Syndromes of Transient Amnesia

For most of us, transient lapses of memory are a familiar and at worst irritating feature of daily life. They are generally brief, item specific and alleviated by a pertinent cue. At the other extreme, the amnesic syndrome is characterised by a profound and usually permanent loss of the ability both to retrieve previously established memories (retrograde amnesia) and to form new ones (anterograde amnesia). A permanent amnesic syndrome is usually caused by extensive bilateral damage to the medial temporal lobes (as in limbic encephalitis or post-hypoxic damage) or to the diencephalon (as in Korsakoff's syndrome), brain regions which play a key role in declarative, 'conscious' memory for facts and events.[1] Some people, however, experience an episode of dense memory loss which is sudden in onset but self-limiting. These syndromes of transient amnesia are the focus of this article.

Transient Global Amnesia (TGA)

The syndrome of TGA has an incidence of 3 to 10 per 100,000 and is characterised by the abrupt onset, usually in middle to old age, of a profound but transient deficit in the retention of new information together with a variable degree of amnesia for past events.[2] At least 50% of cases appear to be precipitated by a variety of acute stressors including exercise, immersion in cold water, sexual intercourse, pain, or a strongly emotional event. The anterograde amnesia is betrayed by repetitive questioning, usually related to attempts at self-orientation such as "What day is it?" or "What am I doing here?" The retrograde amnesia may cover a few hours prior to the attack onset or be much more extensive. There is no impairment of consciousness or of other cognitive functions such as attention, language or perception, and there are no focal neurological deficits. Spontaneous and apparently complete recovery typically occurs within 4 to 10 hours, although the individual is left with a permanent amnesic gap for the duration of the attack. Recurrence is rare, with most recent studies reporting a rate of between 3 and 10% per year. A single, uncomplicated episode requires minimal investigation and no specific treatment.

It is widely accepted that the pathological changes in TGA affect the medial temporal lobes, although precisely what those pathological changes are and why they occur is far from resolved. A number of studies have reported increased prevalence of migraine amongst TGA patients[3] and migrainous accompaniments, including headache, nausea and vomiting, are not uncommon during the amnesic period. This mechanism alone, however, would not explain the limited age range and rare recurrence of TGA. More recent studies using diffusion-weighted imaging have revealed punctate hippocampal lesions, supportive of a vascular aetiology, in a significant proportion of TGA cases.[4,5] Interestingly, given the frequency of Valsalva manoeuvre-like precipitants in TGA, it has also been found that patients have a higher prevalence of jugular vein incompetence than controls,[6,7] lending support to a hypothesis that increased pressure in the superior vena cava causes ischaemia in crucial memory-related brain structures.[8]

Episodes of transient amnesia occurring in the context of epilepsy or head injury and those accompanied by focal neurological symptoms or signs are usually excluded from the rubric of TGA (see Table 1). These are discussed below.

Transient Epileptic Amnesia (TEA)

TEA is a relatively recently described condition in which transient amnesia is the principal manifestation of temporal lobe seizures.[9,10] The attacks are often mistaken for

Table 1: Diagnostic criteria

Transient Global Amnesia (Hodges and Warlow 1993)

1. *attacks must be witnessed and information available from a capable observer who was present for most of the attack*
2. *there must be a clear-cut anterograde amnesia during the attack*
3. *clouding of consciousness and loss of personal identity must be absent, and the cognitive deficit must be limited to amnesia (that is, no aphasia, apraxia, etc)*
4. *there should be no accompanying focal neurological symptoms during the attack and no significant neurological signs afterwards*
5. *epileptic features must be absent*
6. *attacks must resolve within 24 hours*
7. *patients with recent head injury or active epilepsy (that is, remaining on medication or one seizure in the past two years) are excluded*

Transient Epileptic Amnesia (Zeman et al 1998)

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.*

Table 2: Characteristic features

TGA

- *sudden onset often precipitated by exercise, immersion in water, emotional stress, etc*
- *dense anterograde amnesia with repetitive questioning*
- *lasts around 4 – 10 hours*
- *rarely recurs*
- *aetiology unknown*

TEA

- *recurrent, brief (usually < 1 hour) amnesic episodes*
- *often occur upon waking*
- *may be associated with olfactory hallucinations or automatisms*
- *responds to anticonvulsant medication*
- *persistent memory deficits*

Psychogenic amnesia

- *history of 'organic amnesia', psychiatric illness and/or substance abuse*
- *may be triggered by mild head injury or highly emotional event*
- *extensive retrograde amnesia often with loss of personal identity*
- *preserved new learning*
- *duration usually several days at least*

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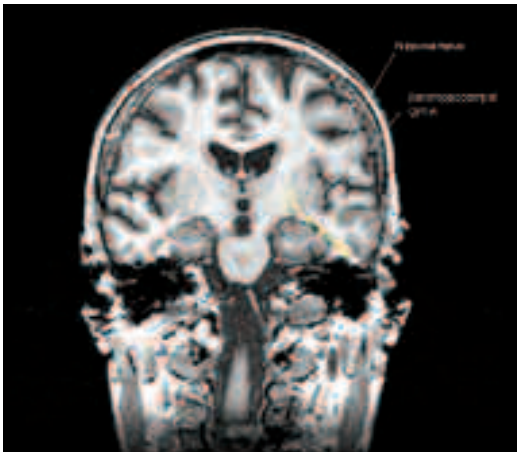

Figure 1: MRI scan showing the location of the hippocampus and parahippocampal gyrus in the medial temporal lobes. These areas are crucial for the processing of declarative memories.

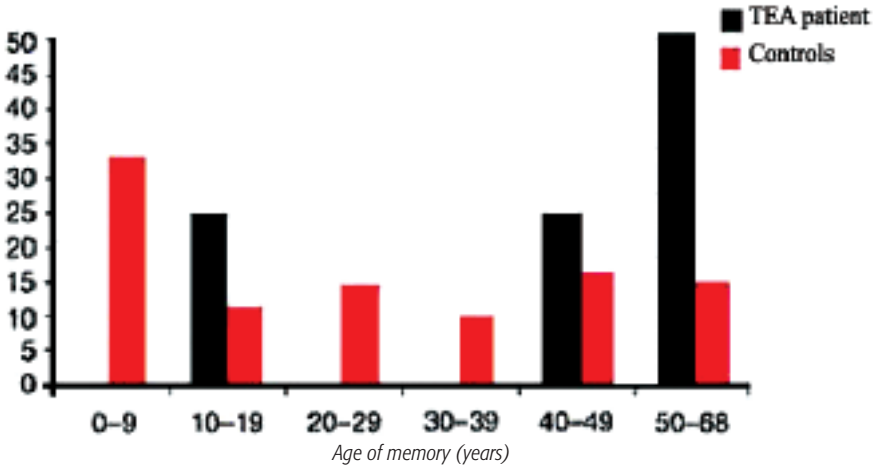

Figure 2: Autobiographical amnesia in TEA. When asked to produce personal memories relating to a particular word (eg 'boat'), a 68-year-old TEA patient failed to retrieve any episodes from his 20's or 30's. His performance on standard tests of anterograde memory was normal.

TGA. They too occur in late-middle to old age and usually involve a mixed anterograde and retrograde amnesia, repetitive questioning and otherwise preserved cognitive functioning. However, there are a number of important distinguishing features. The attacks are recurrent and tend to be briefer than TGA, typically lasting less than one hour. They often occur upon waking and may be associated with other features suggestive of epilepsy such as olfactory hallucinations, oro-alimentary automatisms or a brief period of unresponsiveness. Anterograde amnesia may be incomplete such that, after the attack, the patient may report being "able to remember not being able to remember". The interictal EEG is positive in about one-third of cases, with sleep-deprived recordings having a significantly higher yield. The attacks are usually very responsive to anticonvulsant medication. However, patients frequently complain of persistent memory difficulties that may not be detected by standard neuropsychological testing. In particular, they describe 1) the accelerated forgetting, over days to weeks, of newly acquired memories, and 2) a patchy loss of memories for remote, salient autobiographical events such as holidays or weddings.[11] The extent to which these deficits improve with anticonvulsant treatment is not yet clear.

Closed head injury

During recovery from violent cranial insult, the duration of post-traumatic amnesia, characterised by a severe learning deficit and a retrograde amnesia, is an important predictor of eventual outcome. The precise mechanism underlying this deficit is not understood. Occasionally, minor head injury, such as sustained during sporting activities, appears to trigger an episode of transient amnesia indistinguishable from TGA. The majority of reported cases have occurred in younger patients and several have been associated with a migraine-like headache reminiscent of Matthews' "footballer's migraine".[12,13]

Transient Ischaemic Attacks

It is clear that the majority of TGA attacks are not associated with vascular risk factors and do not entail an increased risk of future cerebrovascular events.[14] However, some transient ischaemic attacks, particularly of the posterior circulation, can result in a transient memory disturbance that resembles TGA. In these cases, the physician should be alerted by accompanying neurological signs such as ataxia, dysarthria, nystagmus or hemianopia.[2]

Psychogenic amnesia

Memory is a psychological function and distinguishing between psychological and physical causes of memory loss is a form of handwaving that reflects our current lack of understanding about the relationship between mind and brain. Nevertheless, certain cases of transient amnesia appear to be triggered by an apparently trivial event, related to periods of emotional stress, and have a neuropsychological profile that is difficult to reconcile with focal neurological dysfunction. These cases have variably been termed 'psychogenic', 'functional' or 'hysterical' amnesia. A distinction is made here from cases of 'malingering' in which the individual is believed to be intentionally deceiving medical personnel.

Psychogenic amnesia is typified by sudden onset of an inability to access memories from an extensive swathe of the past, often including loss of personal identity, a symptom otherwise only seen in the latest stages of degenerative brain disease.[15] In stark contrast, new learning is usually preserved. The memory loss may be associated with a period of wandering – the 'fugue state' – for which the individual is also later amnesic. Neuropsychological studies have not revealed any other consistent pattern of deficit that may help with diagnosis. A history of psychiatric disease or substance abuse is not uncommon and the patient may have experienced an episode of 'organic' transient amnesia in the past. Prognosis is variable with some individuals dramatically recovering their memories in response to a minor cue, and others remaining permanently disabled. However, the duration is usually considerably longer than in TGA or TEA.

Psychogenic memory loss can also be event-specific such as in the context of post-traumatic stress disorder and crime-related amnesia.

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