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Transient Epileptic Amnesia over twenty years: Long-term follow-up of a case series with three detailed reports

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ABSTRACT

Purpose: Transient Epileptic Amnesia (TEA) is a form of adult onset temporal lobe epilepsy characterised by ictal amnesia. The amnesic seizures are often accompanied by interical memory disturbance, involving autobiographical amnesia and accelerated long-term forgetting. Short-term follow-up studies suggest a relatively stable cognitive profile once treated, but recent case reports raise concerns regarding the risk of developing Alzheimer's disease (AD). The current study reports clinical and cognitive outcome in TEA patients over a 20-year period.

Methods: A cohort of ten TEA patients first reported in 1998 were followed up at two time intervals, each 10 years apart. Information regarding clinical outcomes and subjective reports of memory functioning was gained via GP records and clinical interview. Objective memory function was determined at each time point via a comprehensive neuropsychological assessment, where possible.

Results: Information was obtained for nine of the original 10 participants. Over the 20-year period, 4 participants died, with no indication of dementia prior to death. One participant was diagnosed with Vascular Dementia. Seizures were generally well controlled. Subjective reports of memory varied, including no concerns, stable memory difficulties, and worsening memory. Neuropsychological assessment at 10 years showed stable performances across most measures. At the 20-year follow up, there was no evidence of a general cognitive decline. Participants showed stability on some measures, with reductions on others. Performance was not consistent with AD.

Conclusions: No elevated risk of dementia was evident from this TEA series. Although memory difficulties persist over time, the prognosis of TEA appears generally benign.

1. Introduction

Transient Epileptic Amnesia (TEA) is a form of adult onset temporal lobe epilepsy characterised by repeated transient episodes of memory impairment, which occur in the absence of other significant cognitive disruption. For the majority, this ictal amnesia is accompanied by some degree of persistent, interictal memory difficulty, usually autobiographical amnesia [1,2], accelerated long term-forgetting [3–6] or topographical amnesia [7] i.e. memory for routes and places. Although cases of TEA have been described since 1889 [8], the recognition of TEA as a distinctive subtype of TLE is relatively recent, with specific diagnostic criteria outlined in 1998 [9]. As a result, while several studies characterise features at presentation, there is little information regarding long term prognosis. Evidence from shorter term follow up, however, suggests that while interictal memory problems may persist, the cognitive profile remains stable once the seizures are successfully treated with anticonvulsant medication [10–12]. Whether this is true over the longer term is currently unclear.

Longitudinal studies of other forms of TLE suggest that while memory performance of such patients may be below age-matched peers, declines over time do not generally exceed rates seen in normal ageing [13] and are therefore not usually suggestive of a neurodegenerative process. Prognosis in this group has been related to the type of seizure (with greater risk occurring if the patient's epilepsy includes generalised seizures), the number of uncontrolled seizures, and the age of onset (earlier onset predicting a poorer outcome) [14]. This bodes well for people

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with TEA, as the majority do not experience generalised seizures, respond well to medication, and do not develop the condition until their midlife [7].

Nevertheless, TEA was recently described in a woman who developed Alzheimer's disease (AD) 16 years later [15]. While potentially coincidental, the authors suggest that TEA may have been the first sign of this disease. Similarly, cases diagnosed with Epileptic Amnesic Syndrome (EAS) have developed AD [16]. 'EAS' denotes a syndrome closely resembling TEA but also encompassing patients with interictal memory disturbance in the context of subtle, non-amnesic, temporal lobe seizures. Amnesic seizures have been also noted, occasionally as a presenting feature, among patients with Mild Cognitive Impairment and early AD [17,18]. While this is usually in the context of other seizure types, taken together, the emergence of such cases has served as a warning that TEA and EAS may not be as benign as originally thought.

The current study presents the clinical and cognitive outcome of patients with TEA first reported in 1998 who have been long-term participants in the TIME project (The Impairment of Memory in Epilepsy—http://projects.exeter.ac.uk/time/). From the original series of 10 participants[9], we present follow-up information on 9 individuals over a 20-year period, with 3 detailed case reports. These unique long-term data provide insights into the prognosis of TEA.

2. Method

2.1. Participants

All participants took part in the 1998 published study [9] of TEA (T1). The diagnosis of TEA was established via clinical assessment by an experienced behavioural neurologist (AZ). In all cases, the repeated amnesic episodes had been witnessed by the participant's spouse. Evidence of epilepsy was confirmed through any combination of epileptiform abnormalities on EEG, reports of concurrent classically epileptic features (e.g. olfactory hallucinations, automatisms) and/or a positive treatment response to anticonvulsant therapy.

All available participants from the 1998 study were then recruited to the TIME study as part of the 2007 series (T2) [7], and invited to a third follow up 10 years later (T3).

The study was approved by the Multicentre Research Ethics Committee, United Kingdom (MREC 03/10/77). All participants gave written, informed consent.

2.2. Measures

Updated medical information regarding memory complaints, ongoing seizures and other significant medical events was collected either via clinical interview directly with the participant or through their General Practitioner. Where possible, participants also underwent neuropsychological re-assessment. This included administration of the following measures:

- General intellectual functioning: National Adult Reading Test (NART) [19] was used at T1 to estimate IQ. At T2 and T3, the 4-subtest version of the Wechsler Abbreviated Scale of Intelligence (WASI) [20] was used.
- Visuospatial/visuoconstructional skills: Rey Complex Figure Test (RCFT) [21]—copy trial.
- Visual delayed recall: 30 min free recall of the RCFT.
- Verbal immediate and delayed recall: Story 1 (Anna Thompson) from the Logical Memory (LM) subtest of the Wechsler Memory Scale (WMS-R version at T1 and WMS-III version at T2) [22].
- Recognition memory: Warrington Recognition Memory Test (RMT) [23]—Words and Faces subtests
- Semantic memory: Graded Naming Test (GNT) [24,25] at T2 and T3
- Executive function: verbal fluency [26,27] and Wisconsin Card Sorting Test—64 Card Version [28] at T2 and T3.

Data include either age-corrected percentile ranks, or raw scores if these were not available, to interpret performance over time. Clinically significant impairment was defined as test performance that was less than or equal to the 10th percentile. Performance was considered stable if the percentile rank remained within a similar range (e.g. if scores remained within the normal range of 25–75th percentile, above 75th percentile, or below average range 10–25th percentile; or if scores were in overlapping percentile ranges, such as "75–95" and then 75th). Where test norms did not adjust for differences in age over time, stability was assumed if raw scores remained relatively unchanged (i.e. allowing for minor decrements that may be expected from measurement error).

3. Results

Table 1 summarises each participant's clinical presentation, Table 2 the clinical outcomes over the 10–20-year period, and Tables 3a and 3b the neuropsychological test performance. Fig. 1 provides a summary of participant numbers at each time point.

Table 1
Clinical characteristics of TEA participants.

ID	Sex	Age at onset	Duration of attacks	Approx. frequency of attacks	Seizure features	Other epilepsy	EEG	Initial treatment response
1	M	60	30–60 min	Monthly	All on waking, Olf hall	sps	Normal	Yes—LAM
2	M	49	15–30 min	Twice/month	All on waking, Pure amnesia	sps	Epileptic	Yes—CBZ
3	M	68	Hours–days	No pattern	On waking, Olf hall	sps, cps	Epileptic	Yes—SVP
4	F	52	2–24 h	Twice/year	On waking, Pure amnesia	None	Epileptic	Yes—LAM
5	M	78	Hours–days	Twice/year	On waking	None	Epileptic	Equivocal reduction—CBZ
6	M	69	15–30 min	Monthly	On waking, automatisms, déjà vu	sps	Non-specific abnormalities	Not treated
7	M	73	1–3 h	Monthly	On waking, Pure amnesia	none	Non-specific abnormalities	Yes—Phen
8	M	60	2–24 h	Monthly	On waking, automatisms	cps, tcl (1)	Normal	Yes—SVP
9	M	69	20–60 min	Monthly	On waking, automatisms	cps	Some abnormalities	Yes—CBZ
10	M	52	15–30 min	Twice/week	On waking, automatisms	cps, tcl (3)	Some abnormalities	Yes—CBZ

CBZ = carbamazepine; LAM = lamotrigine; SVP = sodium valproate; Phen = phenytoin, sps = simple partial seizures; cps = complex partial seizures; tcl = tonic–clonic seizures; Olf hall = olfactory hallucination.