Chapter 2
Clinical Features, Diagnostic Criteria and Possible Variants of TGA

Abstract This chapter begins with a consideration of the typical clinical features of an attack of TGA. Although relatively stereotyped, nevertheless different authors have used the "TGA" terminology to describe different events characterised by transient amnesia. Following the description of possible boundaries for what might be included or excluded from the TGA label, diagnostic criteria were developed by Hodges and Warlow in 1990 for definite or pure TGA. Whether variants of TGA exist is still uncertain; if so, they are much rarer, gauged by the frequency of published reports.

Keywords TGA · Clinical features · Diagnostic criteria · Variants

2.1 Clinical Features of TGA

2.1.1 TGA Archetype

The clinical features of transient global amnesia (TGA) are best illustrated by citing a typical case history, and it is generally acknowledged that in this regard the descriptions by Fisher and Adams [1, 2] are archetypal:

> Case 1. Man, aged 67
>
> The patient, a brilliant professional man, suffered his attack immediately after he had spent about one and a half hours being interviewed by two journalists at his home. The subject of the discussion was the history of an organization some 33 years ago and the details provided proved accurate and during the interview the journalists noted no abnormality in the patient whatsoever. As the visitors left, the patient bade them goodby [sic] and added a few appropriately humorous words. The members of his family were standing in the hallway 15 to 20 feet away and the patient was in full view and earshot while the visitors were leaving. The patient turned and walked towards his family, not saying anything but looking puzzled. He then asked, "Who are they?" (the visitors), "What are they doing here?" [.] Then he asked how it happened that certain members of his family were present (they had come for a visit the previous day). Then he asked if the family noticed anything wrong with him. The patient was quite worried and clearly appreciated that he could not

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> remember and could not collect his thoughts (one of the family members present was a physician and provided most of the details of the events). For the next hour or hour and a half the patient repeatedly asked somewhat similar questions: "Who was that? What were they doing here? What are you doing here? Do you see anything wrong with me?"[.] As each question was answered he would go on to another, so that the repetition was not wholly automatic. But if he remained quiet for a minute or so he would again begin a repetition of the same questions. There was no dysarthria or dysphasia ([2], p.9).

The typical features of TGA, made evident not only by the accounts of Fisher and Adams by also by earlier authors [3, 4], consist of an abrupt attack of impaired anterograde memory, affecting both verbal and non-verbal components, often manifest as repeated, iterative, circular, questioning, but without clouding of consciousness or focal neurological signs. The questions are usually of a self-orienting nature (e.g. Where am I? What is happening?). Also evident from clinical observation is concurrent retrograde amnesia of variable duration, whereas personal identification and other aspects of memory (working memory, semantic memory, implicit memory) appear to be intact (see Sect. 4.1 for more detailed discussion of the neuropsychological features of TGA).

Patient behaviour during an attack is also characteristic. The insight that something is wrong is not uncommon [5], with the patient manifesting a sense of bewilderment or perplexity to onlookers, sometimes amounting to agitation or distress, although sometimes the affect is rather flattened.

2.1.2 Accompanying Neurological and Psychological Symptoms

Neurological symptoms during an attack may include a complaint of headache (sometimes consistent with migraine), nausea and vomiting, and sometimes dizziness and sleepiness. For example, in a series of 203 episodes of TGA reported by Ahn et al. [6], the most common associated symptoms were headache (14.8%), dizziness (6.4%) and nausea/vomiting (5.4%). A wide variety of other symptoms has also been described on occasion, including chills/flushes, fear of dying (angor animi), paraesthesia, cold extremities, trembling, sweating, winding, and palpitations [7], suggestive of activation of the autonomic nervous system.

Focal neurological signs described in some of the early reports of "TGA" (e.g. dysarthria, dysphasia, visual field defects, hemiparesis) would now be considered to exclude the diagnosis of TGA (see Sect. 2.2). Subtle impairments of smooth pursuit eye movements have been documented using oculographic techniques within a median of 1 day of TGA episodes [8], but whether these are evident to unaided clinical neurological examination during attacks remains to be studied.

Acute changes in mood and anxiety levels have also been documented during TGA, the most common emotional symptoms being anxiety and depression. Inzitari et al. [9] noted symptoms during TGA were similar to those exhibited during a panic attack. A number of studies have subsequently documented symptoms of

anxiety and depression during attacks by administering brief rating scales (respectively, the first part of the State-Trait Anxiety Inventory, and the Adjective Mood Scale or Befindlichkeits-Skala) [5, 10, 11]. Psychological factors may also be predisposing factors for TGA (Sect. 7.10).

2.1.3 Chronobiology: Diurnal Time of Onset

TGA attacks may occur at any time of the day. Diurnal variation in the time of onset, with attack onset most often in the morning or at midday, was reported in both a literature review ($n = 17$) and in a prospective patient cohort reported by Quinette et al. [7]. Attacks apparent on waking from sleep were not found, and indeed this may be an important differential diagnostic point, raising the possibility of an epileptic disorder (see Sect. 3.2 and Sect. 7.12). In the series of Ahn et al. [6], TGA episodes ($n = 203$) usually occurred in the morning (0600–1200 h: 36.5%) or in the afternoon (1200–1800 h: 38.9%). Oehler et al. reported one case "occurring exceptionally while sleeping" [12]. Hoyer et al., analysing data from two large TGA cohorts (n = 404 and 261, respectively), reported bimodal peaks of TGA occurrence at mid-morning and late afternoon in both cohorts, suggesting a robust circadian rhythm in TGA occurrence independent of patient gender and age [13].

Time of TGA onset by day of the week, month or season of the year is considered amongst predisposing factors of TGA (Sect. 7.2).

2.1.4 Attack Duration

Episodes of TGA are of brief duration, usually lasting between 1 and10 h. The mean duration in two large series was 4.2 h [14] and 5.6 h [7]. In more recent series, Agosti et al. [15] reported the duration to be 4.3 ± 3.0 h, and Ahn et al. [6] reported a median duration of 5 h. Episodes lasting less than 1 h were previously considered rare (for example, Quinette et al. recorded only 3 such cases in 142 observed patients [7]) and potentially more suggestive of transient epileptic amnesia (Sect. 3.2). However, "short-duration TGA" (i.e. lasting <1 h) was noted to be quite common (8.8–32.0%) in three large independent cohort studies, with clinical features and long-term prognosis no different from longer episodes of TGA [16].

Because of the brevity of TGA, it is possible that many, if not most, attacks are not brought to medical attention. This has implications for attempts to quantitate disease incidence (Sect. 7.1). Extensive investigation post-event contributes relatively little information, but studies of neuropsychology, neurophysiology and neuroimaging during an attack have contributed to the understanding of TGA (see Chaps. 4 and 5).

2.1.5 Prognosis, Recurrence

The prognosis of TGA is generally excellent (see Chap. 6). There is usually an apparently complete recovery after the acute attack, aside from the absence of recollection for the amnesic period.

TGA attacks are usually solitary, but some patients experience recurrence (Sect. 6.2). Quoted recurrence rates may depend, of course, on the extent and completeness of patient follow-up, but the figure is probably around 5% [7]. A history of recurrent events may broaden the differential diagnosis (see Chap. 3), particularly the consideration of transient epileptic amnesia (Sect. 3.2; Case Study 2.1).

Case Study 2.1: Recurrent Attacks, Was it TGA?
A 60-year-old woman had experienced four episodes of transient amnesia over a 4-year period, all similar in form and all witnessed by her husband. All were associated with exercise (canoeing, cycling twice and swimming in cold water) and were characterised by repetitive questioning lasting between about 2 and 7 h with apparent complete recovery. Because of their recurrent nature, a provisional diagnosis of transient epileptic amnesia (TEA) had been made (MR brain imaging and EEG were both normal) and she was advised to stop driving and start taking an antiepileptic medication. She was not willing to contemplate medication so a second opinion was sought. On the basis of the witness account, the episodes were thought to be more typical of TGA than TEA, despite their recurrence. There were no episodes of amnesia on waking from sleep. On the Mini-Mental State Examination, she scored 30/30 and on the Montreal Cognitive Assessment 29/30. Over a 6-year period of follow-up, no further amnesic events occurred without antiepileptic drug treatment.

2.2 Diagnostic Criteria of TGA

2.2.1 Essential Features and Inclusion/Exclusion Boundaries

Although the clinical features of TGA are relatively stereotyped (Sect. 2.1), nevertheless episodes of transient amnesia may sometimes present diagnostic difficulties (see Chap. 3 for a consideration of the differential diagnosis). It should be remembered that not every paper purporting to describe TGA is necessarily describing TGA!

To investigate a specific condition or disorder, in order to try to understand factors such as its epidemiology (see Chaps. 7 and 8) and pathogenesis (Chap. 9), it is obviously important that only examples of that disorder are examined and no other disorders which might seem clinically similar but which may have different causes. Hence the drive to codify clinical diagnosis by means of developing consensus diagnostic criteria, a project which has encompassed many neurological disorders (e.g. [17]). A similar rationale has been applied in TGA. As will be shown (see Chap. 3),

TGA has a potentially broad differential diagnosis, with a number of possible mimics or phenocopies.

Kane [18] recognised the need for diagnostic precision for TGA and listed ten "essential features" based on an experience of six patients followed up for 2.5 years, specifically:

- no premonitory transient ischaemic attack (TIA);
- risk factors for stroke often absent;
- isolated severe loss of recent memory (<24 h);
- complete clearing once episode is passed;
- patient aware/anxious about deficit;
- sparing of motor, visual and speech systems;
- no change in personality;
- persistence of unimpaired technical skills;
- rarely evolves to more characteristic stroke;
- rarely recurs ([18], p.726).

Perhaps implicit in these features was Kane's assumption that the pathology of TGA was vascular. Whilst these "essential features" have face validity, the definition of diagnostic criteria generally requires a more precise methodology and the examination of many more cases.

Caplan ([19], p.206–7) proposed "boundaries ... of what can be included within the diagnostic category of transient global amnesia, and what should properly be excluded", noting that hitherto such boundaries had been "fuzzy". The strict categorical definition of TGA which emerged was based on a large personal case series and literature review, with four points emerging as central to diagnosis, viz.:

1. "Information about the beginning of the attack should be available from a capable observer who witnessed the onset".

   This stipulation sought to exclude amnesic episodes secondary to trauma or epileptic seizure since these aetiologies could not be easily excluded if the onset of the event was unwitnessed.
2. "The patient should have been examined during the attack to be certain that other neurological symptoms and signs did not accompany the amnesia".

   The ideal of neurologist as examiner was noted to be impractical, since relatively few patients reach medical facilities within the time frame of an attack, and even if they do come to medical attention, clinicians with the skills and knowledge to undertake appropriate examination may not be immediately available. Caplan accepted that information from a "careful, concerned witness" who interacted with the patient would be acceptable, but patient self-report or information from casual companions would not.
3. "There should be no important accompanying neurological signs".
4. "The memory loss should be transient".

The extent of transience was not defined, and in his review, Caplan accepted cases of amnesia ranging in reported duration from 15 min to 7 days (cf. Sect. 2.1.4).

These "boundaries" defined by Caplan are still cited as "Diagnostic criteria for Transient Global Amnesia" in a textbook devoted to diagnostic criteria in neurology published in 2006 ([17], p.52–3) and certainly influenced subsequent thinking on the nature of TGA.

Of note, neither Kane nor Caplan appears to have been explicit about the exclusion of clouding or loss of consciousness in TGA, although this might be implicit in the formulation of "patient aware" [18] and "no … accompanying neurological signs" [19].

2.2.2 Hodges and Warlow's 1990 Diagnostic Criteria

Based upon their extensive clinical experience of TGA cases and a review of the literature, Hodges and Warlow [14] and Hodges ([20], p.6–12) developed seven diagnostic criteria for definite or pure TGA (see Table 2.1). These are explicit, inter alia, about level of consciousness and absence of aphasia.

(An eighth criterion was added by Nishiyama et al. [21], specifically for the diagnosis of transient partial verbal amnesia; see Sect. 2.3.2.)

The Hodges and Warlow 1990 criteria have become widely accepted and used (although, to my knowledge, have never been independently verified), indeed are now sometimes referred to as the "classical criteria" ([22], p.2270). Although the pre-1990 literature on TGA, predating the Hodges and Warlow criteria, will not be ignored in this book, post-1990 published material in which these diagnostic criteria have been applied will generally be given greater weight, as excluding other disorders which enter the differential diagnosis of TGA (see Chap. 3). Retrospectively, there may be caveats about some cases reported as "TGA" prior to the adoption of these criteria; re-analysis of the described clinical features may put some reports out with these diagnostic criteria. The "pure TGA" terminology had been used before

Table 2.1 Diagnostic criteria for definite TGA based on Hodges and Warlow 1990 [14] and Hodges 1991 ([20], p.12)

(a)	Attacks must be witnessed and information available from a capable observer who was present for most of the attack.
(b)	There must be clear-cut anterograde amnesia during the attack.
(c)	Clouding of consciousness and loss of personal identity must be absent, and the cognitive impairment limited to amnesia (i.e. no aphasia, apraxia).
(d)	There should be no accompanying focal neurological symptoms during the attack and no significant neurological signs afterwards.
(e)	Epileptic features must be absent.
(f)	Attacks must resolve within 24 h.
(g)	Patients with recent head injury or active epilepsy (that is, remaining on medication or one seizure in the past two years) are excluded.

this landmark paper (e.g. [23, 24]) and has also been used on occasion since, specifically with respect to what might be termed "symptomatic" cases (e.g. [25–27]).

A reliable witness account of the attack is the first criterion; hence unwitnessed amnesic attacks cannot be diagnosed as TGA (e.g. Case Study 2.2). In their study of 153 cases of acute amnesia, Hodges and Warlow [14] excluded 39 cases (25%), the principal reason being unwitnessed attack ($n = 14$), followed by very limited details (8). In the author's personal series of acute amnesic patients seen over the period 2002–2021, 23 of 73 cases (31.5%) were excluded as not conforming to the Hodges and Warlow criteria (see also Fig. 7.3; note that these figures do not include cases confidently diagnosed as transient epileptic amnesia; Sect. 3.2).

Case Study 2.2: Unwitnessed Attack, Was it TGA?
A 79-year-old man was on a long walking expedition when he had an episode of impaired memory. No direct witness account was available, but apparently he had wanted to stop, had sat down and was asking repetitive questions for about half an hour. His wife attended the clinic with him but had not been with her husband on the walk, and by the time she had seen him several hours after the incident, he was apparently back to normal. A provisional diagnosis of TGA was made. (see Case Study 7.2 for further details.)

One implication emerging from the application of the Hodges and Warlow criteria is that diagnostic labels such as "TGA-like" syndrome (e.g. [28–33]) or "TGA-plus" syndrome (e.g. [34]) are misnomers. By applying the criteria, episodes are defined as "definite or pure TGA" or as "not TGA". To avoid potential confusion, a terminology that avoided the "TGA" label might be desirable to describe events not fulfilling TGA criteria: perhaps "transient amnesia of uncertain origin" or "transient amnesia not fulfilling criteria for TGA" would be preferable to "TGA-like" or "TGA-plus" syndromes.

The Hodges and Warlow criteria are entirely based on clinical history and examination findings, without recourse to any findings from investigations (see Chaps. 4 and 5). A corollary is that if the diagnosis of TGA is based on the use of these criteria then TGA remains a clinical diagnosis, with no current supplementary biomarkers (e.g. to help distinguish TGA from TEA). Whether the Hodges and Warlow criteria should be expanded in the light of more recent findings remains to be decided. For example, the possibility of modifying the criteria in the light of the neuroimaging changes observed in TGA, particularly diffusion-weighted magnetic resonance imaging sequences (Sect. 5.1.2), has been suggested (e.g. [35], p.109; [36]). The acute psychological changes (Sect. 2.1.2) are also overlooked by the Hodges and Warlow criteria, although "patient aware/anxious about deficit" was included amongst the ten "essential features" listed by Kane [18].

2.2.3 TGA Subtypes?

A question remaining unanswered by the Hodges and Warlow criteria is whether there might be subtypes of TGA, related to factors such as whether cases are idiopathic or symptomatic and whether episodes are single or recurrent.

A distinction may be drawn between a primary or idiopathic form of TGA and a secondary or symptomatic form of TGA, for example, TGA occurring secondary to a clear precipitating event, such as cerebral angiography (Sect. 3.1.6) or exposure to cold water (Sect. 1.1 and Sect. 8.3), or associated with a cerebral lesion such as an ischaemic stroke (Sect. 3.1.2) or tumour (Sect. 7.12). There is no evidence to suggest that these are different clinico-pathological entities, although whether the secondary or symptomatic forms shed any light on the pathogenesis of the primary or idiopathic form(s) remains to be established. The label of "spontaneous TGA" or "spontaneously occurring TGA" for those episodes occurring without an obvious precipitating factor is also questionable, as such factors may be identified with deeper analysis (Chap. 8).

At the time of Hodges and Warlow's studies, the only readily available neurological investigations included cerebrospinal fluid analysis, electroencephalography and brain imaging with computed tomography (CT) or single-photon emission computed tomography (SPECT). The greater spatial resolution of magnetic resonance (MR) brain imaging was not then easily accessed, let alone functional MR studies.

Agosti et al. [37] considered the validity of the Hodges and Warlow criteria in the light of a study of 130 consecutive patients with a first episode of TGA who underwent MR brain imaging, of whom 13 (10%) were found to have a structural brain lesion (leptomeningeal cysts 9; falx meningioma 2; cerebellar haemangioma 1; white matter hyperintensities in parieto-temporal region 1). In the light of these neuroradiological findings, they proposed that patients be classified into two subgroups, defined as primary TGA (classical attacks with normal neuroimaging: = TGA-p) and TGA patients with brain lesions (= TGA-b). No clinical or demographic differences were found between the two groups. This was perhaps not a surprising finding, since the brain lesions discovered on imaging were unlikely to be contributors to pathogenesis.

In a subsequent study, Agosti et al. [15] divided TGA patients ($n = 243$) according to whether or not they had evidence for internal jugular vein valve incompetence (IJVVI), a factor that was considered possibly relevant to TGA pathogenesis (Sect. 4.3.3.2 and Sect. 9.2.2). TGA patients with IJVVI showed a higher frequency of precipitating factors (Chap. 8) but had fewer vascular comorbidities (Sect. 7.11) than TGA patients without IJVVI, suggesting to these authors that there may be different mechanisms underpinning episodes of TGA.

Hence, it currently remains uncertain whether there is any merit in distinguishing TGA as either primary or secondary for the understanding of disease aetiology, although patient management in the latter category might be different. Investigations may disclose a symptomatic cause (e.g. the very rare instances of underlying

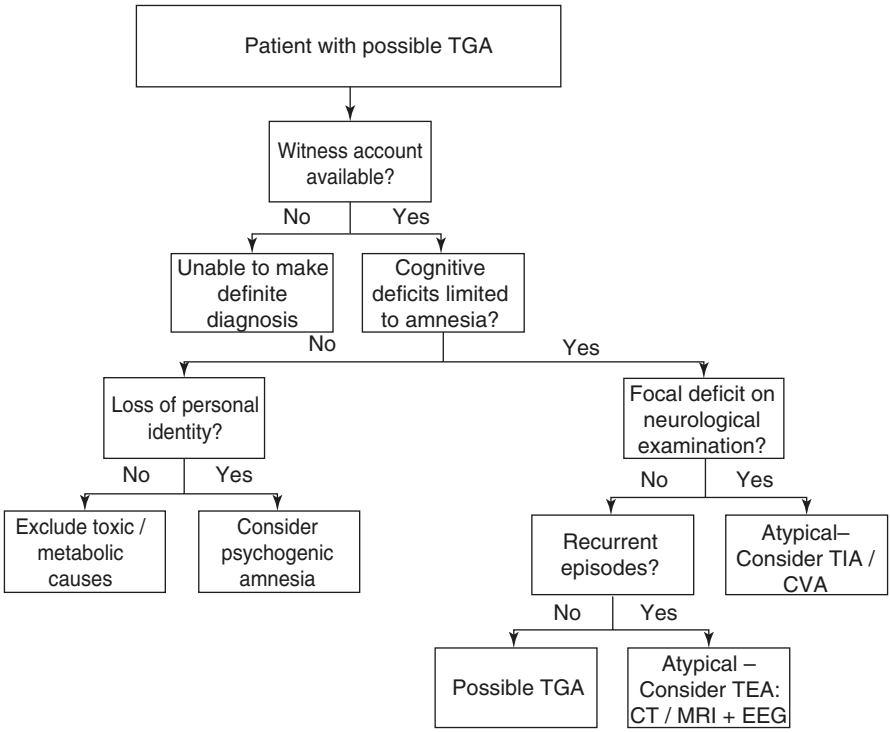

Fig. 2.1 Flow chart illustrating the possible decision-making process in the management of suspected TGA (adapted from [40])

multiple sclerosis [38, 39]) which may have distinct implications for patient treatment and management.

Another issue concerning TGA classification relates to recurrence. Although the annual recurrence rate is low (Sect. 6.2.1), some individuals do suffer recurrent TGA (e.g. Case Study 2.1), and there is some tentative evidence to suggest that these patients may differ in some respects from those with single episodes (Sect. 6.2.2), which might potentially impact on prognosis.

A flow chart illustrating the possible decision-making process in the management of suspected TGA is shown in Fig. 2.1.

2.3 Possible Variant Forms of TGA

TGA subgroups have been suggested on the basis of different precipitating events (see Chap. 8), namely physical exertion in men and emotional upset in women [7]. However, the possibility of distinct TGA phenotypic variants within the broad conceptualisation of TGA as an acute amnesic syndrome is considered here.

Alzheimer's disease (AD), perhaps the most common cause of amnesia encountered in clinical practice, typically presents as a syndrome of episodic amnesia, reflecting neuronal disconnection of hippocampal structures from the cortex by the plaque and tangle pathology typical of AD. However, other variants of AD are well recognised, resulting from pathological change predominating elsewhere in the brain [41]. Hence, logopenic progressive aphasia, visual variant/posterior cortical atrophy and even frontal variants are acknowledged in modern diagnostic criteria for AD [42], and a phenotype resembling corticobasal degeneration has also been described on occasion (e.g. [43]). Might there also be variant forms of TGA?

Memory may be conceptualised neuropsychologically as a non-uniform, distributed cognitive function within which subdivisions in function may be differentiated (Fig. 2.2), which involve various neuroanatomical substrates [44]. Current taxonomies of memory propose a distinction between declarative memory, also known as explicit or conscious memory, and non-declarative memory, also known as implicit, procedural and unconscious memory. Conceptual objections to this distinction are to be noted ([45], p.155–8), but nevertheless this taxonomy is presented here as the one most, if not all, cognitive neurologists current work with. "Working memory" or immediate memory is better conceptualised as an aspect of attentional mechanisms.

Declarative or explicit memories are intentional or conscious recollections of previous experience. Declarative memory may be further subdivided into episodic and semantic components. Episodic memories are specific personal events, sometimes known as autobiographical memories, which are time and place (context) specific. These may be either verbal or non-verbal (visual), with localising value to dominant and non-dominant hemispheres, respectively. Semantic memories, in contrast, are facts, a database of culturally-approved knowledge independent of any specific context. A distinction may also be drawn between anterograde memory, the laying down of new memories, and retrograde memory, the store of previously encoded material. Could any of these memory subsystems or subassemblies, whose anatomical substrates are thought to lie within the circuit of limbic structures proposed by Papez [46], be liable to the same pathological process(es) responsible for TGA, thus producing different variants of TGA?

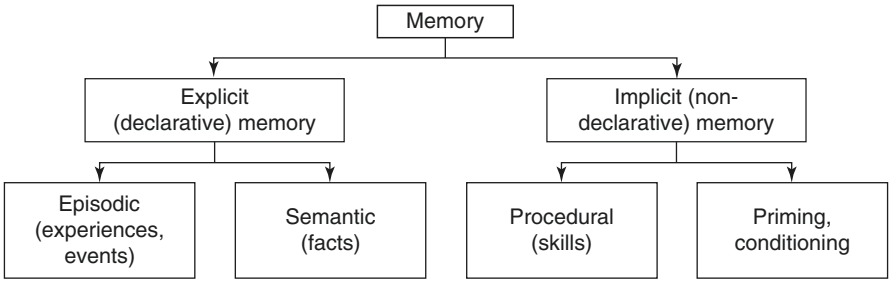

Fig. 2.2 Simplified taxonomy of memory processes (adapted from [40])

A number of potential variants of TGA have been described in the literature: transient topographical amnesia, transient partial verbal amnesia, transient semantic amnesia and transient procedural amnesia. The first two of these suggest the possible fractionation of TGA into non-verbal and verbal variants. These might legitimately be considered as forms of "selective amnesia", a specification that has been used by some authors (e.g. [47–49]). However, this terminology is probably best avoided since "selective amnesia" has passed into the vernacular to denote apparent amnesia about a particular event or events that prove convenient for the person who (apparently) cannot remember.

For clinical completeness, reports of these potential variants are included here. However, such variants, if that is indeed what they are, are either rare or extremely rare and will not be considered hereafter, since they are unlikely either to be encountered clinically or to shed any additional light on the pathogenesis of TGA.

2.3.1 Transient Topographical Amnesia (TTA)

The most frequently reported variant of the possible variants of TGA is transient topographical amnesia (TTA). A number of reports of TTA have appeared, initially single cases, all of them from Italian centres [50–53], and thereafter small series ([54], $n = 8$; [55], $n = 10$), as well as cases from countries other than Italy [54, 56–58]. TTA may be identical to, or overlap with, cases labelled as "transient topographical disorientation" [59].

Stracciari [53] described the case of a woman who experienced three isolated episodes of loss of topographical memory and postulated that this was a rare form of selective non-verbal transient amnesia. Episodes were characterised by the sudden onset of failure to find the way despite spared recognition of the environment, such as landmarks or objects, postulated to reflect transient right (non-dominant) occipitotemporal region dysfunction. Impaired recognition of landmarks may be a feature of some cases (e.g. [57, 59]).

Considering the published series of TTA, these show a female predominance (all ten cases of Stracciari et al. [55]; 6 of 8 cases of Naranjo-Fernandez et al. [54]). Episodes are brief, ranging from 5 to 40 min [55] with the average duration of 24.5 min [54], hence much shorter than in typical TGA episodes (see Sect. 2.1.4). Indeed, some attacks which have been labelled as TTA apparently last only a few seconds [57]. Patient age at time of attack ranged from 51 to 84 years in the series of Stracciari et al. [55], with an average age of 69.13 ± 8.79 years in the series of Naranjo-Fernandez et al. [54]. Recurrence of up to three episodes was noted in 3 out of 10 patients [55], with a mean number of episodes of 1.75, range 1–3 [54], although some patients have many episodes over many years [57].

That TTA may be related to TGA is suggested not only on the basis of the shared brevity of the attacks in the absence of other neurological features, but also the observation of a patient with two episodes of TGA one of which ended in a typical TTA attack [60]. Attacks may occur in patients with a history of migraine ([50], and

[55], case 9), during a migraine attack [58], and may apparently be triggered by swimming [60].

Neuropsychological evaluation in 12 patients 6–12 months after recovery from TTA showed normal performance in all tasks but lower performance compared to controls in a test of spatial (geographical) orientation, but it was not known whether this deficit predated the TTA events [61]. One patient in the series of Naranjo-Fernandez et al. [54] developed dementia 6 years after the acute episode.

No diagnostic criteria have been formulated for TTA to my knowledge. One may question whether a patient with frequent attacks labelled as TTA but associated with tonic rigidity of the left limbs and imaging findings of an angioma at the right cingulate cortex [62] should qualify. Likewise, two patients with transient topographical disorientation accompanied by visual field defects and other cognitive dysfunctions [63] are doubtful as examples of TTA if this phenomenon is pathogenetically related to TGA.

2.3.2 Transient Partial Verbal Amnesia (TPVA)

A number of case reports of patients with transient amnesia characterised by a selective impairment of verbal memory with sparing of non-verbal memory, unlike typical TGA in which both are affected, have appeared [64–67], sometimes labelled transient partial verbal amnesia (TPVA) [21].

Damasio et al. [65] described a patient with relative preservation of orientation to place and familiarity with previously known persons in the context of transient impairment of verbal memory, who subsequently retained partial memory of the event. Matias-Guiu and Codina [66] reported four patients with transient amnesia affecting verbal material, but little clinical detail was provided. Okada et al. [67] reported two patients with some degree of visual memory preservation during an attack of "TGA", with quicker recovery of non-verbal memory.

The fullest account is that of Nishiyama et al. [21]. They reported a 58-year-old man examined during an attack. When sent to the hospital because of his memory problems, manifested by repeated questioning, he was able to remember the faces of newly encountered doctors but not their names. Administered the Wechsler Memory Scale-Revised during the attack, which lasted for about 10 h, there was a discrepancy between verbal (65) and visual (113) memory indices. The delayed visual recall was normal during the attack but delayed verbal memory was severely impaired; the latter normalised by the time of re-testing 2 weeks later. The authors suggested eight points as criteria for TPVA: these were essentially the seven Hodges and Warlow 1990 criteria [14] (Table 2.1) in addition to the requirement that amnesia must be limited to verbal materials.

Yildiz et al. [68] reported a 63-year-old vasculopath who underwent coronary and lower extremity angiography who "experienced transient partial amnesia, headache, and right upper extremity numbness" after repeated injections. No other details of the neuropsychological deficit were given in the publication, but all

symptoms returned to normal on the same day. Brady [69] commented on this article but added no further case. The report by Yildiz et al. [68] would not fulfil the suggested criteria for TPVA published some years earlier by Nishiyama et al. [21].

Mon et al. reported a neurologist who had a brief (<1 h; see Sect. 2.1.4) episode of amnesia during a panel consultation by video link (Zoom), confirmed as TGA by the subsequent observation of the typical magnetic resonance neuroimaging findings (Sect. 5.1.2) who "partially remembered what had happened during memory loss" [70].

The fractionation of memory function into verbal and non-verbal components might be anticipated to result in partial syndromes selectively affecting verbal memory or visual memory (TTA), perhaps reflecting selective or predominant involvement of only one cerebral hemisphere by whatever process(es) underpin(s) TGA.

2.3.3 Transient Semantic Amnesia

Hodges [71] reported a 50-year-old man who suffered an attack characterised by transient loss of memory for word and object meaning during a typical migraine headache. Interictal brain imaging (CT) and EEG were normal. This transient loss of semantic memory but with preservation of anterograde episodic and working memory was suggested to represent "transient semantic amnesia". The literature review identified only one prior possible case: Kapur et al. [72] reported a patient with temporary loss of memory for people. A report of "transient selective amnesia" for merchandise prices [47] might possibly represent a similar entity.

Considering the mental structure of memory processes, such a semantic variant of TGA might be predictable. However, to my knowledge, no subsequent similar cases have been reported, although as Hodges [71] pointed out such cases might easily be overlooked because of the more subtle cognitive dysfunction compared to that occurring in definite TGA.

2.3.4 Transient Procedural Amnesia

As previously mentioned, fractionation of memory into declarative (explicit) and non-declarative (implicit, procedural) components underlies current models of memory function (Fig. 2.2). Although all the possible variants of TGA described hitherto have involved aspects of declarative memory, it would be theoretically and clinically notable if cases of transient non-declarative memory dysfunction were also observed. Preservation of procedural memory during definite TGA cases is well attested to, including activities such as driving long distances (e.g. [73, 74]), teaching school classes [18], being interviewed for a job [75], and undertaking musical performance, either playing an instrument [76, 77] or conducting [78].

In contrast to these observations, Stracciari et al. [79] described the case of a man who experienced transient amnesia for familiar daily tasks which comprised his occupation of bread making. The authors postulated that this was a disorder similar to TGA but which selectively affected procedural memory, hence transient procedural amnesia.

To my knowledge, no subsequent cases have been reported under the rubric of transient procedural amnesia. However, Yamaoka et al. [49] reported two cases of "transient selective amnesia" lasting several hours in which the patients became unable to operate simple machines, respectively, a taxi meter and a fax machine; neither patient had evidence of anterograde amnesia. (Note that the clinical phenotype in these patients appears to differ from that in a previous case reported as "transient selective amnesia" by Finkel [47]). Moreover, both patients showed high-intensity signal lesions in the left hippocampus CA1 region on diffusion-weighted magnetic resonance imaging which disappeared in the chronic phase; such imaging changes are those typically found in TGA cases (Sect. 5.1.2). This appears to be the most compelling evidence presented to date for the existence of selective variants of TGA and might be adduced as rationale for adding neuroimaging findings to the diagnostic criteria (Sect. 2.2.2).

2.3.5 Transient Retrograde Amnesia

The term transient retrograde amnesia has been used on occasion [48, 80, 81], but whether this terminology refers to the same clinical syndrome in each instance is not clear. It has been used to describe a focal deficit in verbal fluency and living/non-living dissociation in an amnesic period following a mild head injury [81]; a syndrome of focal and selective loss of memory for autobiographical events [48]; and retrograde amnesia for recent events following anterior communicating artery aneurysm coiling ([80]; note that TGA has also been described after aneurysm coiling [82]). The duration of some of these events puts them well outside the diagnostic criteria for TGA (e.g. 10 days [81]; no improvement after 2 days [80]). On the basis of the current evidence, a selective retrograde amnesic variant of TGA is not established.

2.4 Summary and Recommendations

TGA is a relatively stereotyped syndrome of dense anterograde amnesia with variably extensive retrograde amnesia, for which clinical diagnostic criteria have been formulated and widely implemented. Whether variant forms of TGA exist, as might be predicted from the current understanding of the fractionated neuropsychological substrates of memory, remains uncertain.

Not all reports of "TGA" predating the clinical diagnostic criteria conform to what would now be considered TGA. Cases labelled as "TGA" which have been reported since the inception of these criteria but which do not apply or fulfil these criteria should be treated with some scepticism and should prompt consideration of the differential diagnosis of TGA, which is elaborated in the next chapter.

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