SHORT REPORT

Are brief or recurrent transient global amnesias of epileptic origin?

Teresa P Melo, José M Ferro, Teresa Paiva

Abstract
To evaluate if short (less than one hour) or recurrent, or both, episodes of transient global amnesia (TGA) have an epileptic origin or carry a subsequent risk of epilepsy a group of patients with these types of TGA attacks was studied. The group was selected from a prospective series of 103 patients with TGA. Sixteen patients had an episode lasting less than one hour, 13 had more than one episode, and five patients had both short and recurrent attacks. For each patient the number of recurrences was small (four or less) and they were separated by months or years. During short attacks of TGA many subjects showed other typical features of TGA including repeated questioning (12 subjects) and performance of purposeful complex acts (eight subjects). Twelve short attacks were closely related to a characteristic precipitating event. During follow up only one patient had a seizure (partial motor). No other association between either short or repeated attacks of TGA and past history of epilepsy or paroxysmal discharges were seen on the EEG. Short or recurrent, or both, attacks of TGA are not epileptic and do not carry a relevant risk of subsequent seizures.

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Transient global amnesia (TGA) is a disorder whose pathogenesis is still unsettled. For most workers who have studied this disorder, epilepsy is an unlikely explanation for TGA.1-4 There are reports, however, of epileptic transient amnesia5-7 and pure amnestic seizures,14 and Hodges and Warlow9-14 have identified a small subgroup (7%) of subjects with short-lived or recurrent, or both, episodes of TGA who developed complex partial seizures on follow up. The objective of this study is to evaluate, in a prospective series of patients with TGA, if short or repeated, or both, episodes of TGA have an epileptic origin or carry a subsequent risk of epilepsy.

Subjects and methods
Since 1985 we have been asking other neurologists to refer patients with TGA and we are conducting a prospective case-control, neuromaging, neuropsychological, and follow-up study of this population.15 Transient global amnesia was defined as an episodic dysfunction of the central nervous system, during which there is a sudden loss of declarative memory for recent events without other neurological signs or symptoms, namely without any disturbance of vigilance, consciousness, language, cognition, praxis, or visuospatial functions.16-20 These attacks had to have been witnessed by a capable observer and there should have been no accompanying focal neurological symptoms or signs. Headache, nausea, and vomiting were allowed as associated symptoms during TGA. Patients who had had a head injury within the 72 hours preceding the amnestic period were not included.

Up to January 1993, 103 patients were enrolled in the study. Fifty-three were referred by other neurologists in the Lisbon area who were aware of our study. The remaining 50 patients were observed by one of the authors (TPM, JMF) at the emergency room (usually called by the neurologist on duty) or at the outpatient clinic. Nine other referred patients were excluded because they did not meet the inclusion criteria for TGA. All patients who had had a head injury within the 72 hours preceding the amnestic period were not included.

For the purpose of this study only patients with (a) short (one hour or less) inception TGA, (b) multiple (more than one) attacks of TGA, or (c) both short and multiple attacks
Patients with more than one episode of transient global amnesia (TGA) and at least one episode of TGA lasting less than one hour

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex/age (years)</th>
<th>Risk factors*</th>
<th>Date of TGA episode (duration (minutes))</th>
<th>EEG results</th>
<th>Seizures on follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>M, 66</td>
<td>HTA</td>
<td>1981 (120); 1984 (30); 1985 (30)</td>
<td>normal</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>M, 69</td>
<td>HTA</td>
<td>Sep 1988 (45); Mar 1989 (30); Apr 1990 (60)</td>
<td>1989 (normal); 1990 (left temporal slow focus)</td>
<td>1989 (focal, motor)</td>
</tr>
<tr>
<td>35</td>
<td>F, 63</td>
<td>HTA, high cholesterol</td>
<td>Dec 1988 (60); Apr 1989 (480); Aug 1989 (720)</td>
<td>three normal; 1989 (one during TGA)</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>F, 62</td>
<td>HTA, migraine, smoker, high cholesterol</td>
<td>1978 (30); 1980 (240); 1985 (120); 1989 (240)</td>
<td>normal</td>
<td></td>
</tr>
<tr>
<td>72</td>
<td>F, 67</td>
<td>HTA, migraine</td>
<td>1989 (60); Dec 1991 (240); Mar 1992 (180)</td>
<td>two normal</td>
<td></td>
</tr>
</tbody>
</table>

*HTA = Hypertension.

(including the inception attack, previous and recurrent attacks) were selected and reported in detail.

**Results**

**DURATION OF ATTACKS: SHORT TGAS**

In sixteen (16%) of 103 subjects with TGA investigated, the inception attack lasted one hour or less. Three short attacks lasted less than 30 minutes, five around 30 minutes, two between 30 and 60 minutes, and six lasted one hour. Three patients were examined by a neurologist during the attack and were judged to have typical TGA. Twelve subjects had repeated questioning and nine performed complex tasks such as driving, cooking, telephoning, and gardening during the episode. Twelve of these short episodes had typical precipitants (emotion, three; driving, one; sexual activity, one; effort, four; cough, one; heat exposure, one; angiography, one). No patient had a past history of seizures. Fourteen had an interictal EEG performed. Two had focal (temporal) $\alpha$ or $\theta-\delta$ slowing but none had paroxysmal EEG discharges. During follow-up (mean (SD) 27 (24) months, range 1–88) one patient, patient 33 (table), had three different recurrent episodes: a typical TGA, an episode of disorientation not detailed enough to be categorised, and a brief motor seizure of his right arm. A repeat EEG revealed a slow ($\theta$) focus on the left nasopharyngeal lead and CT showed a right frontal calcification (probably cysticercosis).

**NUMBER OF ATTACKS: RECURRENT TGAS**

Of the 103 subjects with TGA studied, 13 patients had more than one episode of TGA. Seven patients had an history of TGA before inclusion, four had recurrent episodes, and two had previous and recurrent episodes. Most (eight subjects) had only two episodes of TGA, four had three episodes, and one had four episodes of TGA. The median interval between two contiguous TGA episodes was 24 months (range 3–60) (figure).

Except for patient 33 who had a focal convolution, no other patient had seizures on follow-up.

**SHORT AND REPETITIVE TGAS**

The five patients with both short and repeated TGAs are summarised in the table. Recurrent TGAs were few (four or less) and separated by months or years. Despite EEGs being performed more than once in these patients, paroxysmal activity was never detected.

**Discussion**

The results of our series did not show any association between short (less than or equal to one hour) or recurrent episodes of TGA and epilepsy. There was no association with seizures in the past or paroxysmal discharges on the interictal EEG, and only one subject had a partial seizure on follow up, but not of the partial complex type. Half of our subjects with short attacks performed purposeful, intentional complex praxic acts, which indicates the preservation of procedural memory, in contrast with the disruption of episodic and semantic declarative memory. On the contrary, during partial complex epileptic seizures only relatively short and automatic sets of unlearned complex motor behaviour are displayed. Repeated questioning about the circumstances surrounding the attack is also a typical feature of TGA and was observed in three out of four of our subjects, whereas it is absent in pure amnestic seizures. Repeated questioning indicates awareness of the memory defect and preservation of metamemory. It is in fact an information seeking behaviour, trying to compensate for the memory storage disturbance. These two features seem more important for the differential diagnosis of TGA than simply the duration of the episode.

The idea that short, recurrent attacks of amnesia could have epileptic origin is not new or original. Deisenhammer presented a case
Although TGA patients were whereas about half of Hodges and Warlow’s patients were collected retrospectively, whereas about half of Hodges and Warlow’s patients were collected retrospectively. Although Hodges and Warlow interviewed patients and witnesses again, the time gap between the episode and the interview makes their testimony less reliable and the differential diagnosis between TGA, epileptic transient amnesia, pure amnestic seizures, or a prolonged post-ictal amnesia difficult to make.

Palmini et al19 studied eight patients with pure amnestic seizures. These type of attacks are defined as seizures during which the only clinical manifestation is an inability to retain in memory what occurs during the seizure, coupled with the preservation of other cognitive functions and the ability to interact normally with their physical and social environment. These patients also had unmis-takable conventional complex partial seizures. In seven patients attacks were preceded by a typical aura. During the attacks patients (and observers) were not aware that there was anything wrong with them, becoming aware of that only after the event. Patients with pure amnestic seizures had no retrograde amnesia for events before the seizure. All these patients had interictal EEG evidence of mesial temporal dysfunction.

Epileptic transient amnesia, either ictal or postictal,22,23 should not be confused with transient global amnesia. Epileptic amnestic episodes are not only briefer (usually lasting minutes) but also more numerous (more than four; even more than one a day) and recur at short intervals. Automatisms and staring are seen during some of these episodes and they are often preceded by a typical aura. Patients usually also have other types of partial complex seizures. Transient global amnesia rarely recurs and, as our series shows, recurrent TGAs are few and separated by months or years. Typical precipitant events and repeated questions can be found in about 75% of the short TGA attacks and are absent in epileptic transient amnesia. Anticonvulsant drugs and driving limitations should only be recommended for epileptic transient amnesia. Although the relative prevalence of TGA and pure amnestic seizures is not known, this type of seizure is probably rare. It is rarely seen in epileptic clinics23 and we could not find any such case among all the amnestic spells referred to us.

10 Palmini A, Morreale A, Lorusso S, Pazzaglia P, Lugaresi
Transient global amnesia: epileptic origin?


Nicolaus Petreus Tulpitius (1593–1674) on headaches

Nicolaus Pietersz Dirksz, son of Pieter Dirksz, a merchant, was born in Amsterdam, The Netherlands, on 11 October 1593. He studied under Pauw and Bontius at Leiden. He changed his name, adopting the tulips which adorned the façade of his home on Keizersgracht. A fine anatomist, pathologist, and physician, he provided early descriptions of the ileocecal valve (Tulp’s valve), angina interna, kidney stones, a bronchial cast, beriberi inorum, and tapeworms. Tulp is immortalised by his friend Rembrandt in The anatomy lesson, to be seen in the Rijksmuseum, Amsterdam, which shows Tulp, in an exquisite lace collar and tassels, dissecting before a group of surgeons.

In his “golden work” (Haller) Observationes medicæ, published in 1641 (fig), Tulp described a fat man who had suffered from severe headaches for a considerable time. Several treatments had failed. “He asked nature for help... and lost a great amount of fluid from the nose... (and) was relieved in a short period of time.”

Being a Hippocratic physician, Tulp cited the aphorism (Aph. 10, Book VI): “who has headache, and is very sick, and if matter, water and blood escapes from the nose or ears, will be cured”. We are left to wonder whether this was a transient CSF leak from head injury or hydrocephalus.

Tulp also relates the story of “the carpenter’s wife who had headaches for many years, accompanied by a warm feeling ascending from the foot to the head and back to the big toe. Tulp ordered cupping by which the volatile spirit could drain from the body; the patient recovered soon.”

He distinguishes between cephalia—headache accompanying febrile illnesses, and cephalalgia—recuring endogenous headache.

He tells of an Isaac van Halmaal who: “... in the beginning of the summer season, was inflicted with a very severe headache, occurring and disappearing daily on fixed hours, with such intensity, that he often assured me that he could not bear the pain any more or he would succumb shortly. For rarely it lasted longer than two hours. And the rest of the day there was no fever, nor indisposition of the urine, nor any infirmity of the pulse. But this recurring pain lasted until the fourteenth day...”

The usual treatment with cupping or blister-raising plasters applied to the occiput gave no relief. The description suggests cluster headache although unilateral pain, lacrimation, and redness of the eye were not mentioned.

I have mentioned elsewhere the later account of probable cluster headache by Thomas Willis in De anima brutorum published in 1672, who described a venerable matron who began to suffer every afternoon at 4 pm from recurring severe headache.1 In 1747 Joannes Christoph Ulricus Oppermann published his little acknowledged dissertatio medica inauguralis, entitled Hemicrania horologica which may be the first account of the variant, chronic paroxysmal hemi-crania. The later depiction of cluster headache awaited the doubtful account of Benjamin Hutchinson and the more convincing description of Romberg in his A manual of nervous diseases in man, 1853.

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1 Tulp NF. Observationes medicæ, 5th edn. Book 1, Ch 13, Leiden: Vivie, 1716.


I am greatly indebted to Dr P J Koehler of Heerlen, The Netherlands for his translation and permission to quote from his paper.

Nicholas Tulp (1593–1674). Engraving by L. Visscher (frontispiece to Observationes medicæ).1

See also p. 637
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