Transient Epileptic Amnesia

For over 120 years it has been recognised that episodes of dense memory loss may be the sole presenting feature of epileptic seizures. Recent research suggests that ‘transient epileptic amnesia’ (TEA) should be thought of as a distinct neurological syndrome, with important implications both for clinical practice and for our scientific understanding of human memory.

TEA: development of the concept
In 1888, the renowned British neurologist John Hughlings Jackson described the case of Dr Z, a medical practitioner who suffered from an unusual variety of epilepsy.1 During seizures, Z retained consciousness and was able to engage in complex, purposeful behaviour for which he was later amnesic. On one occasion, whilst at work, he experienced the onset of his typical epileptic aura. He subsequently examined, diagnosed and instigated treatment for a child with pneumonia, yet afterwards had no recollection of the consultation. Some years later, Z’s brain came to autopsy, and a single, circumscribed lesion in the left uncus was discovered.2

The idea that transient, isolated memory loss may be the sole manifestation of epileptic seizures lay dormant in the scientific literature until the mid-twentieth century when debate began about the aetiology of the newly described syndrome of transient global amnesia (TGA). It is now clear that, in the majority of cases, TGA is not caused by seizure activity. However, Hodges and Warlow3 despite using stringent diagnostic criteria, discovered that a significant minority (7%) of TGA patients they studied went on to develop complex partial seizures. These patients tended to have recurrent, briefer amnesic attacks than those with typical TGA.

The term ‘transient epileptic amnesia’ was coined in 1990 by Narinder Kapur4 in an essay in which he reviewed the published case reports, distilled the principal clinical features and concluded that TEA was a distinct neurological entity worthy of further study.

Using the diagnostic criteria of Zeman et al5 (see Box), we have recruited a cohort of over 50 patients with TEA from around the UK, as part of the wider TIME (The Impairment of Memory in Epilepsy) Project. This has enabled detailed study of the clinical, neuropsychological and radiological characteristics of this under-recognised and fascinating syndrome.6,7

Clinical features of TEA
The amnesic attacks of TEA typically begin in late middle-age, the mean age of onset being 57 years. Males outnumber females by a ratio of two to one. As with most forms of epilepsy, the frequency of attacks is highly variable but, on average, they occur about once per month. A helpful clue to the diagnosis is that episodes of TEA characteristically occur upon waking, with around 70% of patients experiencing at least some attacks in this context. During the amnesic episodes, patients are unable to remember recent events (‘retrograde amnesia’) and often cannot retain new information.

Diagnostic criteria for TEA [5]
1. A history of recurrent witnessed episodes of transient amnesia
2. Cognitive functions other than memory judged to be intact during typical episodes by a reliable witness
3. Evidence for a diagnosis of epilepsy based on one or more of the following:
   a. epileptiform abnormalities on electroencephalography
   b. the concurrent onset of other clinical features of epilepsy (e.g. lip-smacking, olfactory hallucinations)
   c. a clear-cut response to anticonvulsant therapy.

Figure 1: Radiological localisation of the seizure focus in TEA: (a) MRI scan showing high signal on T2-weighted imaging in the left medial temporal lobe of a patient with a flurry of attacks of TEA. (b) PET scan showing hypermetabolism in the left hippocampus at the time of the attacks. (c) with resolution after successful treatment 1 month later [Reproduced from10].

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As mentioned above, complaints of interictal memory difficulties are common amongst patients with TEA. Nevertheless, patients are typically unimpaired on standard neuropsychological tests of memory.8 Instead, they describe problems that are invisible to these tests but have a significant impact on everyday life.

Remote memory impairment: 70% of patients with TEA report loss of memories for salient, personally experienced events from the remote past. For example, they may be unable to remember holidays they have been on or family weddings they have attended. A recent study confirms that there is a life-long depletion of autobiographical memories, particularly affecting the recollection of episodic details.9 Memory for public events was also affected, but to a lesser degree and only for recent decades. A subgroup of patients also complains of difficulty in recognizing familiar places and navigating along familiar routes.10

Accelerated long-term forgetting (ALF): 44% of patients describe the excessively rapid fading of newly acquired memories over a period of days to weeks. One patient was able to discuss the merits of a film he had seen with his daughter on the following day, but one week later had no recollection of the movie.11 Patients with TEA as a group show evidence of ALF on objective testing (Figure 2b). Those who specifically complain of the problem show especially severe longterm forgetting.11

The cause of remote memory impairment and ALF in TEA is unknown. They are not related to the volumes of MTL structures as measured on MR brain imaging,12 but it is possible that they are due to more subtle structural damage yet to be detected. An alternative explanation is that they result from disturbance of normal brain function in the MTL, or elsewhere, by subclinical seizure activity. Reports of improvement of ALF upon treatment with antiepileptic medication are in keeping with this suggestion.12,13 Further research is clearly needed, particularly in the light of evidence that remote memory impairment and ALF also occur in the wider population of people with epilepsy.14

Conclusion

Transient epileptic amnesia is a distinctive variety of temporal lobe epilepsy causing brief, recurrent, treatment-responsive attacks of transient amnesia, often on waking, generally in middle aged and elderly people. It is usually accompanied by interictal memory deficits including remote memory loss and accelerated long-term forgetting.

Pathophysiology of TEA

Several features of TEA suggest that the medial temporal lobes (MTLs) are the seizure source. The MTL is critically involved in the laying down and retrieval of memories,1 as well as being a common site of seizure onset in temporal lobe epilepsy. The cognitive deficit in TEA attacks is characteristic of that observed with MTL dysfunction. Further anatomical clues are the high frequency of olfactory hallucinations and oroalimentary automatisms, and the localisation of epileptiform activity, which can be detected by EEG. Evidence obtained from EEG monitoring indicates that the amnestic spells of TEA can occur either as an ictal or a post-ictal phenomenon.11

When structural abnormalities are detected, they consistently impinge on the temporal lobes. A single case was studied at the time of a flurry of attacks: MRI scanning revealed high signal in the left hippocampus with hypermetabolism in the left hippocampus on peri-ictal PET which had resolved after successful treatment of his seizures (Figure 1).12 As a group, the 50 patients studied by Butler et al had mild but significant bilateral hippocampal atrophy.10

Neuropsychology of TEA

In most cases, general intellectual functioning is normal in patients with TEA. Indeed, the cohort of patients recruited to the TIME Project had an average mean full scale IQ of 118. This may reflect the difficulty of recognising TEA in the absence of an articulate description of its symptoms.

REFERENCES