‘Les ictus amnésiques’ and Transient Global Amnesia

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Key Words

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Abstract

In March 1909, R. Benon was probably the first to report a typical case of what we now call transient global amnesia. In 1956, Bender, and independently, Guyotat and Courjon described clinical and epidemiological features of transient amnesic attacks. The condition achieved general recognition after the term *transient global amnesia* (TGA) was introduced by Fisher and Adams in 1958. Their historic work is the main focus of this review. They reported 17 patients, with an abrupt anterograde amnesia of short duration. Classification and criteria are outlined. Various aetiologies have been postulated, but although TGA remains a clinically distinct syndrome, usually with a good prognosis, evidence of neither ischaemia nor epilepsy is demonstrable in most patients. Theories of jugular venous reflux may be relevant in some but probably not in most cases of this heterogeneous disorder.

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History

Various forms of the Greek word ἀμνηστία for oblivion, from not remembering, were used occasionally in English in the 16–17th century in Latin and Greek forms.

In 1786, Benjamin Rush in his *Influence of Phys. Causes in Med. Inquiries and Observations* (1793) II. 5 noted: ‘The loss of memory has been called “amnesia”’. Since Louyer-Villermay used the term *amnésie* in 1819 [1], there have been several reports of patients with more or less quickly reversible episodes of disturbed memory [2, 3]. However, during the 19th century, transient memory impairment became associated with hysteria, a period that had its peak in 1898 when Ganser [4] reported the transitory amnesic state with *vorbeireden* (approximate answers) now known as the Ganser state. The first mention of the *ictus amnésique* – subsequently used by Guyotat, Bender, Fisher and Adams – appears to have been by Jean Alfred Fournier [5] who in 1879 reported amnesic spells (with few details) in patients with tabes and general paresis, which he was the first to have linked with syphilitic brain infection. Allan Hamilton (1878) and, independently, Charlton Bastian (1880) described amnesic states, but in none of these clinical accounts are there recognisable characteristics of transient global amnesia.

In March 1909, R. Benon was probably the first to report a typical case of what we now call *transient global amnesia* (TGA) [6]. Benon defined *ictus amnésique* as ‘a clinical psychopathological state with abrupt onset, of short duration, with diffuse, widespread, retro-antegrade amnesia of various depth’. His paper was intended to present cases of ‘organic’ amnesia (i.e. non-hysterical) in patients without syphilitic general paresis (he had published a paper on amnesia in general paresis in the preceding year) [7].

Fig. 1. C. Miller Fisher (left) and Raymond D. Adams (right).

Benon reported 4 patients with different conditions, suggestive of stroke or degenerative dementia in 3 of them, while his *Observation II* corresponds to a typical case of TGA in a 66-year-old woman. At the age of 50, she had had strokes, from which she recovered fully with no cognitive dysfunction or weakness. Ten years later, she had four episodes of acute, transient amnesia over 2 years.

Benon reported that the patient typically asked repeated questions: 'But where am I here? Where am I here? Where am I here?' He noted: 'One explains it to her, but she goes on asking ... She knows whom she is, during this amnesic state, but she does not remember her age. She recognizes her husband, her children, but not everybody who would come to the house ... She is asking for news of all her children, including those who died over 30 years ago ... In her amnesic state, she cannot give any detail on recent events, but she can speak of the past. She does not know, for example, since when she was last with her children, but she can well tell in detail an old family event ... She forgets from one moment to the other what she has just said or what she has just done ... During the spell, she seems to realize that something may be wrong with her and she says: "This is stupid to be like that", but after the episode she has forgotten everything'. Benon insisted on the fact that there was no associated neurological dysfunction, and that the patient had no hallucinations or delusional ideas, and he concluded: 'This state of amnesia lasts only four to five hours and the patient comes back to her normal state. She is a bit tired and has no memory

of what happened to her'. During a follow-up of another 3 years, no further episode occurred.

In 1956, Bender [8] described 12 elderly patients with sudden inability to form new memories for longer than a few seconds, accompanied by amnesia for recent events before the onset (retrograde amnesia). Frequently, patients asked the same questions repeatedly. Neurological examination was otherwise normal. Bender said attacks lasted a few hours and observed no recurrence. Independently, Guyotat and Courjon [9] briefly described clinical and epidemiological features of transient amnesic attacks ('ictus'), the latter based on their study of 16 patients. They took a particular interest in describing the epidemiological characteristics (age, context of occurrence, duration, cognitive disorders, medical history and medical examination). Their clinical details were succinct, describing 'transient loss of retrograde memory without diffuse loss of brain function'.

But physicians seem to have neglected or perhaps acquired amnesia for these early accounts, since the disorder was not generally part of the diagnostic armamentarium until the name *transient global amnesia* (TGA) was introduced by C. Miller Fisher and Raymond D. Adams (fig. 1) in 1958 [10] and amplified 6 years later [11]. It remains a satisfyingly distinctive clinical diagnosis bearing a good prognosis.

Their detailed, lucid papers described attacks suffered by 17 patients, usually in middle or old age, characterized by the abrupt onset of anterograde amnesia. With the exception of amnesia and the attendant anxiety, they re-

corded no neurological symptoms. They observed that attacks lasted a matter of minutes or hours and the ability to lay down new memories was gradually recovered, leaving only a dense amnesic gap for the duration of the episode and often for the preceding hours. Patients repeatedly asked agitated questions about their own, or their families' whereabouts, and what had been happening to them. The retrograde amnesia was initially for days, but diminished gradually during the subsequent few hours. Perception, cognition and personal identity were preserved, and there were no other neurological signs during or after the attacks. Two of their classic 1964 case descriptions justify repetition:

(1) 'A man of 67 developed his attack immediately after a prolonged interview with two journalists, who had noticed nothing amiss. He turned to his family after bidding the visitors goodbye, looked puzzled and asking "Who are they? What are they doing here?" He then asked how it happened that certain members of his family were present (they had come for a visit the previous day). He was obviously worried and appreciated he could not remember or collect his thoughts. For the next hour and a half he repeatedly asked similar questions ... There was no dysarthria or dysphasia. He tested his arms and legs periodically to assure himself they functioned normally. He did not remember that the journalists had made appointments a few weeks previously, nor did he recall special events of the day before or of the morning hours preceding the interview.'

'... After one and a half hours he lay down and slept for an hour, following which he appeared to have recovered fully. A retrograde amnesia remained permanently for the period of the interview and the hour prior to this. He also proved subsequently to remember very little of the day following the attack, although he appeared to his family to have recovered in three hours.'

(2) 'A physician aged 55 was examining a patient he had known for some twenty years when the telephone rang. He showed obvious difficulty in taking the message, became flushed, anxious and perplexed ... He told his patient he was having a lapse of memory, asked her who she was and why she was there. He asked over and over again what day it was and why his secretary was not available (he had given permission for a vacation ten days before). Ultimately his wife called at the office bringing his daughter and granddaughter who were scheduled to be taken to the airport. He had forgotten the arrangements and remained perplexed asking reiterative questions as they drove to the airport. There he met an old friend, greeted him by name and was proper in his responses ... then agreed to be seen by a physician. He named the doctor of his choice and recalled the number of the hospital where he could be contacted ...'

'At the hospital, some four hours after the onset, he was perplexed and restless ... But he recognized the physician immediately and reminded him of a case they had discussed some three or four years before. He vaguely recalled seeing his granddaughter first thing that morning, seemed to realise he had seen a woman

patient and remembered her name, and vaguely remembered seeing his daughter and granddaughter off on the plane ... but did not recall the journey to his office or to the hospital. He repeated six or seven times the circumstances of his sister's death ten months before. He gave the day and date correctly and knew where he was. The digit span was 6 forwards and 6 backwards. He could recall nothing of a name and address after ten minutes and had no recollection of being asked to remember them. Speech was normal and mathematical ability unimpaired. No abnormal neurological signs were found.'

'When re-examined a few hours later some of the memory of the day's events was returning in a rather patchy manner ... Subsequently he remained well, though with permanent amnesia for the two hours preceding the attack and for most of the events during the eight hours following it' [11].

Pathogenesis

Modern research has so far failed to yield a consistent pathogenesis. Fisher and Adams's original papers rejected psychiatric explanations and stated that epilepsy too was unlikely in view of the very infrequent recurrence of attacks and the absence of other epileptic features. Heathfield et al. [12] in 1973 described a series of 31 patients with attacks of sudden loss of memory. Two-thirds had TGA. They related the amnesia to bilateral temporal lobe or thalamic lesions, yet none were demonstrated. In some patients they claimed evidence of ischaemia.

TGA is distinct from the briefer *transient epileptic amnesia syndrome* characterised by multiple attacks on waking, epileptiform discharges on EEG, concurrent onset of other seizure types, and a response to anticonvulsants [13]. Certain common precipitating situations have emerged as possible clues, e.g. swimming in cold water, taking a hot shower, sexual intercourse and pain. In his overview, Caplan [14] also included the frequent occurrence of emotional stress, pain, angiography, and driving. He suggested a migrainous basis in some instances.

Many subsequent reports confirm that attacks are usually solitary with infrequent recurrences [10, 15], which makes both transient ischaemia and epilepsy improbable. A recurrence of between 2 and 15% cases has been reported, however [16]. In a case-controlled study [17], vascular risk factors carried no increased risk of TGA (n = 64). In contrast to TIA control subjects (n = 64), no TGA patient suffered stroke, myocardial infarction or TIA during the follow-up period. Migraine was more common in TGA patients than in control subjects.

It is known that the amnesia depends on lesions, demonstrable within 6 h of onset in hippocampal CA-1

Table 1. Transient global amnesia

Diagnostic criteria (after Hodges and Warlow)	
1	Attacks must be witnessed and information available from a capable observer who was present for most of the attack
2	There must be clear-cut anterograde amnesia during the attack
3	Clouding of consciousness and loss of personal identity must be absent, and the cognitive impairment 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 h
7	Patients with recent head injury or active epilepsy (that is, remaining on medication or one seizure in the past 2 years) are excluded

neurons of Sommer's sector of Ammon's horn [18]. Many precipitating factors relate to a Valsalva manoeuvre. Observers have therefore speculated that a higher rate of retrograde jugular venous flow during this manoeuvre in combination with jugular venous reflux could be a causal mechanism [19–21]. But this is not likely to be the common cause since the typical morphology, time course, and MR-signal characteristics of the lesions resemble neither venous congestion [22] nor infarction [23].

Diagnostic Criteria and Classification

Hodges and Warlow [23] reported an important series of 153 cases and provided a rational classification by assessing diagnostic criteria (table 1) for definite TGA. The main diagnostic groups (table 2) were based on the outcome of the 114 TGA patients that was excellent with the exception of a small subgroup with atypically brief or recurrent attacks, who later developed temporal lobe epilepsy. Computerised tomography in 95 patients was normal. By contrast, the 39 patients who did not meet the criteria for TGA fared worse with a high incidence of major vascular events.

These criteria were validated by Caplan [24] and Quinette et al. [25], who added their own hierarchical cluster analysis, which showed that episodes are mainly associ-

Table 2. Transient amnesia: major diagnostic groups [23]

1	Pure TGA – attacks fulfilling the strict criteria, and of >1 h in duration which do not require detailed investigation
2	Probable epileptic amnesia – attacks of <1 h or rapidly recurrent
3	Probable transient ischaemic amnesia – a minority of cases with additional focal neurological deficits during the attack

ated with emotional precipitants in women, and with physical precipitants in men. As in other controlled studies [26], no link was found with vascular risk factors. Recent comparisons of vascular risk factors and magnetic resonance imaging markers of small-vessel disease between TGA patients, with and without diffusion-weighted imaging (DWI) lesions and normal controls, show no higher rate of cerebrovascular abnormalities in either the total group of TGA patients or TGA DWI-positive patients [27, 28].

Other occasional contributory aetiological associations reported include migraine [29], mitral valve prolapse or myxomatous degeneration [30], and cortical spreading depression [31].

Using strict criteria, TGA remains a clinically distinct syndrome of uncertain aetiology, with a good prognosis, evincing evidence of neither ischaemic nor epileptic basis in most patients.

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