

# Chapter 1

## History of TGA



**Abstract** This chapter considers the history of TGA. This may be dated from the first use of the term “transient global amnesia” by Fisher and Adams in their publications of 1958 and 1964, but the characteristic clinical features had been described earlier than this under different appellations, in both the English (“episode of confusion with amnesia”) and French (“les ictus amnésiques”) literature. To date, the earliest probable case noted is that published by Benon in 1909. The reports retrospectively identified as suggestive of TGA had already described the associations with catheter angiography of the vertebral arteries and with migraine.

**Keywords** TGA · History

### 1.1 Beginnings: Fisher and Adams’ First Accounts of TGA

The syndrome of transient global amnesia (TGA) was first described as such by the neurologists C. Miller Fisher (1913–2012) and Raymond D. Adams (1911–2008) in 1958 [1] and 1964 [2].

In an interview with Raymond Adams, his biographer Robert Laurenco asked him whether he recalled any of his cases:

RA: Our first case was the wife of the dean of a medical school, who brought her to me. They had been at their summer place. It was their practice to get up in the morning to go for a swim in the cold north shore water. She set the breakfast table. When they returned from the swim, she had no memory of having set the table or having gone for the swim. Her memory for the day before was virtually nil. He called me and brought her to the Massachusetts General Hospital that afternoon and by then she was completely recovered. She did not remember the episode or the events of the preceding hours. That was our first case, several years before our publication ([3], p.107).

In their first published report, of 1958, Fisher and Adams described 12 cases with a relatively uniform and stereotyped clinical picture consisting of a profound but transient amnesic syndrome which they believed had not previously been described in the medical literature and which they called “transient global amnesia” [1]. Only

later did it become apparent that not all mnemonic function is impaired in transient global amnesia (see Chap. 2 and Sect. 4.1.1) and hence that “global” may be a misnomer. At the time of this publication, the deeper fractionation of mnemonic processes, much of it related to work on patient HM [4], had not yet impacted clinical practice.

Fisher and Adams’ subsequent paper, published in 1964, was an altogether more substantial affair, indeed comprising an entire supplement of the journal *Acta Neurologica Scandinavica*. This was an amplification of the earlier paper, now presenting 17 extensive case descriptions as well as discussions of the possible aetiology of TGA, of which their favoured explanation, albeit tentative, was “a special type of focal cerebral seizure” [2]. Caplan’s biography of Fisher adds no other details about these inaugural TGA papers [5].

TGA represents just one of Raymond Adams’ many major contributions in neurology, as listed in Laurenco’s biography [3]. However, whether this could be labelled as an “original” contribution is moot. Although new neurological diseases do sometimes emerge, it would seem a priori that TGA was not a new condition when Fisher and Adams described it, contrary to their statement that it “appeared to represent a distinct clinical syndrome which heretofore had not been delineated in the literature” [2]. Indeed, prior reports documenting cases similar to, and almost certainly representing examples of, what Fisher and Adams called TGA (and of which they were apparently unaware) may also be found in the literature, accounts which might be figuratively termed the “prehistory” of TGA.

## 1.2 “Prehistory” of TGA

In 1956, Morris Bender described 12 patients who experienced an “isolated episode of confusion with amnesia”, which was characterised by a “single brief period of defective memory and confusion with a complete retrograde amnesia”. Repetition of the same questions by the patient was a frequent clinical observation. Attacks were reported to last for a few hours but did not recur. Bender found it difficult to classify these events, but favoured a “transient circulatory disturbance of the brain” [6]. A later paper by the same author detailed the clinical features in 26 patients and emphasised the absence of recurrence [7]. Jaffe and Bender subsequently reported on 51 patients, with particular reference to electroencephalographic (EEG) findings [8] (Sect. 4.2.1).

Contemporaneously with Bender’s first (1956) account, though the authors were evidently unknown to one another, Guyotat and Courjon writing in the French literature described 16 patients with “l’ictus amnésique” [9], a syndrome of “transient loss of retrograde memory without diffuse loss of brain function” (translation of Pearce and Bogousslavsky; [10], p.189). In contrast to Bender’s report, six of their sixteen patients had more than one episode. The possibility of recurrence of amnesic attacks was subsequently also mentioned by Fisher and Adams [2].

Prior to Guyotat and Courjon [9], the term “ictus amnésique” had been in use, apparently originating with Jean Alfred Fournier in 1879 who reported patients with amnesic spells in the context of tabes and general paresis ([10], p.188). The term was also subsequently used to describe other cases which appeared in the French literature which are likely to have been examples of TGA ([11], p.3).

In 1954, Hauge described three cases of acute and transient memory loss following catheter angiography of the vertebral arteries. Some patients had visual disturbances which resembled migraine following the injection of contrast media [12]. Retrospectively, it seems likely that these cases probably correspond with what Fisher and Adams called TGA. Other cases of TGA associated with angiographic procedures have subsequently been described (see Sect. 3.1.5 and Table 3.6).

When John Hodges published his influential monograph on TGA in 1991, it was thought that Hauge’s account was probably the earliest description of TGA ([11], p.3). Hodges did note, however, that earlier cases of TGA might have been “immersed in the literature on psychogenic amnesia” ([11], p.4) and cited possible examples from the 1939 publication of Kanzer [13]. Hodges noted the concurrent decrease in reports of “hysterical amnesia” and increase in reports of TGA from the 1960s onwards. Gil et al. later challenged Hodges’ contention, finding a “clear differentiation between hysterical amnesia and amnesia triggered by an emotional shock” in the 1900 textbook of Paul Sollier (1861–1933), a student of Charcot, dating from the late nineteenth century [14]. Gil et al. also state that Sollier’s 1900 book portrayed “characteristic descriptions of transient global amnesia after a violent emotional shock” [14].

However, the earliest report which, at time of writing, seems to be acknowledged as likely to be a typical case of TGA, as noted by Berrios ([15], p.22), is that presented by R Benon in 1909, under the rubric of “ictus amnésique” [16]. Of the four patients reported, one (“*Observation II*”) documented a 66-year-old woman who had an episode lasting 4–5 h characterised by an amnesic state with repetitive questioning, a retrograde amnesia of at least 30 years, but without other neurological signs (see the translation in Pearce and Bogousslavsky’s paper [10] which commemorates the 100th anniversary of Benon’s publication). There was no recurrence during a 3-year period of follow-up. Benon drew a distinction between these cases of “organic” amnesia and those which occurred in the context of general paresis (syphilis) on which he had published previously [17].

Daniel ([18], p.2) states that the French clinician Théodule-Armand Ribot (1839–1916) “described transient amnesic states suggestive of TGA” in his 1881 volume on *Disorders of Memory*. This claim for the priority of Ribot has also been made by other authors writing on TGA [19, 20], but likewise eschewing quotation or precise page citation from Ribot’s book. Consulting the English translation of the book made by William Huntington Smith and published in New York in 1882 [21], Ribot certainly addresses the subject of temporary amnesia, as compared with periodic and progressive amnesia. The most suggestive account is simply a citation ([21], pp. 123–7) of a case previously presented in 1835 by “Kömpfen” [22] which followed a head injury, an exclusion criterion for TGA (see Sect. 2.2.2). Hence, I

find no compelling account of TGA in Ribot [23], contrary to previous claims to that effect [18–20].

Berrios claims descriptions of transient global amnesia in the works of Jules Falret (1865) ([15], p.18) and Forbes Winslow (1861) ([15], p.16, 22). In the latter’s *On obscure diseases of the brain and disorders of the mind*, in the chapter (XIV) devoted to “Acute disorders of the memory” [24], I find no account suggestive of TGA (Berrios [15], p.22, quotes from this chapter, but his page citation, p.372, is incorrect; the quote is from p.342). Trimble states that “In the nineteenth century ... examples of what we now refer to as transient global amnesia were reported” but gives no references ([25], p.176–7).

This is not to say, of course, that TGA did not occur before the twentieth century: absence of evidence is not equivalent to evidence of absence. The ontological challenge to the persistence of disease over historical time, suggesting as it does in this situation that mechanisms of mnemonic hippocampal function have changed, is simply not credible [23].

### 1.3 After Fisher and Adams

It is acknowledged that TGA achieved general recognition as a distinct neurological condition after the term was introduced by Fisher and Adams ([10], p. 188), but this recognition was not achieved immediately.

Poser and Ziegler in 1960 reported cases of temporary amnesia which they ascribed to “cerebrovascular insufficiency” [26]. Despite the brevity of their clinical descriptions, Hodges ([11], p. 3) was “almost certain” that these represented cases of TGA. Amongst these were patients with an existing diagnosis of migraine (see Sect. 3.4.1 and Sect. 7.9), probably the first report of the concurrence of these conditions. (Incidentally, Poser did later adopt the term “transient global amnesia”, although the patient reported under this nomenclature had memory problems for several days [27]. Nevertheless, Caplan included this case in his 1985 literature review [28].) The possible link between TGA and migraine was later emphasised by Caplan et al. in 1981 [29].

Evans in 1966 reported three patients with transient loss of memory, of whom two had attacks suggestive of TGA in the context of a history of migraine. The third patient had a history of temporal lobe epilepsy and the reported attack lasted more than 48 hours so is unlikely to have been TGA [30]. Another early report was that of Bolwig, in 1968, who presented four cases and favoured “transient ischemia in the hippocampal region” as the aetiological explanation [31].

Recurrence of TGA attacks, although previously mentioned in the literature, for example, by Guyotat and Courjon [9] and by Fisher and Adams [2], was made explicit by Lou [32] (Sect. 6.2), although at least one patient in this series almost certainly had an ischaemic aetiology (see Sect. 3.1).

Just as early accounts of patients with what would now be called TGA may be found in the literature on psychogenic amnesia ([11], p.4), it is also possible that

some cases labelled as having Korsakoff's syndrome might in fact be examples of TGA. From 1887 onwards, Sergei Korsakoff described cases of dense anterograde amnesia in alcoholic patients, although earlier accounts had appeared, for example, that of Robert Lawson in 1878 [33, 34]. Reports of "transient Korsakoff's syndrome" but with clinical details suggestive of TGA may be found in the literature, predating the widespread awareness of the TGA construct [35, 36].

An example of the increased recognition of the condition, and the ascendancy of Fisher and Adams' proposed TGA nomenclature, was provided by the consecutive editions of Whitty and Zangwill's textbook devoted to the subject of amnesia. In the first edition of 1966, Whitty and Lishman, in their chapter entitled "Amnesia in cerebral disease", mentioned only Fisher and Adams' original 1958 paper, under the subheading of "Transient vascular occlusions" ([37], p.51). However, by the time of the second edition of the book, published in 1977, a whole chapter was devoted exclusively to TGA, including a case personally observed by Whitty [38].

During this period, cases of TGA also began to be reported in languages other than English (e.g. [39–42]). Perhaps the first monograph on the subject was published by Gerhard Frank in 1981, reporting 27 personally observed cases [43].

An issue that emerged with these early reports, particularly noted in retrospect, related to exactly what qualified for inclusion as "TGA" as conceptualised by Fisher and Adams, and what did not, what was distinct and hence possibly a different disorder or disorders. In other words, the term "TGA" might have been applied somewhat loosely in these early accounts. By the time of Caplan's 1985 review [28], he was able to present data relating to 485 TGA patients reported in the literature and suggested some boundaries for inclusion and exclusion (see Sect. 2.2.1). This trend inevitably culminated in the formulation of diagnostic criteria for TGA, proposed by Hodges and Warlow in 1990 [44], based on their clinico-epidemiological study of TGA (Sect. 2.2.2). These proposals were somewhat more stringent than Caplan's proposed inclusion/exclusion boundaries.

These developments coincided with the advent of the widespread availability of neuroimaging techniques, initially computed tomography (CT), in neurological practice. Although CT contributed rather little to the understanding of TGA (Sect. 5.1.1), it was the harbinger of the rapid development in neuroimaging techniques, particularly magnetic resonance imaging, which has contributed to understanding of the condition and which will be discussed later in greater detail (Sect. 5.1.2).

The volume devoted largely to TGA which was edited by Markowitsch in 1990 [45] and the monograph by Hodges published in 1991 [11], the latter based on the seminal publications of the Oxford TGA study (e.g. [44, 46–48]), indicated that TGA had become a widely recognised condition and a legitimate subject for ongoing investigations. Since then, Hodges and Warlow's diagnostic criteria [44] have been increasingly applied to TGA case definition. Retrospectively, there may be caveats regarding cases labelled as "TGA" which were described prior to the adoption of these criteria (e.g. see specific cases in the series reported by Evans [30] and Lou [32], as mentioned above).

Notable contributions in more recent years have been the extensive review by Quinette et al. in 2006 of 142 personally observed cases and 1353 cases found in the

literature [49]. Daniel (2012) reviewed several hundred publications related to TGA in his book [18], to my knowledge the most recent book length publication devoted exclusively to TGA prior to the first edition of this book published in 2017. Recourse to a PubMed search using the title words “transient global amnesia” returned 668 hits to the end of 2016 (accessed 02/01/2017) and 830 hits to the end of 2021 (accessed 31/12/21). This is certainly an underestimate of all publications related to TGA, since papers describing cases do not necessarily have this term in the title (Sect. 1.4). Of these articles, major series and systematic studies have until recent times been relatively few (e.g. [50, 51]), most publications reporting only single or a few cases.

## 1.4 A Note on Nomenclature

As well as “ictus amnésiques” [9], a number of other terms have been used on occasion to describe what appear to be typical TGA episodes. These include:

- episodic global amnesia (by Adams, cited in Laurenco [3], p.145). This may owe something to the terminology of “episode(s) of confusion with amnesia” used by Bender [6, 7] and Jaffe and Bender [8].
- amnesic episodes (e.g. [39, 52], perhaps related to the appellation in German (“Amnestische Episoden”, e.g. [43]).
- transitory global amnesia (e.g. [39, 53–55], perhaps related to the appellations in French (“amnesia global transitoire”, e.g. [56]) and Spanish (“amnesia global transitoria” or AGT, e.g. [57]).
- paroxysmal memory loss [58].

In this text, the familiar “transient global amnesia” terminology coined by Fisher and Adams [1, 2] will be used throughout.

## 1.5 A Note on Methodology

Because TGA is a relatively rare condition, the majority of publications have been single case reports or small case series. This anecdotal, opportunistic and unsystematic literature constitutes the lowest rung on the ladder of clinical evidence (e.g. [59, 60]) and has been previously criticised [48]. Although this evidence is not ignored here, the findings may be less robust than those emerging from case–control studies, population cohort studies (e.g. [50, 51]), systematic reviews (e.g. [61]) and meta-analyses (e.g. [62, 63]). These studies are far less common, but will be emphasised in this text.

## 1.6 Summary and Recommendations

Although first described as such in the late 1950s and early 1960s, the syndrome of transient global amnesia has probably been reported in the medical literature under other nomenclature since the beginning of the twentieth century. It would seem likely that the human brain has always been vulnerable to this syndrome.

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