Transient global amnesia is a syndrome involving sudden and complete disruption of short term memory, with no other neurological signs or symptoms. It is often referred to physicians and stroke teams in primary/secondary care.

Epidemiology

It classically affects people between the ages of 40 and 80 years with the average age of onset being 62 years.\(^2,3\) It has an incidence of five per 100,000 population per year. There has been no racial or sexual predilection reported.\(^4,5\)

Clinical history

Transient global amnesia is widely regarded as one of the most remarkable neurological conditions in terms of its history, symptoms and signs. It presents classically with a sudden onset of severe anterograde amnesia.\(^1\) We describe here the epidemiology, clinical features, and management of this poorly recognised condition.

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Clinical history

Transient global amnesia is widely regarded as one of the most remarkable neurological conditions in terms of its history, symptoms and signs. It presents classically with a sudden onset of severe anterograde amnesia. During the episode patients are incapable of producing any new memories. The amnesia is so profound that both verbal and non-verbal memories cannot be formed often despite repetition. Immediate recall memory is preserved as is that of remote memories; however a degree of retrograde amnesia has also been reported in some cases.\(^1,6,7\)

Due to the sudden and alarming nature of the above described events, patients are often noted to have a high level of agitation and anxiety. This can lead to repetition and perseveration with those affected typically asking the same questions again and again in a very methodical manner, and often with similar gestures and vocal intonation. It has been likened to a sound track being repeatedly re-run.\(^8\)

During the event patients remain fully conscious and alert. They can continue to communicate and perform complex tasks such as driving. This suggests language, visuo-spatial skills, attention and social skills are preserved.

Symptoms generally last between two and eight hours, and are always less than 24 hours.\(^2,5\)

For trial purposes diagnostic criteria have been set out by Hodges et al and as a result are often used for a clinical diagnosis also. These are:\(^9\)

- Witnessed event
- Acute onset of anterograde amnesia
- No other cognitive impairment
- No alteration in conscious level
- No associated focal neurological deficit
- No associated features of seizure like activity
- No recent head injury
- No active history of epilepsy
- Symptoms should resolve within 24 hours.

Differential diagnosis

Although such a striking condition, many clinicians have not encountered it in their practice and hence it can often be mislabelled. Patients are often referred/admitted to
secondary care as this condition is sometimes considered a stroke mimic.

Subsequently TGA accounts for many consultations in TIA clinics. Differentials to consider in patients with suspected TGA include:

- Acute confusional states
- Epileptiform activity
- Transient epileptic amnesia
- Transient ischaemic attack/cerebrovascular event
- Atypical migraine
- Syncope episodes
- Psychogenic amnesia.

The above should all be considered and excluded through careful history taking and clinical examination, however the unique nature of TGA and its typical clinical presentation described above means it is often unmistakable.

Pathophysiology

The underlying causes have been extensively investigated, and varying hypotheses exist. It is however understood that the areas of the brain affected are likely to involve the mediobasal temporal region, hippocampus and parahippocampus which all play an integral role in memory formation.\(^{10,11}\)

Certain precipitants have also been noted in a large proportion of TGAs through case reporting. These include: \(^{12}\)

- Vigorous exercise
- Sudden temperature change
- Emotional instability.

Epilepsy is thought to be unlikely as a cause of TGA. This is due to the fact that episodes tend to occur in complete consciousness and have a low recurrence rate. Furthermore EEG studies have been largely unremarkable both during and after events. Transient Epileptic Amnesia (TEA) is thought to be a separate condition in itself, but one that can cause diagnostic confusion. TEAs tend to affect the young and episodes certainly last less than one hour.\(^{12,13}\)

Migraine has also been mooted as a potential cause of TGAs. The theory is based around the release of glutamate following emotional triggers, which leads to hippocampal dysfunction. Some studies have reported an association of TGAs occurring more frequently in those who suffer with migraines, but others have not found this relationship. Again the demographics of the affected vary, with migraines affecting a younger cohort. Only a small minority of TGA cases have reported a history of headache preceding or during the event.\(^{12,14}\)

The relationship with Valsalva triggers lead some to believe TGAs may have been due to a paradoxical embolus through a patent foramen ovale. This theory was refuted as the prevalence of PFOs is no higher in those affected by TGA. However the sudden onset nature of the symptoms means there are still many proponents of a vascular/ischaemic theory. Many have speculated that it may well be a form of a transient ischaemic attack or cerebrovascular event, however those who have been affected by TGA have not been found to be “arteriopath” and have no increased incidence of myocardial infarctions, peripheral vascular disease or strokes.\(^{14,15}\)

Another theory suggests that rather than arterial ischaemia, venous ischaemia may well be a causative factor. Valsalva manoeuvres have been shown to briefly raise cerebral venous pressure. The hippocampus has been found to be especially sensitive to such pressure changes, which reflects potentially why symptoms can occur without any other neurological deficit. These significant pressure changes are often exacerbated with jugular vein valve insufficiency which leads to further venous congestion, and selective ischaemia. However this alone does not fully explain the mechanism as prevalence of jugular insufficiency is no higher in the TGA group than in the general population.\(^{6,12,16,17}\)

Other postulated theories include drugs and alcohol. Some
suggested a relationship between the use of statins and TGA but no significant correlation was found. It has been suggested that psychological disturbances are a key factor. A link to psychiatric conditions and certain personality traits has also been put forward by some, where others feel it may be linked to hyperventilation and consequent cerebral vasoconstriction.2,7,12

The reality is that despite much research and studies, the exact aetiology remains elusive. Much investigation using MRI Diffusion Weighted Imaging, PET scanning, SPECT and MR spectroscopy have highlighted the various areas of the brain affected, but exactly how and why remains unclear.

Management

Regardless of the causes behind TGA it is widely felt to be a benign condition requiring no further treatment. The mainstay is reassurance to the patient and family. Naturally, patient concerns centre around ruling out tumours and strokes. Family members are often very distressed and perturbed upon witnessing their loved one go from “normal” to being unable to remember anything so acutely.

Prognosis

Episodes of TGA resolve spontaneously and are self-limiting. Recurrence rates have been reported varyingly with figures varying from 3% to 20% having repeated episodes in five years. The DVLA do not need to be informed about episodes of TGA and there are no implications on the ability to drive.2,6

Conclusion

Transient global amnesia continues to cause much diagnostic uncertainty, and its exact aetiology remains poorly understood. However it is a remarkable and dramatic condition presenting with sudden onset memory loss and an inability to retain new information. It resolves spontaneously, and is self-limiting with low risk of recurrence. It requires no formal treatment or follow-up.

Conflict of interest: none declared

References