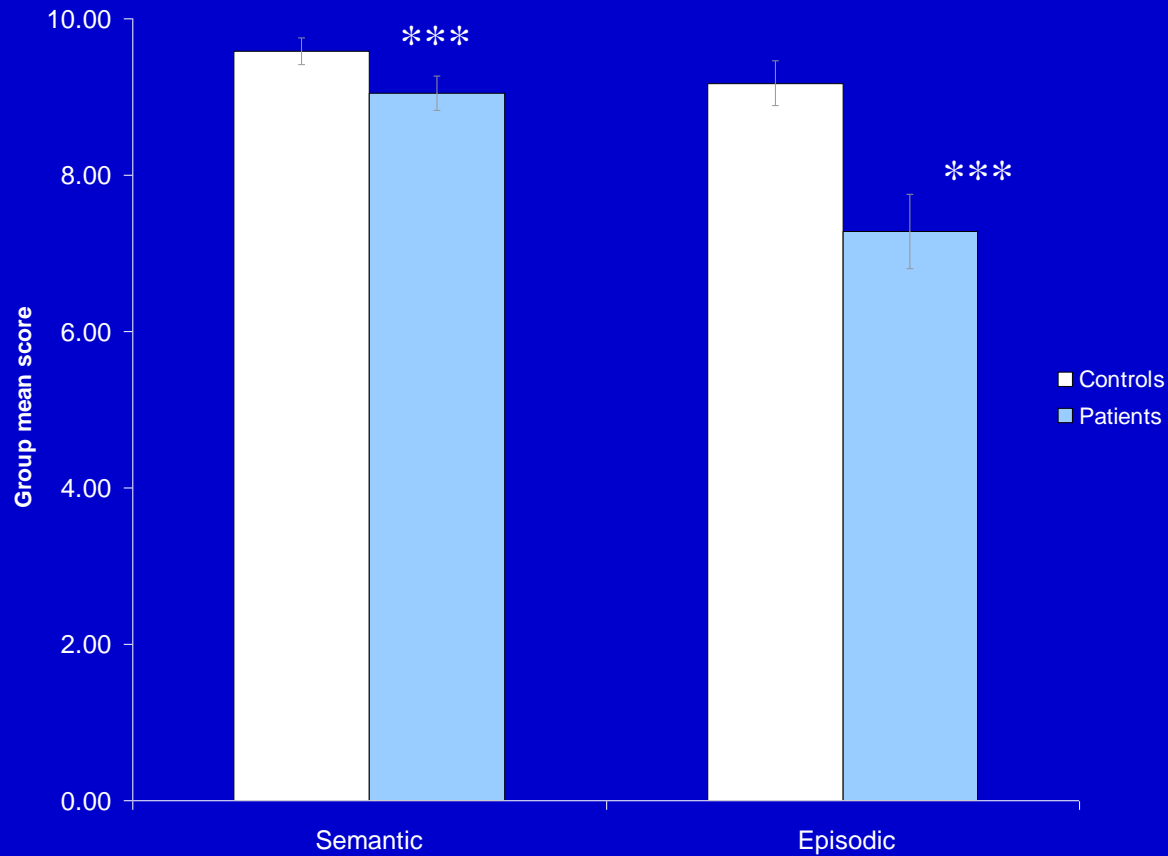
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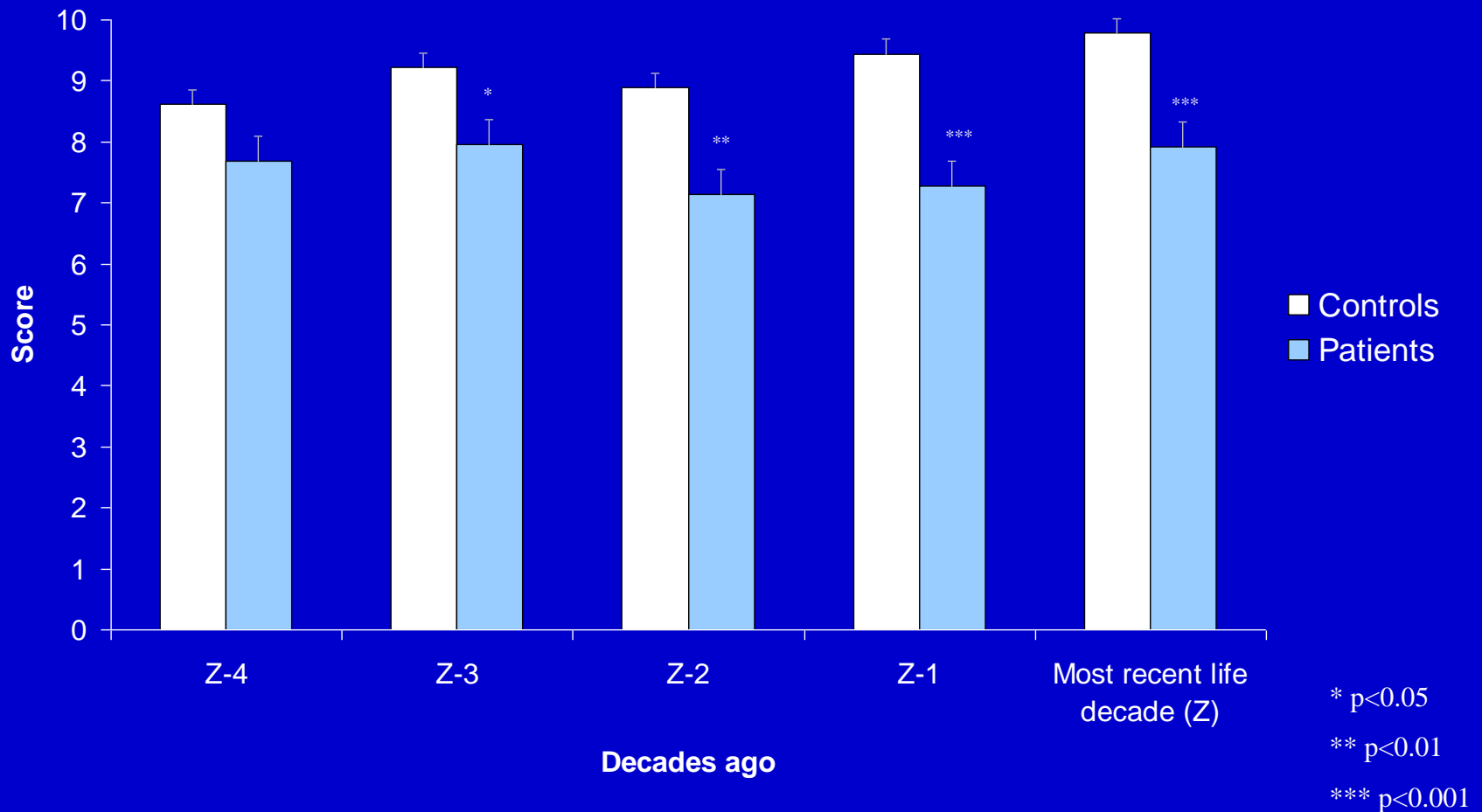
Manes et al Brain 2001;124:499-509

MAMI: average lifetime scores

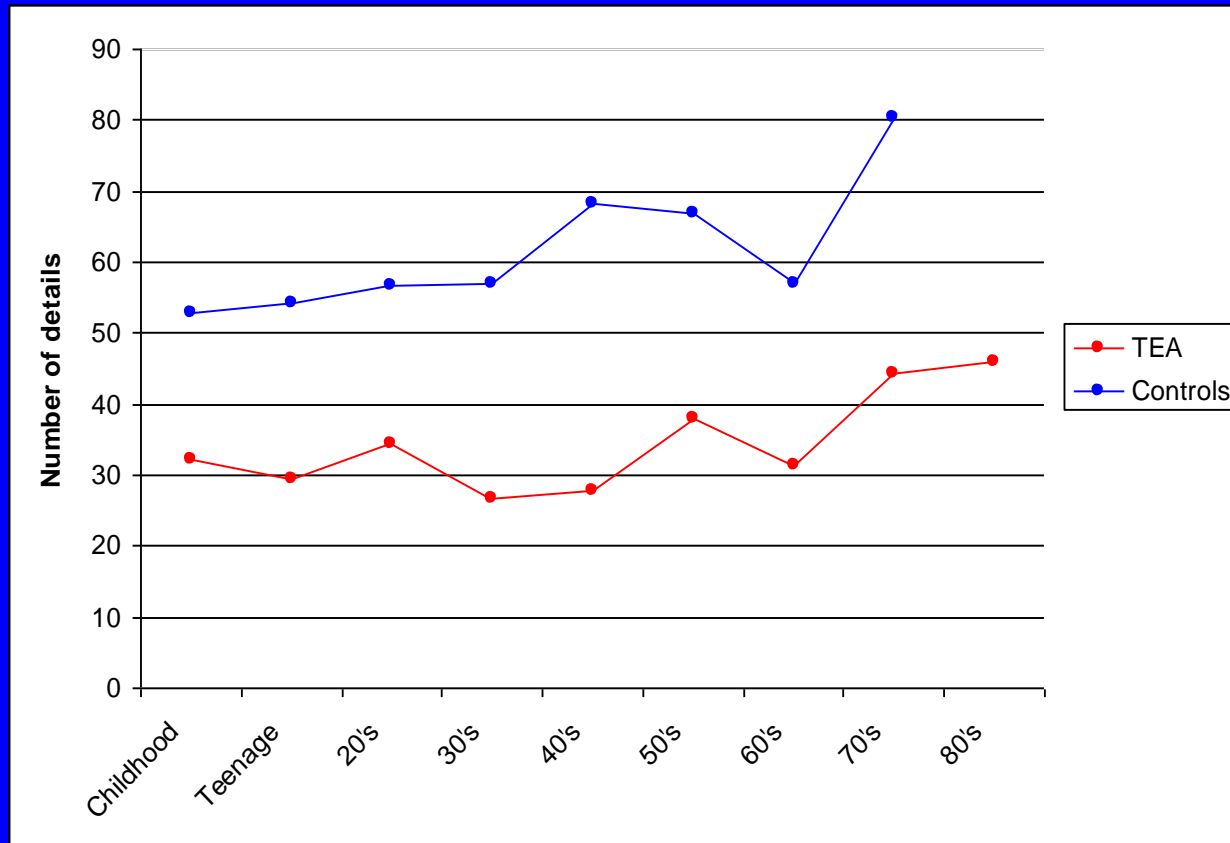


*** p<0.001

MAMI: episodic score by decade



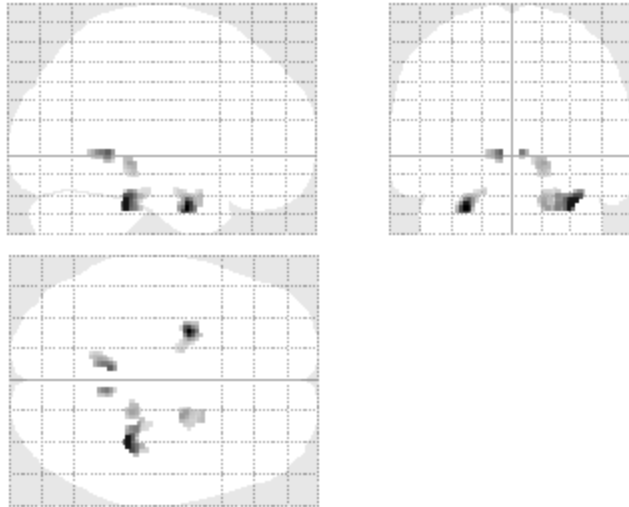
Internal details



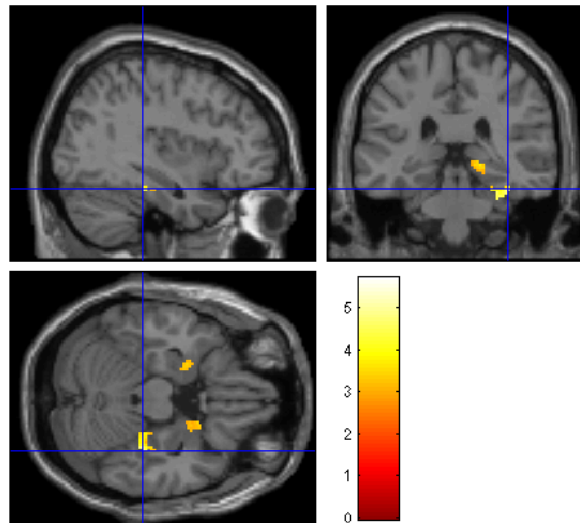
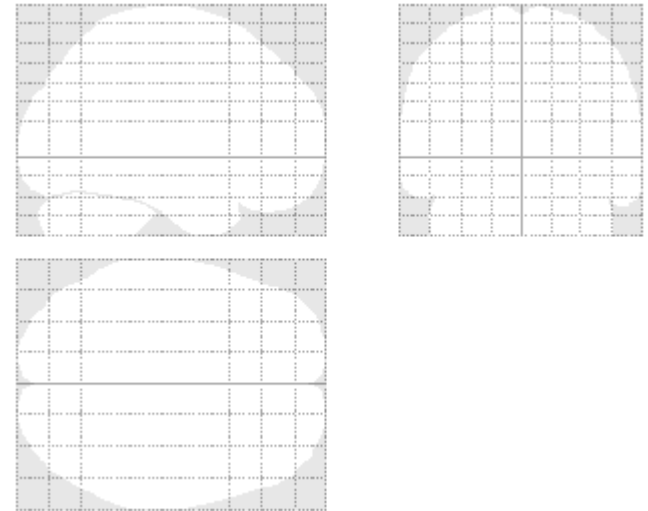
Milton et al, Brain 2010:133:1368-1379

AM – Category (MTL ROI)

Controls



Patients

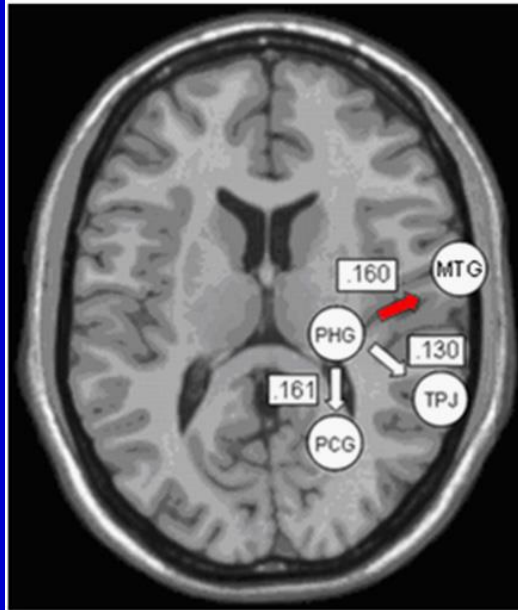


Milton et al Neuropsychologia 2012

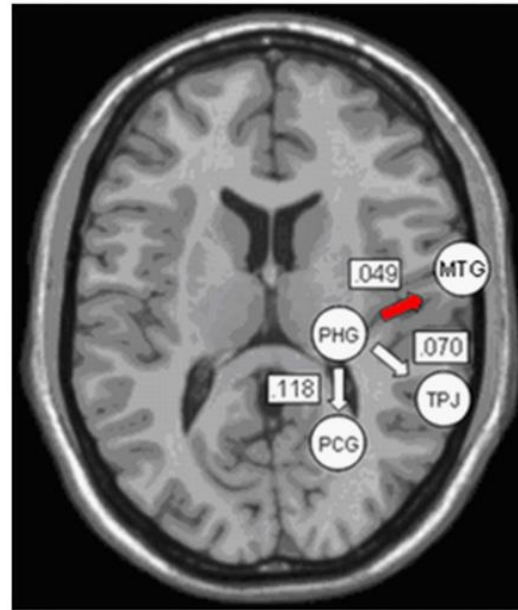
50:3528–3541

($p < .005$, cluster size > 10)

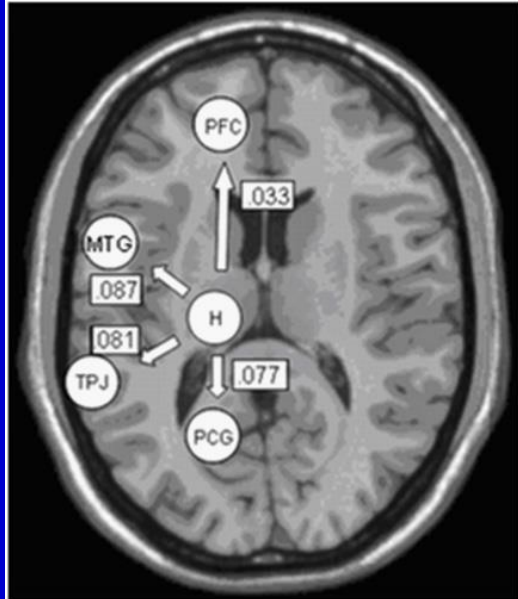
a **Controls**



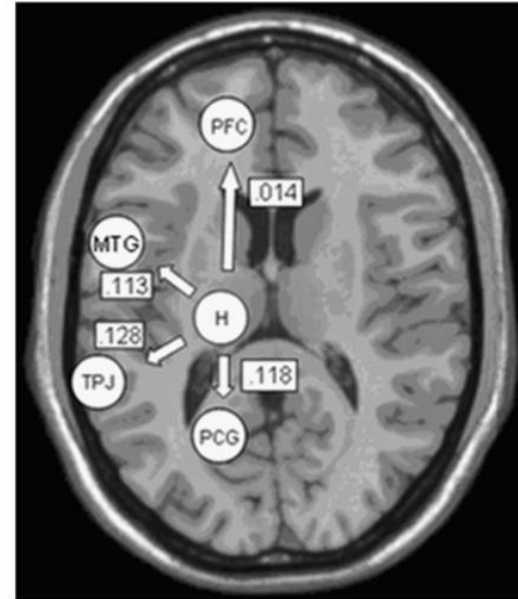
Patients



b **Controls**



Patients



Temporal lobe epilepsy

- autobiographical memory loss

- Chronic refractory

- eg Viskontas, 2000; Lah, 2006; Addis, 2007

- Temporal lobectomy

- eg Barr, 1990; Lah, 2004; Noulhiane, 2007

- Adult-onset drug sensitive

- Tramoni, 2011

- As presentation of TLE

- Subtle seizures

- Jansari, 2010

- Prodromal

- Hornberger, 2010; Tramoni, 2011

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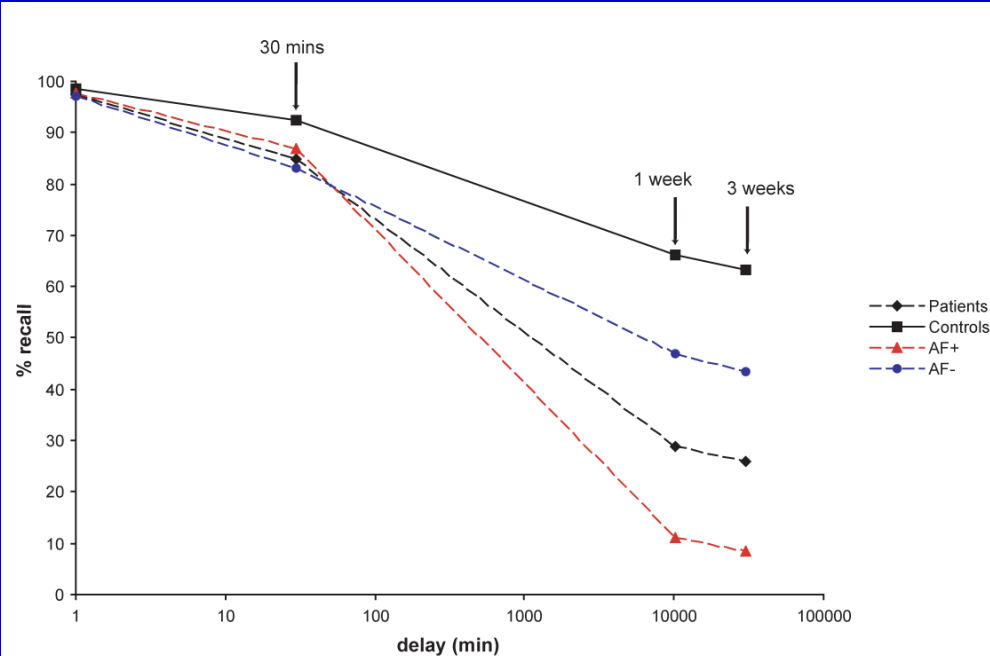
Focal Aba in other contexts

- Diffuse pathology
 - Evans et al 1996, 2003
- Right temporofrontal pathology
 - Levine et al 1998, 2009; Piolino et al 2005; Kopelman et al 2003
- Visual deficit amnesia
 - Rubin & Greenberg 1998
- Functional amnesia
 - Kopelman 2002; Kritchevsky et al 2004
- Temporal lobe epilepsy

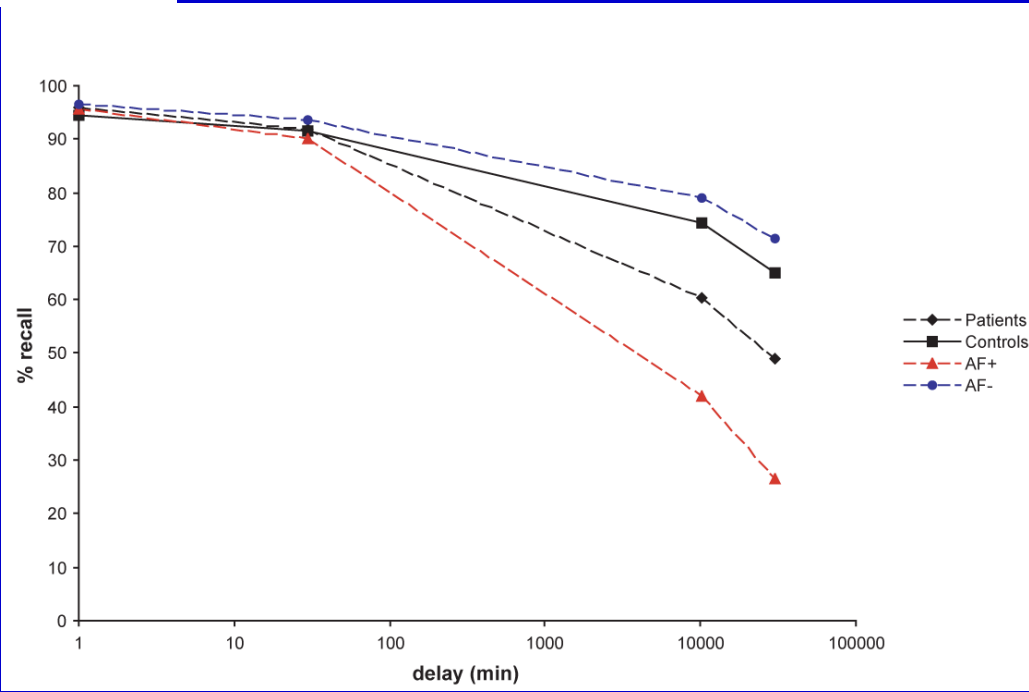
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Word list



Designs



(Butler et al *Ann Neurol* 2007)



a)

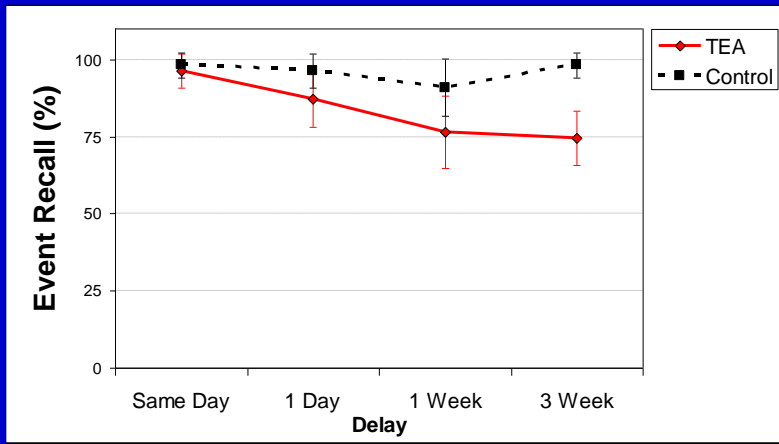


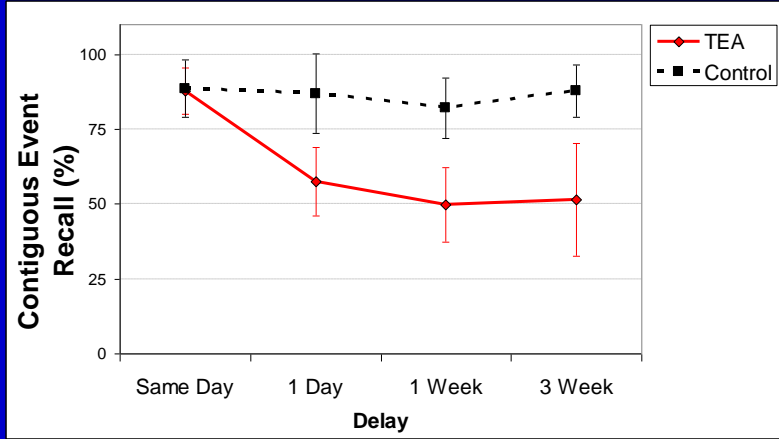
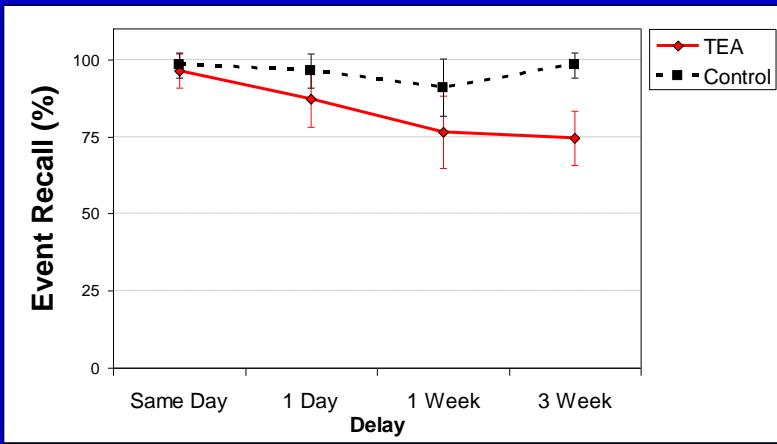
SenseCam

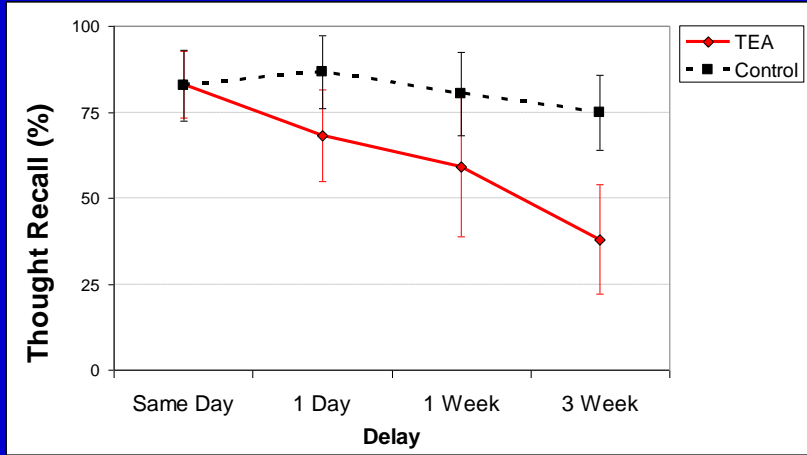
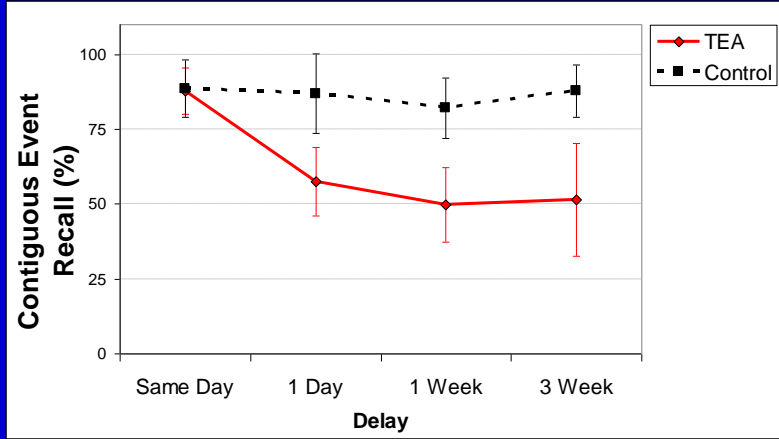
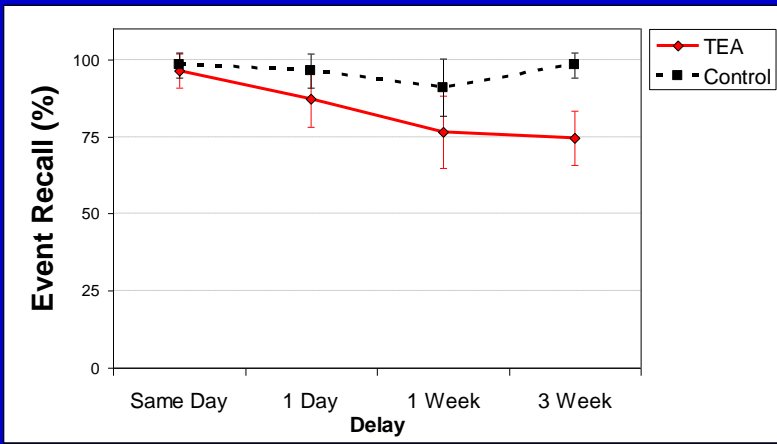
b)



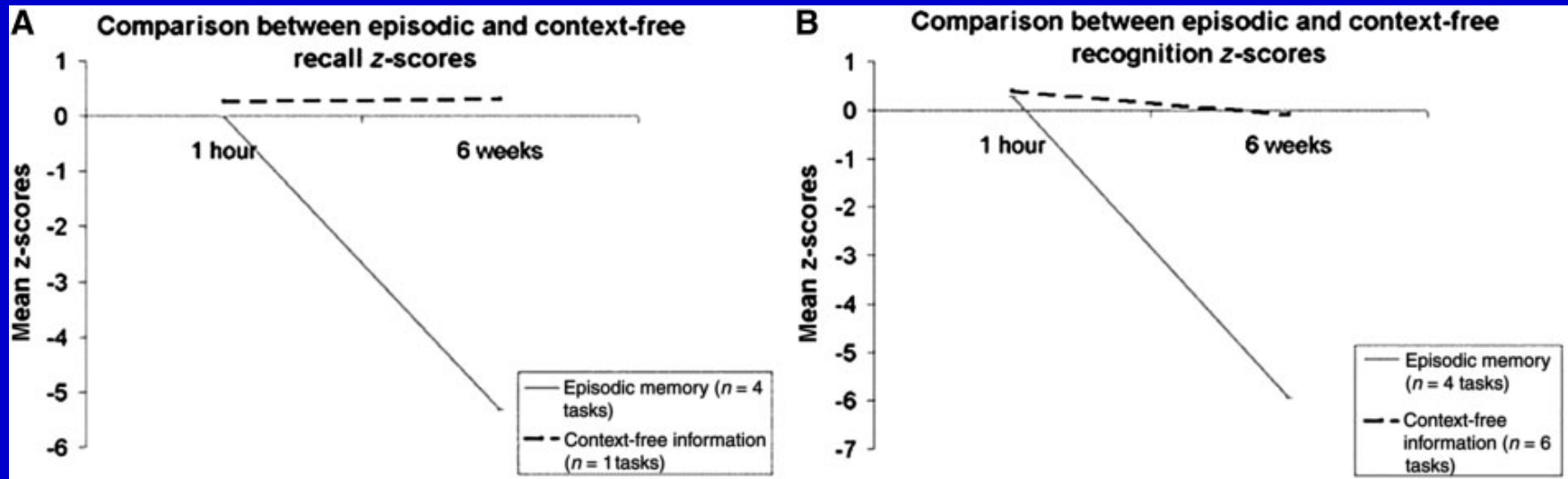
Time



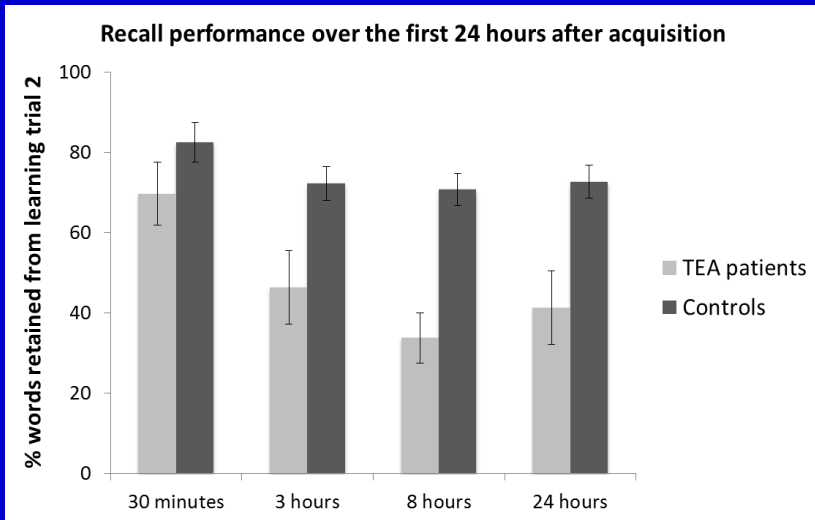




Muhlert et al,
 Neuropsychologia 2010
 48:3235-3244



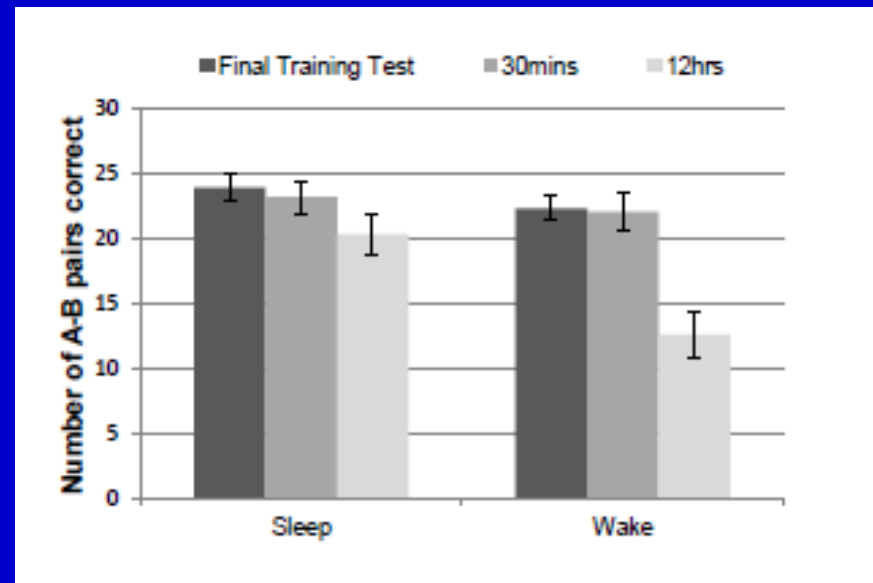
Tramoni E et al Brain 2011 134:816-831



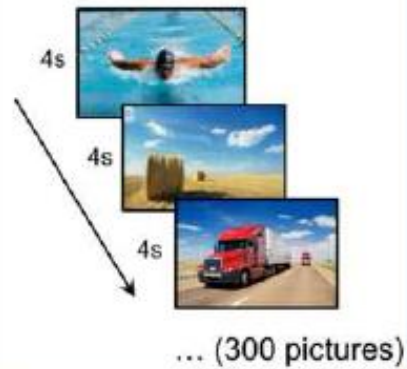
**Hoefijzers et al Neuropsychology
2014**

<http://dx.doi.org/10.1037/neu0000114>

**Atherton et al Cortex
2014;54:92-105**

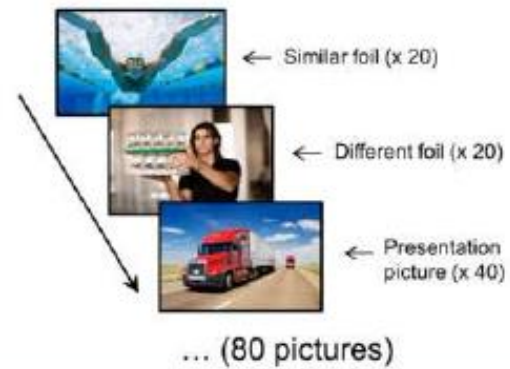


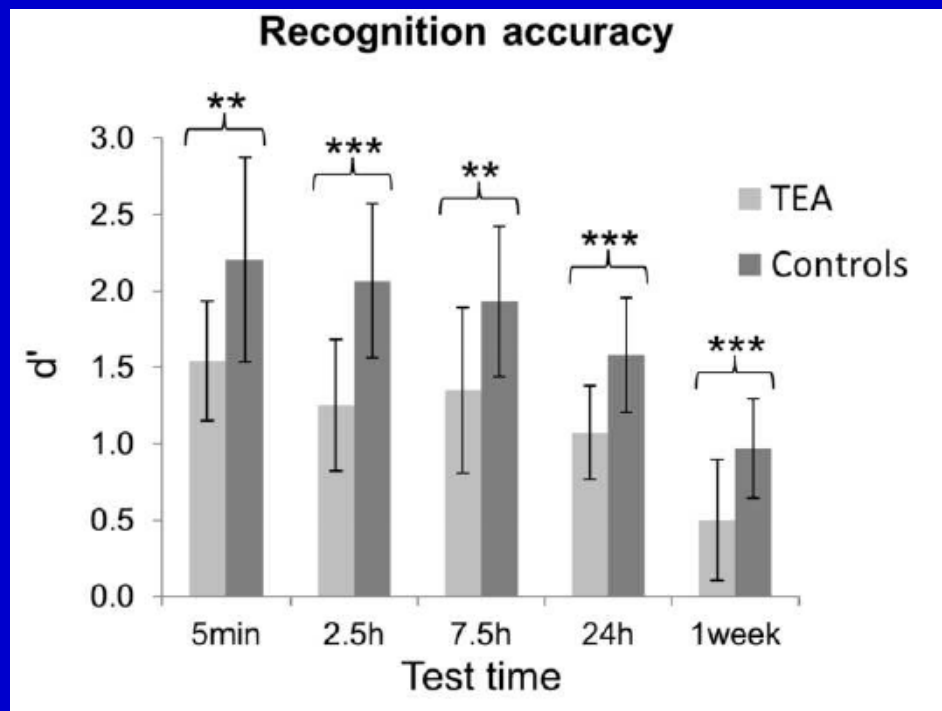
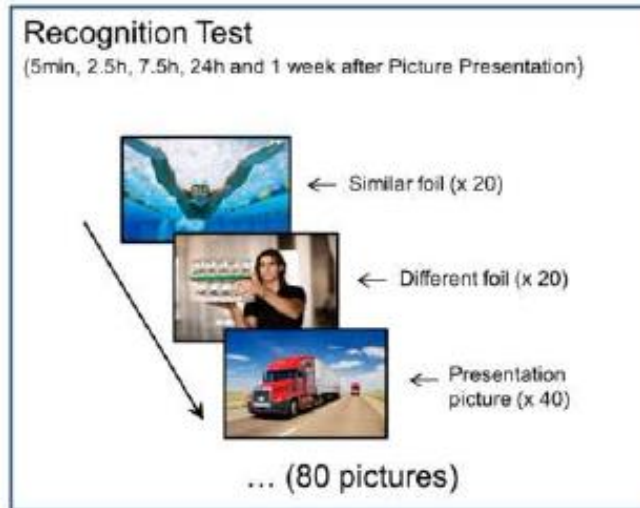
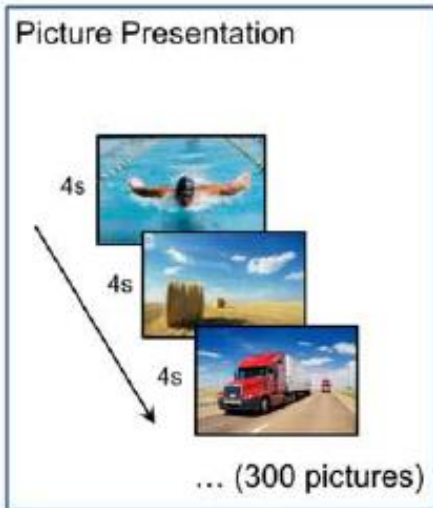
Picture Presentation



Recognition Test

(5min, 2.5h, 7.5h, 24h and 1 week after Picture Presentation)





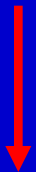
Dewar et al
Epilepsy and
Behavior
2015;42:107-
116

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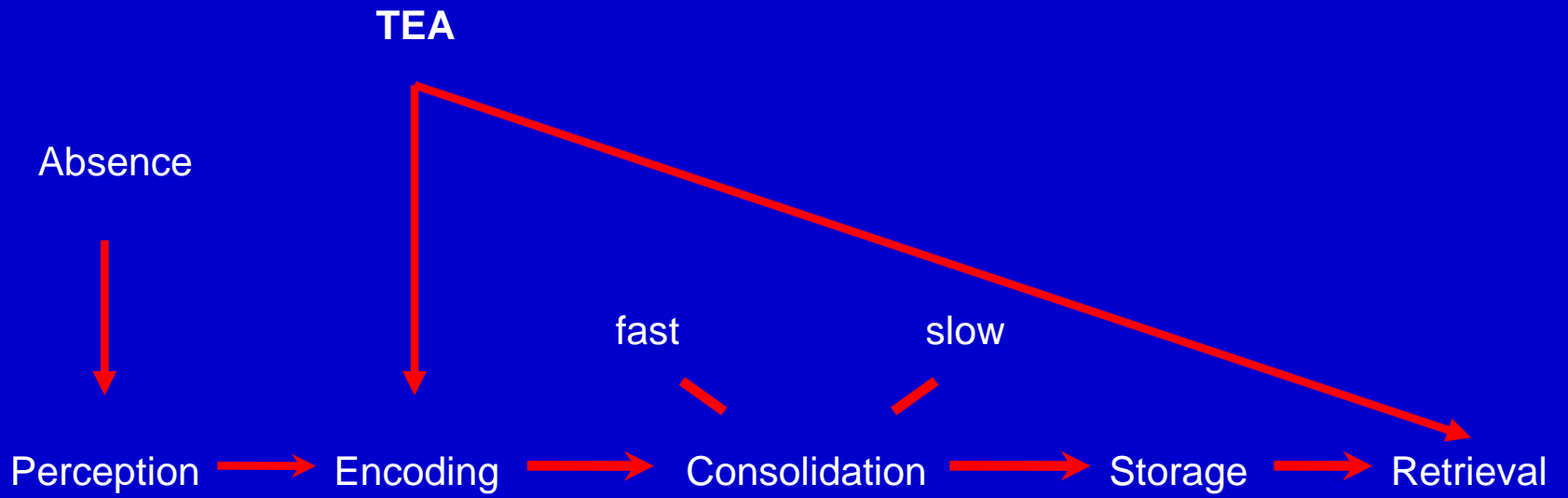
Absence

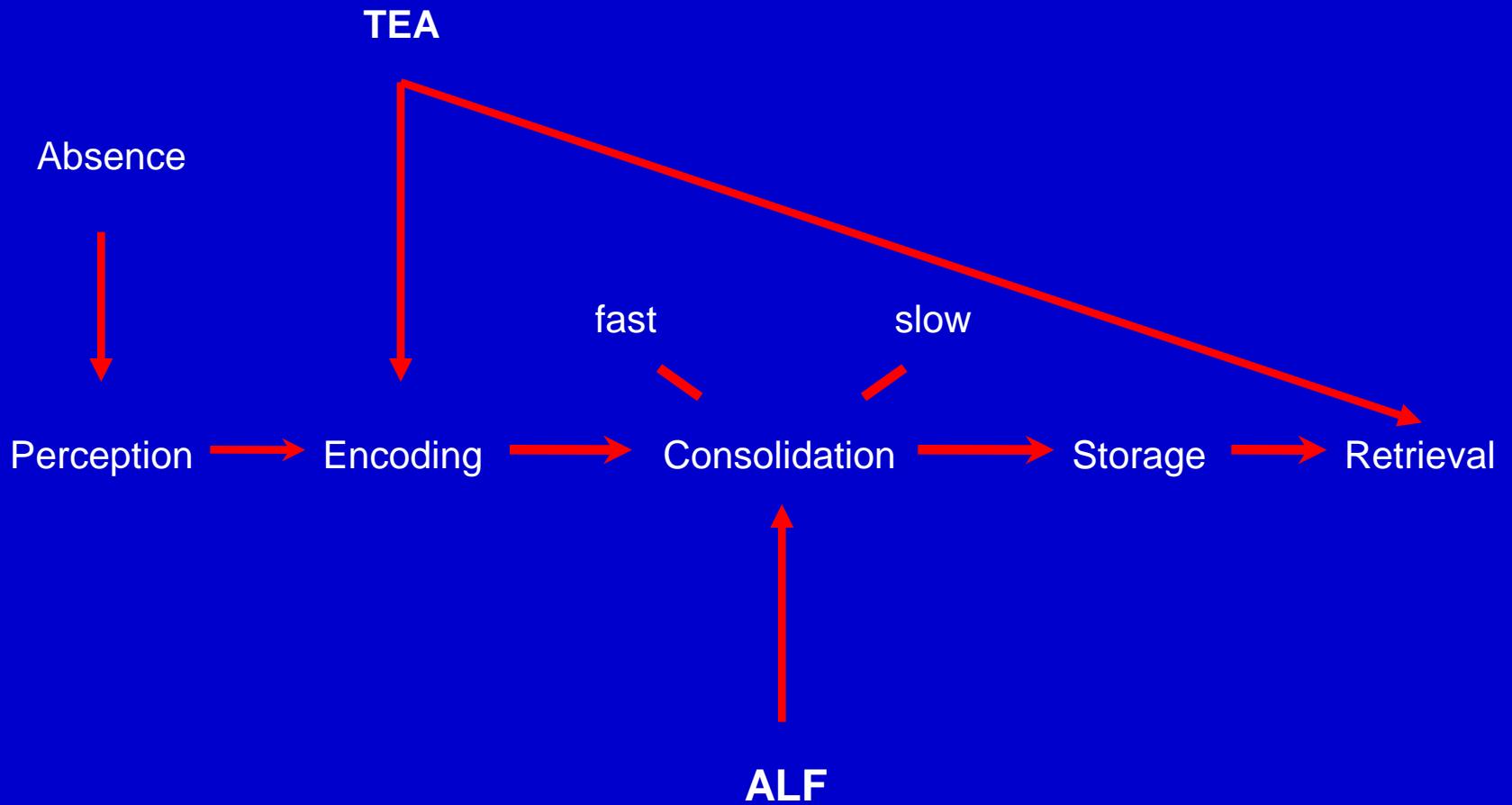


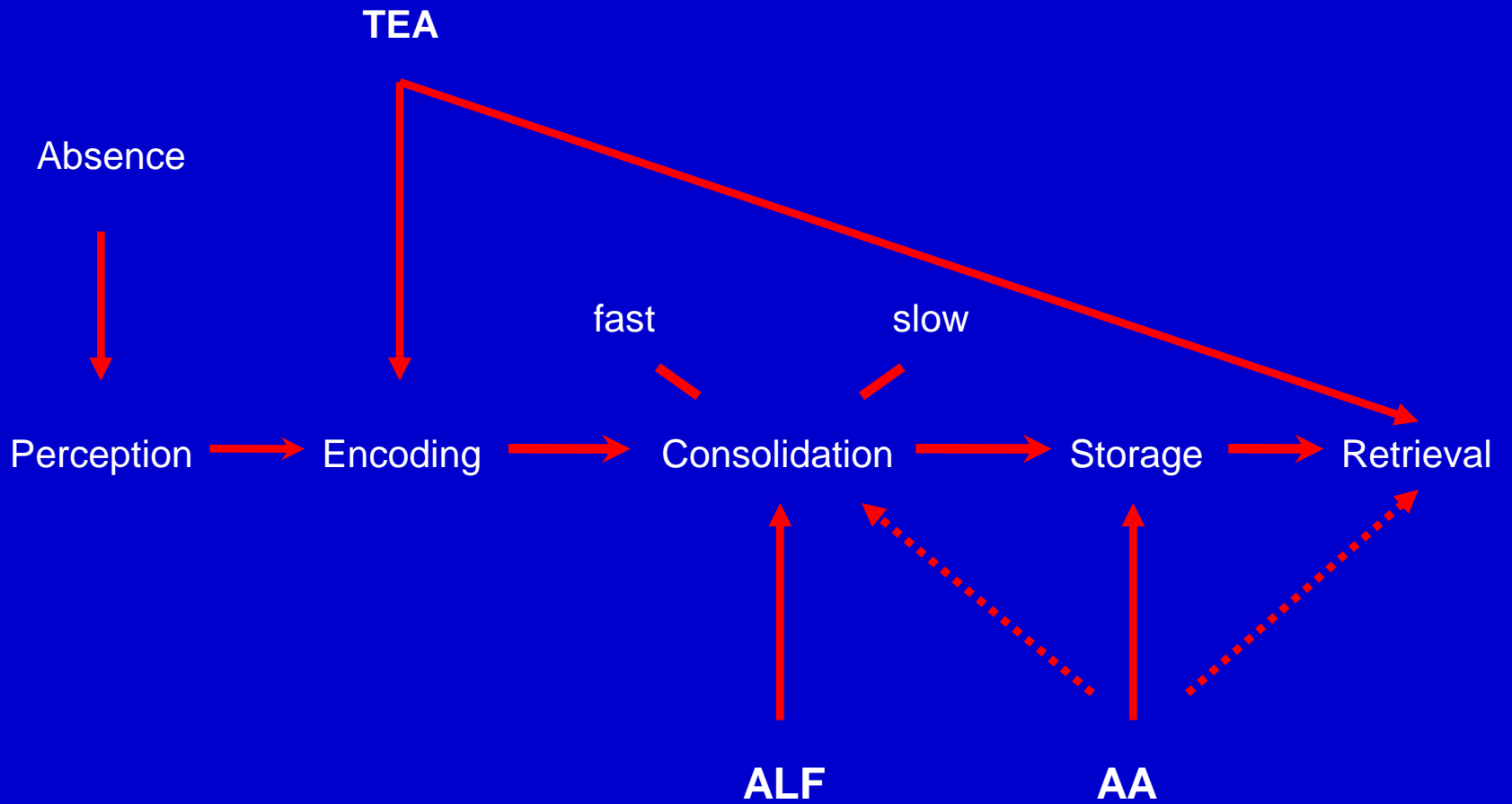
fast

slow









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conclusions & future directions

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ALF & AbA

conclusions & future directions

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 - What causes it?
 - What is its prognosis?
- Autobiographical amnesia
 - Functional or structural?
 - Acquisition, consolidation, storage or retrieval?
 - Distinctive patterns in different disorders?
- Accelerated long-term forgetting
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 - Acquisition or consolidation?
 - An early feature in other disorders?

ALF & AbA

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'Having last week makes me functional, to a very large degree. What it means not to have last year is very hard to describe...my primary symptom is the void that is my past'



People

Exeter

Fraser Milton
Sharon Savage
Adam Zeman

Oxford

Chris Butler
Kathryn Atherton

Cardiff

Kim Graham
Nils Muhlert

London

Narinder Kapur

Edinburgh

Michaela Dewar
Serge Hoefeijsers
Sergio Della Sala
Joanna Wardlaw

Sydney

John Hodges

Buenos Aires

Facundo Manes

Funding

Academy of Medical Sciences
Dunhill Medical Trust
Epilepsy Research UK
ESRC
Great Western Research
Health Foundation
Microsoft Research
Mrs Dale Medical Neurology Fund
Patrick Berthoud Charitable Trust
Wellcome Trust

Recruitment

BNSU



- <http://projects.exeter.ac.uk/time/>