

Transient epileptic amnesia — a clinical update and a reformulation

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Abstract

While absence attacks and complex partial seizures have been well documented in patients with epilepsy, the delineation of pure episodes of memory loss without additional clinical manifestations remains poorly characterised. The recently described condition of transient epileptic amnesia (TEA) is critically examined, and four new cases are described, in each of which there were episodes of pure memory loss which subsequently proved to be epileptic in origin. The anatomical and pathophysiological basis of TEA is presumed to be similar to transient global amnesia (TGA), that is, it is likely to be primarily hippocampal in origin, but with more variable involvement of limbic and adjacent temporal lobe neocortical structures.

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We have previously described or reviewed a number of cases of amnesia associated with epilepsy.¹⁻³ Hodges and Warlow⁴⁻⁵ specifically identified a subgroup of patients with transient amnesia related to the presence of epilepsy, and provided statistical information on the clinical features separating these patients from those with transient global amnesia (TGA), namely duration of attacks and number of attacks. In spite of these and similar studies, there remains a considerable lack of awareness of transient epileptic amnesia (TEA) as a distinctive neurological condition. For example, a recent textbook on epilepsy does not have this term in its index—and makes only passing reference to the condition.⁶

The purpose of this review is:

- 1) To present a clinical update on the condition of TEA in the light of my further experience with four additional cases, and in the light of published evidence of similar cases.⁷
- 2) To offer a subclassification of four types of TEA.
- 3) To provide a revised diagnostic framework to help distinguish TEA from clinically similar forms of transient memory disorder.
- 4) To outline a neuropsychological and anatomical framework within which TEA can be understood, so that it can be more readily incorporated into our existing knowledge of memory disorders.

In the series of probable TEA cases which I reviewed,³ there were a range of clinical features which appeared to stand out as

supportive of a diagnosis of TEA and as rather atypical for TGA. These clinical features included:

1) An absence of repetitive questioning and perplexed, anxious state,⁸ with the presence of partial rather than global anterograde amnesia during the episode.^{9,11}

2) Severity of retrograde amnesia may appear to be disproportionate to the degree of anterograde amnesia, and for some episodes it may present as the sole disturbance, as noted by Meador *et al*,¹² and in case 4 reported below.

3) The occurrence of amnesic episodes first thing in the morning or after waking from a period of sleep.^{2,8,11,13,14}

4) An unusually large number of episodes of memory dysfunction.^{2,5,9,15}

5) The brief duration of some of the episodes of memory dysfunction.^{5,11,16,17}

6) The reduction or cessation of amnesic episodes after the introduction of anti-epileptic medication.^{11,13-15}

7) The presence of episodes where memory loss for a period of time only became evident by chance on a later occasion, with no evidence of acute memory dysfunction at the time of the presumed attack,^{2,15} this 'later occasion' was usually hours later, though in one case it was several weeks later.¹²

8) Evidence of inter-ictal EEG abnormality.^{2,15}

9) Evidence of seizures on occasions other than those of the transient memory loss.¹²

10) The occurrence of involuntary automatic behaviour, or a period of unresponsiveness, during or immediately preceding the amnesic episode.^{18,19} Many researchers, however, would regard such accompanying features as excluding a diagnosis of pure transient amnesia and simply reflecting the occurrence of complex partial seizures.

More recently, Palmmini *et al*⁷ have reported several cases which they have indicated represent instances of 'pure amnesic seizures', and which have many of the features of transient epileptic amnesia. In their cases, such seizures never occurred without other types of seizures also being present on other occasions. Many of the features outlined above for patients with TEA were present in the cases reported by Palmmini *et al*, with most of the amnesic episodes of their patients presenting subclinically rather than clinically. However, they did remark on the *absence* of any retrograde amnesia during the amnesic episodes of their patients, in contrast to point 2 above. In addition, most of their patients had long-standing intractable epilepsy, compared with the more recent illness onset of the majority

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of published cases.

I will now describe four further cases of TEA. I have indicated why each would not have fulfilled standard criteria for TGA.²⁰⁻²²

CASE 1

A 63-year-old woman, worked as a supermarket assistant. Her non-identical twin sister had suffered from epilepsy. She had a previous history of migraine, and first experienced transient amnesic episodes in August 1988. She experienced around 35 episodes in the following three years. The attacks were more frequent after a period of sleep, such as an afternoon nap. They largely stopped in late 1991, when she was put on sodium valproate.

Witnessed descriptions of the episodes were obtained both from her husband and from her son. They thought that the episodes ranged in duration from several minutes to several hours. There were no precipitating factors, such as physical stress or exposure to hot/cold. During some attacks, she would lose colour, move about rather slowly and appear in a daze, but she would respond when spoken to and otherwise appeared quite normal. In a few instances she would smack her lips and make gulping sounds before the attack. However, there were a number of episodes where the only manifestation of the attack was impaired memory. During the episode, her memory would be poor for familiar material or for recent happenings, for example, she would not have memory for a recent event or would forget the name of a family member, but she would not appear perplexed and would not appear to have poor ongoing memory. On some occasions, there was evidence of significant retrograde amnesia. For example, for one episode she thought her children, aged 25 and 23 years, were still at school. There would be no loss of personal identity, and she would always recognise her husband. There would be recovery of her memory dysfunction within 2-3 hours, but she would have a 'memory gap' for the period of the attack.

Her husband and her son thought that in between attacks her everyday memory was normal, though she herself thought it was a little impaired.

An EEG showed mild temporal lobe abnormality, with less alpha and more theta activity over the left temporal region. A CT scan was normal.

Neuropsychological investigations showed moderate impairment on an anterograde faces memory task, and also some evidence of impairment on tests of retrograde memory. From a frequency of one episode every 6-8 weeks, her attacks reduced in frequency to 1-2 attacks a year.

This patient would not have fulfilled standard criteria for TGA because of the episodes of involuntary bucco-facial movements that accompanied some of the episodes, the focal EEG abnormalities and the beneficial effects of anti-epileptic medication.

CASE 2

A 67-year-old woman, presented in February 1984 with, in her doctor's words, a "story of temporary amnesia lasting about 40 minutes". This was characterised by a sudden onset of disorientation for place or why she happened to be there. After the episode, she had a memory loss for this period of 40 minutes. She had a similar episode five weeks later while driving home with her husband. On this occasion it was possible to obtain more detailed information. They had been travelling for some time when she said to her husband—"I don't know where I am". This sense of spatial disorientation continued for about 30-40 minutes, after which his wife gradually recovered her memory, so that after a further 20 minutes her memory was back to normal.

Neither she nor her husband felt that she asked questions repetitively during the attack. This feature was considered to apply in the case of most other episodes, and her husband thought that the short period of pre-ictal amnesia was a more prominent feature of the attacks than any ongoing memory disturbance. When recalling the episode several years later, she had no recollection of most of the car journey, though she did recall setting off and experiencing a feeling of disorientation.

In one of the other episodes, she and her husband had been to visit their daughter. Fifteen minutes after departing, she said to her husband that she did not know where she was. At this time, she also could not recollect having visited her daughter's flat. It appeared that during her time in the flat her memory had also been a little suspect, since she had been shown a coat by her daughter, but 15 minutes later made a remark about the coat as if she had never seen it before.

When seen by a consultant neurologist in July 1984, she had two further attacks. Two features of the episodes were considered by the neurologist to be unusual—she could recall a few items of information from the actual episodes, and on three occasions she had some form of warning that they would occur. Later in the same month, her husband reported that she had suffered a further episode, this one lasting for 35 minutes. Since starting phenytoin, she has had no further attacks. At no time, however, had there been any record of an epileptic fit having occurred, and there is no evidence that her level of responsiveness changed during an amnesic attack.

An EEG in August 1984 showed a mildly abnormal record, with minor episodic disturbances in both hemispheres, more prominent in the left fronto-temporal region. A further EEG in September 1985 showed irregular focal theta and slower frequencies, especially in the left anterior temporal region, with evidence of some deterioration in EEG activity since the recording taken in 1984. A CT scan in January 1986 did not show any abnormality.

She was seen for purposes of neuropsychological assessment in November 1988.

Neither she nor her husband considered that her current everyday memory was impaired. They also thought that her memory for past personal events was intact. Her score on an adult reading test was equivalent to an IQ of 126. On a series of learning and recognition memory tests, and on a test of retrograde amnesia, she did not show any deficit.

This patient would not have fulfilled standard criteria for TGA because of the EEG abnormalities, and the cessation of episodes as a result of the introduction of anti-epileptic medication.

CASE 3

A 28-year-old right handed man, worked as a warehouse assistant manager. He first had an episode of transient amnesia in November 1989. While some of the attacks had occurred at work, others had been witnessed by his wife at home. The attacks initially occurred once every two months, but later progressed to once a month. The usual duration of an episode was one day, though a few had been known to last for two days. There was no warning that the episode would occur, nor did they occur after events such as physical stress, exposure to hot/cold, etc. They would invariably start first thing in the morning when he woke up—he would ask what day it was, and would repeat this all day. His wife might serve him coffee, and ten minutes later he would ask whether he had yet drunk his coffee. Throughout the episode, he would be rather anxious and perplexed.

In a few instances, he showed involuntary or stereotyped movements during the attack—his wife observed occasional chewing movements or that he was unresponsive to others in the room. On another occasion he kept pouring a drink into a glass till it poured over onto his jeans and settee, but when his wife later pointed this out to him he denied that he had done it! His wife indicated that for around half of the 20 or so episodes which had occurred, there was evidence of a pure amnesic attack, that is, without any clinical signs such as involuntary motor movements, inappropriate behaviour, etc. She indicated that the initial episodes took the form of these pure instances of memory loss. It was only later that the episodes began to have additional clinical features suggestive of epilepsy.

At the time of the amnesic episode, he would have a period of retrograde amnesia lasting 1–2 days, and this would not recover. There was never any loss of personal identity nor failure to recognise his wife. For most attacks, which lasted one day, he would subsequently have memory loss for the day in question.

Physical examination was normal. A CT scan with contrast enhancement showed some asymmetry of the tip of the temporal horns, with minor enlargement on the left side and a small area of subependymal low attenuation in this region. An MRI scan confirmed these features.

EEG showed generalised bursts of low amplitude spike and wave discharges in both temporal lobes, more on the right. He was

started on carbamazepine, this being later changed to phenytoin, and he has had no further amnesic attacks since that time.

On neuropsychological testing, he showed some impairment on faces matching and faces recognition memory tests, and on a verbal paired associate learning task. On remaining tests, his scores were within normal limits.

This patient would not have fulfilled standard criteria for TGA because of the episodes of involuntary movements that accompanied some of the episodes and the EEG abnormalities which were found.

CASE 4

A 61-year-old woman first presented in September 1990. Her attack of transient amnesia occurred late at night and was therefore unwitnessed, but it was described by her in such detail that there appeared to be little doubt as to its authenticity. The attack occurred in September 1990. She had returned a few days earlier from holiday, and had gone to bed at around 10.30pm. Around 1am, she awoke and when she looked around her room it seemed to her to be totally unfamiliar. She looked at her husband and she did not recognise him. She went to the bedroom next door, and she did not recognise her son or grandson who were sleeping there. There was no loss of personal identity at this time. She felt as if she was in the wrong home, as if she was an intruder in the house. After 10–20 minutes, she did recognise a suitcase which was half-opened in the bedroom, and she recalled that she had recently come back from holiday. However, she still did not recognise her husband. She then saw her cat, and did recognise it as familiar. She went downstairs, and recognised a photograph which was that of her daughter who had died in 1974. She came back upstairs and still did not recognise her husband. At this time, her grandson woke up and asked her about a trip he had mentioned to her earlier in the day, but she did not have any recollection at all about this earlier conversation. She then looked out of the window, and was able to recognise houses across the street. Shortly afterwards, the attack came to an end. She then went back to sleep, and the next morning she felt perfectly normal.

The account given by her was offered six months after the episode and she indicated that it was still very vivid in her mind. There was thus no loss of memory for the period of 'confusion' such as one finds in TGA.

One month later, in October 1990, a further but rather different episode occurred when she was out shopping with her daughter. On this occasion, her daughter was a witness to the event. After she came out of the butcher's shop, she was totally confused for ten minutes, and 'did not know anything or anybody'. She recovered quickly, but then indicated to her daughter that she had to get some meat, thus forgetting that she had just been to the butcher's shop.

In terms of general cognitive symptoms, she thought that her everyday memory had

perhaps become slightly impaired over the past year, and also that her spelling had deteriorated over the past two years.

In June 1991, she suffered a complex partial seizure—witnessed by her daughter—during which she suddenly went red, passed out, and on recovery started to scratch her arms and head, then ran outside and laughed. During this time, she was vacant and inaccessible. The episode lasted for fifteen minutes. Her daughter also described weekly episodes of 'falling' which appeared to be epileptic.

She was subsequently prescribed carbamazepine, and has had no further episodes.

A CT scan showed an old left frontal infarct, and it was not possible to be certain whether this was related to the amnesic episodes. EEG showed 'a mild left anterior temporal abnormality with a slight paroxysmal tendency'.

This patient would not have fulfilled standard criteria for TGA because of her clear memory for the amnesic episode itself, and because of the frank epileptic episodes which subsequently occurred.

Discussion

These four cases of transient amnesia associated with epilepsy permit reassessment of TEA. Retrograde amnesia may be present during the attack, without a corresponding severity in anterograde memory, and sometimes with no apparent loss of anterograde memory (cases 1 and 4), thus providing a contrast with what is often found in TGA. As both Kapur *et al*² and Palmieri *et al*⁷ reported for their cases, there are episodes where memories are not laid down, but where this does not become apparent until some time later. Whereas other researchers⁴ and I have all remarked on the brevity of the episodes, one of our cases (case 3) appeared to have impaired memory for a period of a day and sometimes two days.

A) GENERAL CLASSIFICATION OF TEA

There is now sufficient clinical evidence to outline general diagnostic criteria for the presence of TEA. The criteria which I propose supersede those described earlier.³ For a condition such as TEA, which probably has several subsidiary conditions and where the number of well-documented cases remains fewer than one would like, the criteria may need to be further refined in the light of subsequent experience. At present, there are no firm physical markers for a diagnosis of TEA—routine EEG, CT and MRI may often be reported as normal. Any abnormalities may only show up on 24 hour or depth electrode/multi-electrode recording formats or after high resolution/quantitative MRI analysis. TEA therefore remains a diagnosis which is dependent on careful clinical examination.

I propose that the condition of TEA be reserved for those instances of sudden onset of memory loss (that is, loss of a previous normally acquired memory) or memory dysfunction (that is, impairment in the ability to

retain new information), where there are no other clinical manifestations of seizure activity at the time of the attack, but where there is additional evidence to suggest the presence of epilepsy. This additional evidence may include EEG changes in the temporal lobes with/without spike abnormality, additional epileptic clinical features on other occasions, and reduction or cessation of the attacks with the introduction of anti-epileptic medication. Some clinicians may wish to make a distinction between 'pure' TEA and 'seizure-related' or 'mixed' TEA—the latter would represent cases of 'post-ictal' or 'ictal' amnesia where there was evidence of subtle clinical changes preceding or during the episode of memory loss. TEA would usually be a particular manifestation of complex partial seizures of temporal lobe origin. The diagnosis of TEA would be fairly straightforward in cases where there is clear clinical evidence of seizure activity on other occasions. Some cases may, however, exist where no such concomitant evidence of epilepsy is present, and this may be so particularly in the early stages of presentation of TEA. I would therefore propose that in such patients a diagnosis of TEA is made where there is sudden memory loss, as outlined above, and where at least four of the following eight features are present. Such a diagnostic proforma must of necessity be regarded as tentative and somewhat arbitrary, and would need to be validated in a prospective study of transient amnesia.

1 An absence of repetitive questioning and perplexed, anxious state with the presence of partial rather than global amnesia during the episode of memory impairment.

2 The occurrence of a significant degree of retrograde amnesia, without a correspondingly severe degree of anterograde amnesia.

3 The occurrence of amnesic episodes first thing in the morning or after waking from a period of sleep.

4 An unusually large number of episodes of memory loss (two or more within a six-month period).

5 A brief duration for at least 50% of the episodes of memory dysfunction (less than an hour).

6 The reduction or cessation of amnesic episodes by the introduction of anti-epileptic medication.

7 The presence of episodes where memory loss for an earlier period of time or for an established fact only became evident by chance on a later occasion, with no evidence of acute memory dysfunction at the time of the presumed attack.

8 Evidence of inter-ictal EEG abnormality.

It is important wherever possible to have witnessed information, especially in respect of the presence of concomitant seizure activity at the time of the TEA episode. This information is critical, so that TEA can be distinguished from 'ictal amnesia' related to post-ictal memory dysfunction^{23,24} and from 'absence' states.²⁵

On the basis of the case studies presented here, and in the light of published studies, I

propose a four-fold classification of TEA. *Anterograde TEA* would comprise those cases where there is impaired ability to retain new information but where memory for information acquired before the attack is normal. *Retrograde TEA* would comprise those cases where there is a sudden loss of memory for information which was normally acquired prior to the onset of the episode.²⁶ *Global TEA* would include cases where there is both anterograde and retrograde amnesia at the time of the attack. *Subclinical TEA* would include cases of anterograde TEA where there is subsequent evidence of amnesia for an event which lasted for a discrete period of time, usually several hours, though occasionally shorter or longer than this, but where there was no awareness at that time, either by the patient or by an observer, of any abnormality in memory or other aspect of behaviour.

The concept of subclinical epileptiform activity is not in itself new, and I would see subclinical TEA as having similar mechanisms to those described for other manifestations of transient cognitive impairment.²⁷⁻²⁹ Although instances of subclinical TEA have many similarities to the amnesic episodes of cases, such as the patient Dr Z, described by Hughlings Jackson,³⁰ and the 'pure amnesic seizures' described by Palmizi *et al.*,⁷ some of these patients had a warning sign or symptom before the attack, and I would therefore regard such cases as slightly different from subclinical TEA. Cases of retrograde TEA may sometimes be difficult to distinguish from cases of subclinical TEA, but there may be factors which would tilt a diagnosis one way or the other. For example, if there was clear 'shrinkage' of the amnesia, then this would favour a diagnosis of retrograde TEA. Conversely, loss of memory for a discrete event that had occurred over a specified period of time, as opposed to amnesia for familiar material such as an item of knowledge, would favour a diagnosis of subclinical TEA. Some of the cases I have described in this paper would appear to suggest that retrograde TEA may sometimes occur in conjunction with subclinical TEA.

B) DIFFERENTIAL DIAGNOSIS WITH RESPECT TO OTHER FORMS OF TRANSIENT AMNESIA

In most of the patients whom I have seen, and in many of the published cases, the initial attacks were of pure TEA—similar to the pure amnesic seizures described by Palmizi *et al.*⁷—and only later was there clinical evidence of the presence of epilepsy. An initial erroneous diagnosis has often centred around two alternative possibilities—TGA and transient psychogenic amnesia. As is evident from large-scale series of TGA cases,^{4,11} and from more general series of cases of transient amnesia,³¹ a few patients may present with all of the features which fit the classical description for TGA, but only later will they show evidence for the presence of epilepsy. Since TEA remains a relatively recently recognised form of memory disorder, it may be helpful to

provide a 'distinctive features' table which can help channel clinicians towards a correct differential diagnosis (Table 1). Some aspects of the differentiation of TGA and TEA from psychogenic amnesia have been discussed in more detail elsewhere.³²

C) NEUROPSYCHOLOGICAL AND NEUROANATOMICAL PERSPECTIVES OF TRANSIENT EPILEPTIC AMNESIA

Patients with TEA will tend to show interictal evidence of neuropsychological impairment more often, and to a greater degree, than patients with TGA. This may be due to a number of factors—neuropsychological deficits related to the lesion which underlies the TEA, deleterious effects from amnesic or non-amnesic epileptic episodes, and possible cognitive side-effects from any anti-epileptic medication. Memory impairment has been the most consistent finding across the reported studies of TEA patients, and was also evident in the cases reported here. One feature of this memory impairment which appears to be particularly common is an anterograde memory deficit for faces² (also, cases 1 and 3 of this series). More speculatively, my clinical impression is that repeated episodes of TEA appear to interfere with long-term consolidation processes in the hippocampal formation/temporal lobes, such that patients may perform at normal or near-normal levels on traditional anterograde memory tests, apart from faces memory, but will be impaired in their ability to recall events that have occurred months or years previously.³³ This is naturally rather difficult to assess formally, and it may often be based on observations reported by the carer. In some cases of TEA, I would further speculate that this interference with long-term consolidation may affect memories laid down years earlier, and this may therefore account for the focal retrograde amnesia which we found in one case of TEA.² The pattern and severity of memory impairment will probably vary from case to case, and depend on a number of factors, including the number of TEA episodes which have occurred, the temporal distribution of such episodes (massed or spaced over time), and the type and severity of the attacks. It may well be the case that a large number of attacks of TEA, spaced over several years, may damage long-term consolidation of memory for public and personal events which were encoded during that period and during a 5–10 year period immediately preceding the onset of the illness. Memory impairment—albeit relatively mild—as a residual sequela of TGA has also been reported in a few studies.³⁴⁻⁵ Although formal comparisons between two sets of matched TEA and TGA patients remains to be made, it would appear that memory impairment is rather more frequent and more marked in TEA patients, and that it can affect both verbal and nonverbal memory in TEA patients—whereas it appears to involve verbal memory more selectively in TGA patients.

At the anatomical level, I would agree with

Table Summary of distinctive clinical features of three forms of transient amnesia

	Features supportive of transient epileptic amnesia	Features supportive of transient global amnesia	Features supportive of transient psychogenic amnesia
Background information	Younger age-group. Personal or family history of epilepsy. History of past or present structural brain lesion in or near temporal lobe. EEG epileptiform abnormality. Inter-ictal neuropsychological evidence of temporal lobe dysfunction. Presence of olfactory or gustatory hallucinatory phenomena in clinical history.	History of migraine. History of hypertension.	Present or past history of psychiatric symptoms. Present or past history of alcohol or drug abuse. Present or past history of criminal activity.
Frequency and duration of amnesic episodes	Large number of amnesic episodes. Short duration of attacks, often less than an hour.	Single attack within a two year period. Duration of episode around three hours.	Loss of memory may continue several days.
Precipitating and presenting features	'Aura' may occur prior to occurrence of attack. Occurrence after a period of sleep.	May be preceded by physical exertion or sudden exposure to hot/cold.	Recent stressful event. Secondary gain for occurrence or continuation of memory loss. May often present to non-medical agency.
Behaviour during and after an episode	Patient may show partial or minimal impairment of ability to retain new information. Lack of responsiveness, inappropriate speech or behaviour and involuntary, stereotyped movements may precede or occur during some episodes. Patient may feel rather exhausted after an episode. Patient may show evidence of subclinical amnesia—that is, poor consolidation of new memories, but with no clinical evidence or awareness by the patient of any abnormality in memory or other functions. Patient may subsequently retain some memory for the episode of amnesia.	Patient may be rather perplexed and anxious. Poor ability to retain new information, even over short periods—often characterized by repeating the same questions again and again. Patient will subsequently have a blank period in his memory which will correspond to the episode of amnesia. Patients will usually make a good neuropsychological recovery, with little or only mild residual impairment.	There may be total loss of memory for past, perhaps extending to childhood, with relative preservation of ability to retain new information. In cases of simulated anterograde memory loss, there may be features such as impaired performance on simple memory tasks (for example, digit span), less than chance performance on recognition memory tests, approximate answers to some questions, and inconsistent responses between similar tests or across test sessions.
Characteristics of retrograde memory loss	In some cases, retrograde amnesia may be the sole feature of the patient's memory loss. It may cover memory loss for a period of time or loss of specific knowledge. The latter will tend to recover with time, but the former may remain lost from memory, suggesting a past episode of subclinical anterograde amnesia.	Memory loss for a period which may initially be several years, with subsequent gradual shrinkage of this amnesia to a period of a few hours. Temporal gradient to retrograde amnesia, such that older memories are less impaired than more recent memories.	Patient displays loss of personal identity. Patient may show loss of memory for close family members that persists for days. The retrograde amnesia may recover suddenly. Intact memory for public but not personal events which occurred during any fugue state.

the conclusions reached by Palmini *et al*⁷ that bilateral medial temporal lobe dysfunction plays a part in the amnesic episodes associated with TEA. Some support for the importance of medial temporal lobe structures has come from an MRI study of an unusually pure amnesic state associated with epileptic seizure activity.³⁶ I would, however, propose that this explanation may only account for some TEA episodes. Those episodes with a major retrograde memory component, and also those with a combined anterograde and retrograde memory component, require a broader anatomical explanation. I would propose that Retrograde TEA results from pathological involvement of temporal lobe neocortical and white matter structures, perhaps in the temporal pole or anterior-inferior temporal lobe gyri, as has been found in cases of chronic focal retrograde amnesia.³⁷⁻⁸ I would also propose that global TEA results from abnormality in both the hippocampus and in those structures lateral to it. Anterograde TEA would then follow from a pathophysiological change largely restricted to the hippocampus. The anatomical locus of subclinical TEA is more difficult to characterise. It would probably reflect abnormality in any of the structures or pathways associated with anterograde TEA, but without the critical involvement of neural mechanisms underlying awareness. I would presume that these latter mechanisms would be cortical in

location, since absence of awareness of amnesia would essentially require a mismatch to occur between the individual's memory for an event or piece of information and feedback from his environment that the event had not taken place/that the information was not available. It is therefore likely that subclinical TEA occurs with pathophysiological changes confined to structures in the hippocampal formation, with perhaps more focal/less severe abnormality than that which occurs for anterograde TEA. Indirect support for this possibility comes from studies of memory performance during subclinical hippocampal seizures.³⁹

Conclusions

There is now ample evidence to support the existence of a condition which has the features of TEA. Further well-documented cases are needed to substantiate the four-fold classification proposed in this paper, to establish the clinical and neuropsychological features associated with the various forms of TEA, and to define the anatomical mechanisms which underlie such amnesic episodes. Such knowledge should not only have spin-offs for the proper management of such patients, including early diagnosis and prompt introduction of anti-epileptic medication, but it would also provide us with new

approaches to understanding mechanisms underlying amnesia.

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