

Clinical Aspects of Transient Amnestic States: Lessons from Transient Epileptic Amnesia and Transient Global Amnesia

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Transient amnesias

Sudden-onset and time-limited

Includes entities such as:

Post-traumatic amnesia

Psychogenic amnesia

Transient global amnesia

Transient epileptic amnesia

Post-ictal amnesia

Alcohol-related “blackouts”

Transient Global Amnesia (TGA)

“A neurological syndrome exclusively defined by clinical features” (Quinette et al., 2006)

History

First described in 1956 by
Guyotat and Courjon

Term coined in 1964 by Fisher
and Adams

Diagnostic criteria published in
1985 by Caplan

Broadly accepted features

Onset in middle to older age

Abrupt onset of an anterograde
amnesia with repetitive
questioning

Absence of any other
neurological deficits

Duration in the order of hours

Dense amnesic gap for the
duration of the episode, and
sometimes the lead-up, *as the
only cognitive symptom*

Recurrence is rare

Ictal memory in TGA: A case of forget-able sex

Dense or “global”
amnesia

Some preservation of
non-episodic memory
functions (semantic,
working, and implicit or
procedural memory)

De-contextualized
fragmentary recall

At onset: “what is it we’ve been
doing?”

During attack: “What is it I’ve
been in?”

**Do you remember how this
started:** “no-its the one that you
have when you have sex...I've
been away with the birds”

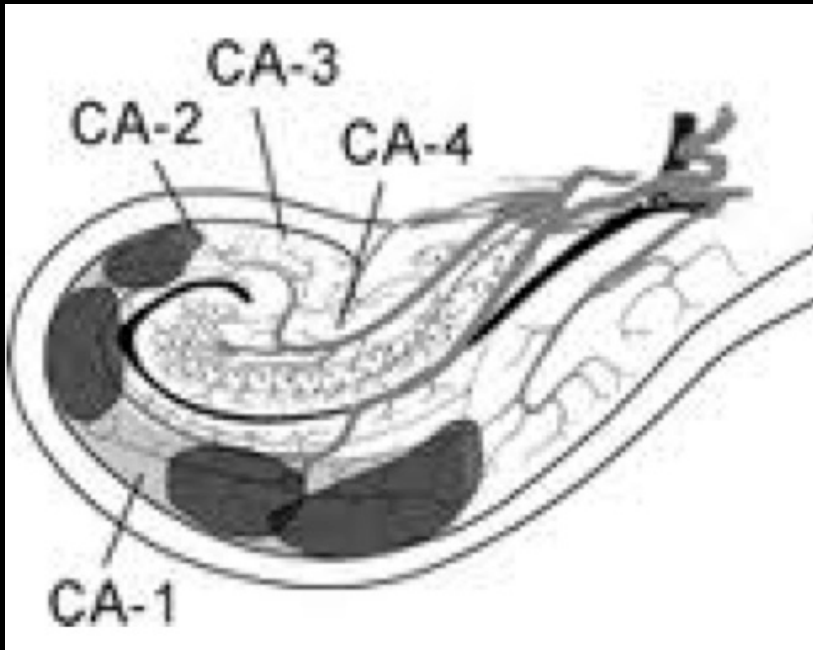
**Do you remember what
happened:** no-I’ll take a stab and
say sexual intercourse

How do you know: maybe I read
about it in one of the textbooks

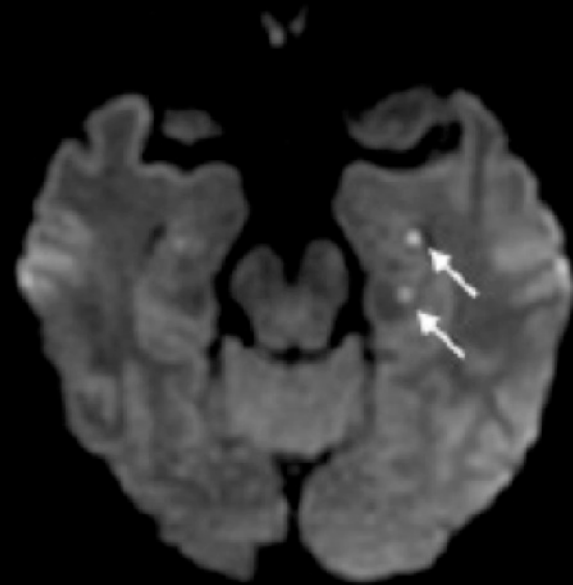
Caplan's (1985) criteria for TGA

1. Attacks must be witnessed and information available from a capable observer who was present for most of the attack
2. There must be clear-cut anterograde amnesia during the attack
3. Clouding of consciousness and loss of personal identity must be absent, and the cognitive impairment limited to amnesia
4. There should be no accompanying focal neurological symptoms during the attack and no significant neurological signs afterwards
5. Epileptic seizures must be absent
6. Attacks must resolve within 24 hours
7. Patients with recent head injury or active epilepsy are excluded

Reversible lesions in TGA



Bartsch and Deuschl, 2010



Seung-Leob et al., 2008

Psychological factors in TGA

Emotional precipitants, such as:

News of disease or illness in family members

Witnessing serious road accidents

Involvement in house fires

Attending a funeral

Giving evidence at a medical tribunal

(Hodges and Warlow, 1990)

Risk factors include:

Personality disorder

Panic attacks

Emotional instability

(Quinette et al., 2006)

An hypothesized mechanism

1. Trigger precipitates metabolic stress of CA1 neurons
2. Transient evolution of diffusion lesion with reversible T2 prolongation
3. Perturbation of CA1 networks leads to TGA
4. Rapid compensation in 4-12 hours

Bartsch and Deuschl (2010). *Lancet Neurol*; 9: 205-14

Towards a classification

“Transient amnesia is a heterogeneous clinical syndrome” (Hodges and Warlow, 1990)

	Pure TGA	Non-TGA
Age at presentation	50-80	30-80
Duration of attack	4.2 (9% < 1 hour)	7.0 (25% < 1 hour)
Precipitating factors	Swimming in cold water, sexual intercourse, severe pain, medical procedures, emotional stress	Emotional or physical exertion in 24%
Seizure outcome	Epilepsy predicted by multiple attacks, and shorter duration	

Dr Z and “double consciousness”

“I was attending a young patient...with some history of lung symptoms...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...was speaking to another person. I was interested to ascertain what had happened [to my previous patient], and had an opportunity an hour later of seeing him in bed, with a note of a diagnosis I had made of pneumonia of the left base.” (Quaerens, 1870)

Dr “ Z” aka “Quaerens” aka Dr Alfred Thomas Meyers, London

Died in 1894 of an overdose of chloral hydrate

At autopsy, a “very small patch of softening in the left uncinat gyrus” on “naked eye” examination (Hughlings Jackson, 1888)

The coronal section provided by Jackson (Hughlings-Jackson and Coleman, 1898, p. 588), shows the lesion just lateral to the fundus of the collateral sulcus, a zone of transition between the ento- and perirhinal cortices (Insausti, et al., 1998).

Transient Epileptic Amnesia (TEA)

History

First case described by Quaerens (1870) and Hughlings Jackson (1888)
Small series published by Lou (1968)
Recognized as a distinct entity by Gallasi et al. (1986)
Term coined by Kapur (1990)

Broadly accepted features

Onset in middle to older age
Attacks are brief (< 30 min), recurrent, and often occur on waking
No consistent triggers, but preceded by unusual feelings
Amnesia is typically the sole feature, but sometimes accompanied by focal seizure semiology
Attacks respond to anti-epileptic medication
Persisting forgetfulness over days or weeks, and “patchy but dense” loss of remote autobiographical memories

Ictal memory in TEA

“TEA represents a distinctive but under recognized syndrome” (Butler et al., 2007)

Brief recurrent amnesic attacks occurring in the second half of life

Partial recall in 40% of cases - “able to remember not being able to remember”, suggesting incomplete anterograde amnesia during the attack (Zeman et al., 1988)

In some attacks no anterograde amnesia is evident. A memory gap might only become evident in chance conversation – “retrospective amnesia”, suggesting a pure consolidation failure

Retrograde amnesia may be the most prominent ictal feature

Proposed criteria for the diagnosis of transient epileptic amnesia

Zeman and Butler (2010). Transient epileptic amnesia. *Current Opinion*, **23**, 610-616

History of recurrent witnessed episodes of transient amnesia [or recurrent episodes of retrospective amnesia]

Cognitive functions other than memory judged to be intact during typical episodes

Evidence for a diagnosis of epilepsy

Clear-cut response to anticonvulsant therapy

Overlap between TEA and dementia

Hogh, P., Smith, S. J., Scahill, R. I., Chan, D., Harvey, R. J., Fox, N. C., et al. (2002). Epilepsy presenting as AD: Neuroimaging, electroclinical features, and response to treatment. *Neurology*, *58*(2), 298-301.

Sinforiani, E., Manni, R., Bernasconi, L., Banchieri, L. M., & Zucchella, C. (2003). Memory disturbances and temporal lobe epilepsy simulating Alzheimer's disease: A case report. *Functional Neurology*, *18*(1), 39-41.

Rabinowicz, A. L., Starkstein, S. E., Leiguarda, R. C., & Coleman, A. E. (2000). Transient epileptic amnesia in dementia: A treatable unrecognized cause of episodic amnestic wandering. *Alzheimer Disease and Associated Disorders*, *14*(4), 231-233.

Case: TEA precursory to early-stage SDAT?

82 year old man

Events:

looks odd on waking, nausea, déjà vu

Travels back to an earlier time in his life,

Recalls parts of a car buying experience and details of the vehicle, but does not recall purchasing it

Inter-ictal retrograde amnesic gaps becoming evident two years later

Simple partial seizures 4 years after onset

Initial neuropsychological examination (6 year post onset):

Retroactive interference effect, and impaired arbitrary association

ADL's intact

Neuropsychological follow-up (7 years post-onset)

Broader memory impairment, now involving new learning

Decline in reasoning ability

Decline in some ADL's

SPECT:

Bilateral temporoparietal, posterior cingulate, and posterior frontal hypoperfusion

A perfect storm: Converging pathways of epilepsy and Alzheimer's dementia intersect in the hippocampal formation (Noebels, 2011)

Three-fold increase in seizures in AD

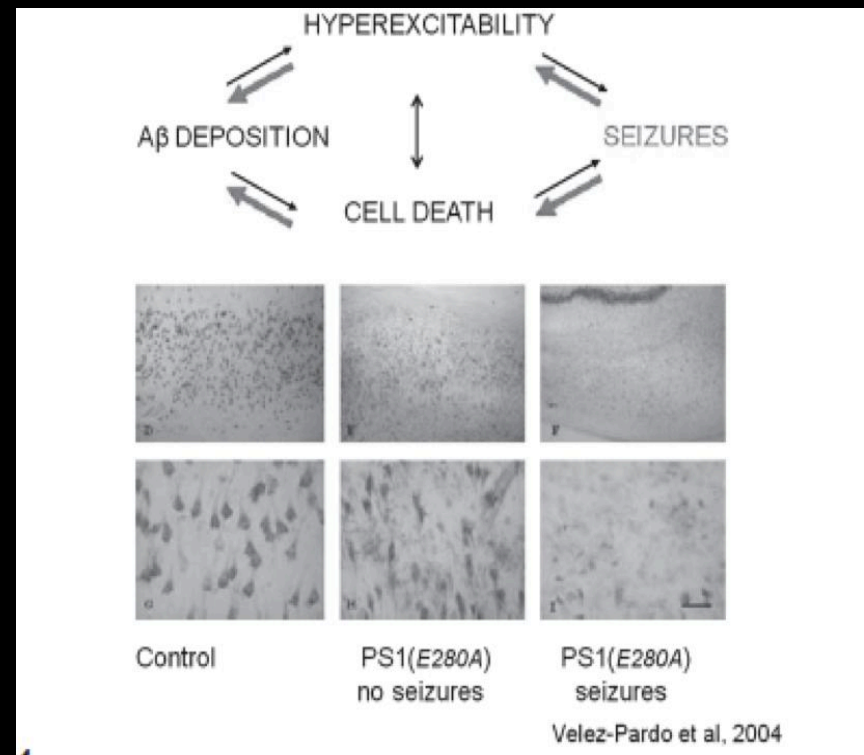
Seizures are complex partial in most cases

Onset of DAT might be masked by transient amnestic events ("epileptic pseudodementia")

Epilepsy a striking co-morbidity in APP, PS1, and PS2 mutations

Non-convulsive seizures in AD mouse models

Hyperexcitability and neuronal remodelling in AD pathology



Concluding comments

1. Pure TGA is not associated with adverse outcomes such as cerebrovascular disease or dementia, and single vents are more common than recurrences. Psychological triggers are not uncommon.
2. Brief and recurrent amnesias are more likely to represent an underlying epilepsy. There is growing evidence that these events are co-morbid with or precursory to DAT.
3. The cognitive semiology of TEA is sometimes counter-intuitive, and represents a challenge to traditional views of memory loss, and differential diagnosis.