# Transient epileptic amnesia

Christopher R Butler

*Practical Neurology* 2006;6;368-371
doi:10.1136/jnnp.2006.107227

NEUROLOGICAL RARITY

Practical Neurology 2006; 6: 368-371

# Transient epileptic amnesia

Christopher R Butler

In 1889, the British neurologist John Hughlings Jackson described the case of Dr Z, a medical practitioner who suffered from an unusual variety of epilepsy. During his seizures, he retained consciousness and was able to engage in complex, purposeful behaviour for which he was later amnesic. On one occasion he felt the onset of a seizure while examining a patient. During this attack, he correctly diagnosed pneumonia, prescribed treatment and wrote in the patient's notes, but later had no recollection of having done so (fig 1).

Reports of pure amnestic seizures have appeared sporadically in the literature over the past 50 years. Recent work, however, has suggested that such cases are underrecognised and appear to have several clinical features in common.

## CASE STUDY

A 69 year old, retired teacher of French, was staying with her daughter over the Christmas period. She awoke one morning and asked her husband "Where are we? What day is it? Why are we here?" She had no recollection for events of the previous few days and, when reminded, appeared to be unable to retain the information. She was understandably concerned by this, but her appearance and behaviour were otherwise normal. By the time she had got up, dressed and had breakfast, her repetitive questioning had stopped and memories for the past had returned. She had a hazy recollection of what had just happened to her. Apart from treated hypertension and hypercholesterolaemia, her past medical history was unremarkable, there were no symptoms of depression or anxiety and physical examination was normal. A diagnosis of transient global amnesia (TGA) was made and she was reassured that the problem was unlikely to recur.

However, she went on to have 35 similar episodes over the next two years. Many occurred upon waking in the morning and some were preceded by a "woozy feeling" or the sensation of a strange metallic taste. The amnesia included loss of memories for events of the previous few days (retrograde amnesia) and an inability to hold onto new information (anterograde amnesia). Other cognitive functions were intact: she proved that she was still able to drive a car, sight-read new piano pieces and perform French-English translation

**Dr C R Butler**
Visiting Neurology Fellow, Memory and Aging Center, University of California at San Francisco, Suite 502, 350 Parnassus Avenue, San Francisco, CA 94143, USA; cbutler@memory.ucsf.edu

10.1136/jnnp.2006.107227

during her attacks. The amnesia typically lasted about 30 minutes. Afterwards, she was usually able to recount at least some details of the episode in her diary.

The recurrence of so many attacks was not at all typical of TGA. Further investigations including brain CT and MRI, echocardiogram and 24 hour ECG monitoring were all normal. The patient's general practitioner wondered whether "stress" might be playing a role and started her on an antidepressant. Eventually, after an extensive internet search, the patient's daughter raised the possibility of epilepsy. Routine EEG was normal but a sleep-deprived recording showed bilateral, independent epileptiform abnormalities over the temporal lobes (fig 2) Carbamazepine abolished the attacks.

However, she then began to notice persistent problems with her memory. In particular, she found that newly acquired memories seemed to fade more rapidly than expected. For example, she had to write up the minutes from committee meetings immediately or she would forget what had been discussed. On another occasion she found she had no recollection of a visit to London she had made two weeks beforehand. An apparently separate problem was that certain episodes from the very distant past had completely disappeared from her memory, including a holiday in Kenya in 1980 and her daughter's wedding in 1985. Even looking at photographs or her diary entries did not trigger any sense of familiarity.

## TRANSIENT EPILEPTIC AMNESIA: CLINICAL FEATURES

There are fewer than 50 reported cases of transient epileptic amnesia (TEA) in the literature. However, it is likely often misdiagnosed. In the most comprehensive review of the subject to date, Zeman *et al*[1] reported 10 new cases and reviewed a further 21 from the literature.

They proposed the following diagnostic criteria:

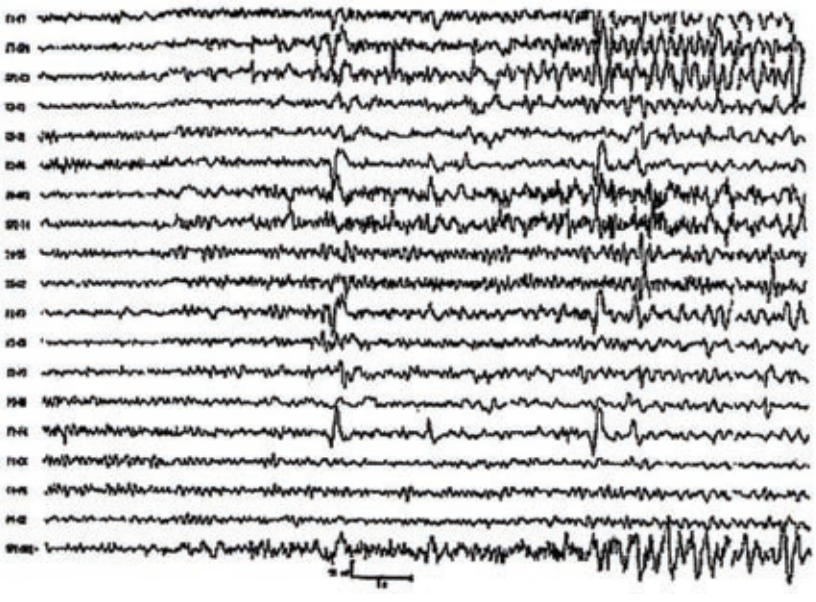
- recurrent, witnessed episodes of transient amnesia
- cognitive functions other than memory judged to be intact by a reliable witness during the attack
- evidence for a diagnosis of epilepsy based on one or more of:
  - epileptiform EEG abnormalities
  - co-occurrence of other clinical features of epilepsy (for example, automatisms, olfactory hallucinations)
  - clear-cut response to antiepileptic drugs.

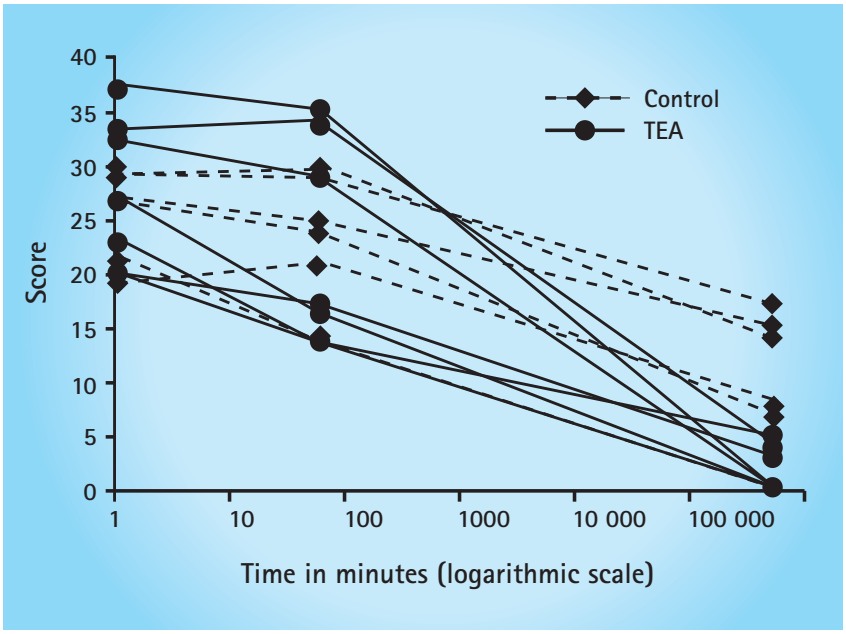
Transient epileptic amnesia typically starts in late middle age. The attacks, which often occur on waking, involve a mixed anterograde and retrograde amnesia. The patient may repeatedly ask questions about recent events, indicating an awareness of the memory deficit but an inability to hold on to new information. About 30% of patients experience only pure amnesic attacks. In the rest, the amnesia is sometimes accompanied by hallucinations of smell or taste and lip-smacking or chewing movements.

**Figure 1**
John Hughlings Jackson (1835–1911) documented the case of Dr Z, who describes one of his amnestic seizures in the extract (*Brain*, 1889).

"(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 diagnosis had been. I was a good deal surprised, but not so unpleasantly as I should have thought probable."

**Figure 2 (Bottom)**
The patient's interictal EEG revealed spikes arising independently from both temporal lobes.





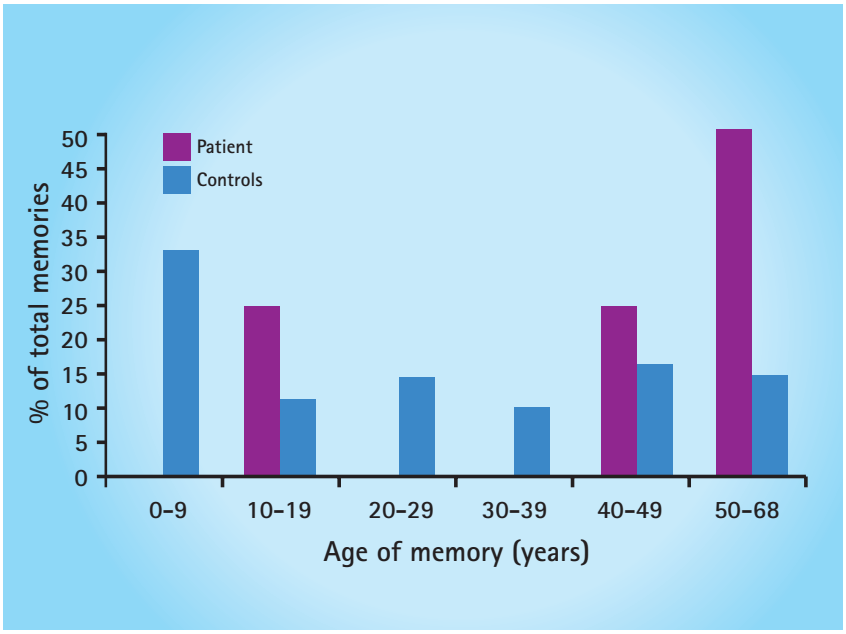




**Figure 3 (Top)**
Seven patients with transient epileptic amnesia (TEA) were as good as controls at learning a short story and remembering it over 30 minutes. However, after a delay of six weeks, the patients' recall was significantly impaired. (Reproduced from Manes *et al*[2] with permission.)

**Figure 4 (Bottom)**
When asked to produce personal memories relating to a particular word (for example, "boat"), a 68 year old epileptic patient failed to retrieve any episodes from his twenties or thirties. His performance on standard tests of anterograde memory was normal.

However, the preservation of other cognitive functions such as attention, perception, language, and executive functions is revealed by a continued ability to respond appropriately to conversation and act in a purposeful manner. The attacks characteristically last 20–30 minutes, but much longer episodes, even persisting over a number of days, have been reported. These may be due to ongoing seizure activity (non-convulsive status epilepticus) or persistent post-ictal dysfunction of memory related brain structures. Once memory functions have returned, the patient sometimes has a complete "gap" for events that occurred during the attack but often describes being at least vaguely "able to remember not being able to remember".

In common with other forms of late onset epilepsy, TEA attacks usually respond well to a low dose of an antiepileptic drug. Despite this, many patients complain, sometimes bitterly, of ongoing memory difficulties.[2] In particular, they describe the unusually rapid forgetting of recently acquired memories over a period of days or weeks (fig 3). Thus, although immediately after viewing the first episode of a TV serial they may be able to discuss the plot in detail with their family, by the time the next instalment is broadcast one week later, they have no recollection of ever having seen the programme before. Another common complaint is a patchy but dense loss of memories for important personal events from the remote past (fig 4). Characteristically, the patient finds that certain holidays or weddings, that perhaps occurred 30 or 40 years ago, have completely vanished from their memory. Finally, many patients notice that their ability to navigate around new or familiar routes is impaired. Importantly, these types of memory difficulty, accelerated long term forgetting, remote autobiographical memory loss, and topographical amnesia are not detected by standard neuropsychological tests and therefore need to be asked about directly.

The diagnosis of TEA can be difficult. A witness account is crucial, and a careful search must be made for other evidence of epilepsy such as olfactory hallucinations, automatisms, or brief losses of responsiveness. The interictal EEG is normal in many cases, although sleep-deprived recordings have greater sensitivity. An MRI scan should be obtained to rule out a structural cause, but is often unremarkable. In some cases, a trial of antiepileptics may be justified without confirmatory evidence from investigations. Once started, treatment usually needs to be lifelong so careful consideration should be given to potential adverse effects, concurrent medical conditions, and drug interactions.

## DIFFERENTIAL DIAGNOSES

Distinguishing TEA from other causes of transient amnesia is important, particularly because the amnesic attacks may be associated with more typical complex partial seizures or even progress to secondary generalisation.

10.1136/jnnp.2006.107227

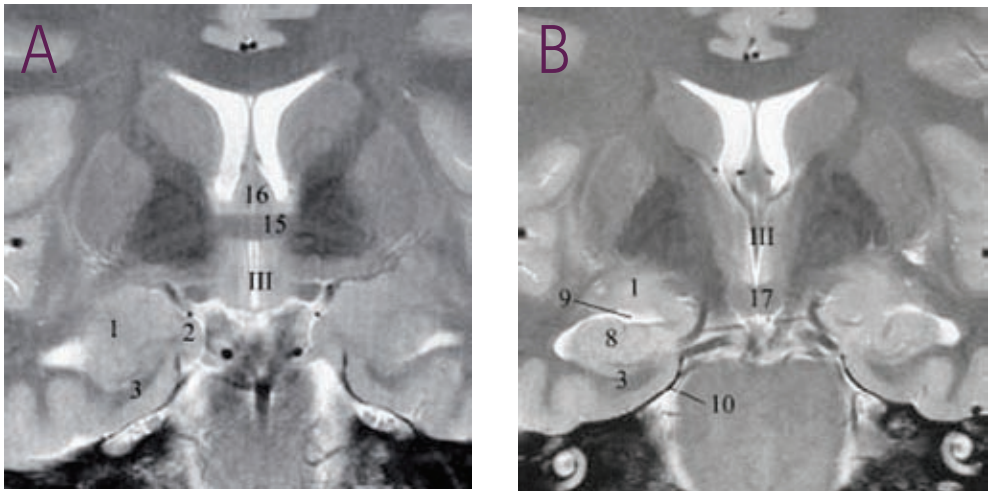



**Figure 5**
Coronal T2-weighted MR images of the anterior temporal medial lobe (B is posterior to A). The medial temporal lobes, including the hippocampus, are essential for the formation and retrieval of certain types of memory. It is thought that they hold an "index" that links together different aspects, stored elsewhere in the cortex, of the remembered episode. Bilateral dysfunction of this area results in dense amnesia of the type seen in TGA and TEA. Closely associated is the uncus, an area involved in olfactory processing. (1) Amygdala; (2) uncus; (3) parahippocampal gyrus; (8) hippocampal head; (9) uncal recess of the temporal horn; (10) free margin of tentorium; (15) anterior commissure; (16) fornix; (17) mamillary bodies; (III) third ventricle.

## Transient global amnesia

Transient global amnesia (TGA) occurs in a similar age group to TEA. Its aetiology is not yet known but recent evidence favours transient haemodynamic disturbance in the medial temporal lobes. In contrast to TEA, TGA has a low recurrence rate (3% per year) and attacks usually last for several hours. It is often triggered by emotional or physical stress. Repetitive questioning and a dense anterograde amnesia (so the patient is later unable to recall anything at all about the episode) are almost universal. Besides amnesia, there are no additional localising neurological signs or symptoms, although non-specific features such as headache or nausea may be present. TGA has a very stereotyped presentation and any atypical features should prompt further investigation.

## Psychogenic amnesia

Transient epileptic amnesia may also be confused with transient amnesia due to "psychological" rather than "organic" factors. Psychogenic amnesia or "fugue" is often triggered by a stressful life event and characteristically involves an extensive loss of autobiographical memories, including self-identity, in the context of preserved new learning and absence of repetitive questioning.

## WHAT'S GOING ON IN THE BRAIN?

The aetiology and pathophysiology of TEA are not known. It is predominantly a condition of later life and some have suggested that it may be triggered by cerebrovascular disease, although there is not yet any convincing evidence of this. Patients can be reassured that the condition does not appear to be a precursor of dementia. The amnesic attacks of TEA may be either ictal or post-ictal (a "Todd's paresis of memory"). The nature of the amnesia, the frequency of olfactory hallucinations, and the location of EEG abnormalities when present all point towards temporary dysfunction in the medial temporal lobes (fig 5). It remains to be seen whether the interictal memory impairments seen in TEA are related to the same or different brain regions, and whether they are due to ongoing, subclinical epileptic activity or to underlying structural pathology. Experience so far suggests that these problems do improve, but only partially, with the initiation of antiepileptic treatment.

## PRACTICE POINTS

- Transient epileptic amnesia usually begins in late-middle to old age.
- Amnesic episodes are brief, recurrent, often occur on waking, and may be associated with olfactory hallucinations and automatisms.
- Attacks respond well to antiepileptic drugs.
- Persistent memory difficulties, including accelerated forgetting and autobiographical amnesia, are common but undetectable by standard neuropsychological tests.
- It is often misdiagnosed as transient global amnesia or "psychogenic fugue".

## REFERENCES

1. Zeman AZ, Boniface SJ, Hodges JR. Transient epileptic amnesia: a description of the clinical and neuropsychological features in 10 cases and a review of the literature. *J Neurol Neurosurg Psychiatry* 1998;**64**:435–43.
2. Manes F, Graham KS, Zeman A, *et al.* Autobiographical amnesia and accelerated forgetting in transient epileptic amnesia. *J Neurol Neurosurg Psychiatry* 2005;**76**:1387–91.