Chapter 6
Prognosis and Management of TGA

Abstract This chapter considers the prognosis and management of TGA. Generally, prognosis is benign, although some mild deficits of memory function may persist as well as a gap for the period of TGA. There is a finite recurrence rate, around 3–6% per year, and it may possibly be the case that recurrent TGA is not as benign as single-episode TGA. Uncertainties remain about long-term risks of developing dementia, epilepsy, stroke and depression.

Keywords Cognition · Recurrent TGA · Epilepsy

A number of studies investigating the prognosis of TGA have appeared (e.g. [1–13].), with variable methods of case ascertainment and duration of follow-up. Generally, these have confirmed the benign outlook in TGA, as has a systematic review [14] although subtle cognitive deficits may persist and there may possibly be increased risk of dementia and epilepsy.

6.1 Recovery and Persisting Cognitive Deficit

In most patients with TGA, recovery of memory function is rapid, with apparent restoration to normal with the exception of the amnesic episode per se (see Sect. 1.1, Sect. 2.1.5 and Sect. 4.1.3). However, some formal studies have suggested that memory function may not return entirely to normal.

In the recovery phase of an acute attack of TGA (post-acute phase), retrograde amnesia recovers before anterograde amnesia, but the shrinkage of the former may be heterogeneous, with or without a temporal gradient [15]. Kapur et al. attempted to fractionate memory tests in patients recovering from TGA and found that resolution of a naming deficit more closely paralleled recovery from retrograde amnesia rather than anterograde amnesia. Within retrograde amnesia for public events, there was a temporal gradient of memory loss, with more recent events affected to a

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greater degree than earlier events. Within anterograde amnesia, picture recognition memory preceded recovery of story recall memory [16].

Persistent retrograde memory deficit after TGA has been described on occasion. Roman-Campos et al. presented a patient with a 5- to 10-year period of retrograde amnesia after the acute episode. However, these authors reported EEG changes suggestive of a left temporal lobe lesion [17], and hence, the possibility that this was an epileptic amnesic attack, rather than TGA, cannot be excluded. Mazzucchi et al. reported deficits in verbal long-term memory and verbal IQ in sixteen TGA patients [18], and Cattaino et al. reported permanent memory impairment in 15/30 patients followed up for a mean interval of 20 months [19]. However, the majority of patients in this study had vascular risk factors, prompting concern that some of these patients suffered from amnesic stroke rather than TGA ([20], p.37–8). A review by Mueller dating from 1989 included eight studies in the literature encompassing 622 TGA patients and 122 patients from a personal survey and reached the conclusion that a "residual syndrome of disturbed long term verbal memory may be seen even after a single attack" [8].

Hodges and Oxbury ([21]; see also [22], p.90–6) studied 41 TGA patients 6 months after their attacks. Compared to age-, sex- and IQ-matched controls, there was no evidence of general intellectual decline, and immediate (working) memory for both verbal and non-verbal material was normal, but there was inferior performance on long-term memory tests (paragraph recall). Remote memory was also impaired, as assessed by the Famous Faces test (identifying famous people from previous decades) and famous events (dating significant previous events; recognition, an easier test, was not impaired). The temporal gradient observed in dating famous events seen in the acute phase (Sect. 4.1.1.3) was not seen in the 6-month follow-up. On the Crovitz test of cued autobiographical memory, there were impairments. Longer-term non-verbal memory, assessed by recall of the Rey–Osterrieth Complex Figure and by learning a supraspan block tapping sequence, was intact. Hence, the anterograde memory deficit appeared to be material-specific. The authors posited a mild hippocampal–diencephalic dysfunction preferentially affecting left-sided structures.

Le Pira et al. documented cognitive dysfunction after clinical recovery in a group of 14 TGA patients compared to matched controls. Quantitative differences were found in performance on the California Verbal Learning Test (CVLT) and the Rey–Osterrieth Complex Figure Test, with reduced categorical learning and attention that were ascribed to a prefrontal impairment [23].

Guillery-Girard et al. investigated 32 patients 13–67 months post-TGA attack and reported deficits in the retrieval of recent semantic information and episodic memories which they thought most likely to be due to difficulty accessing memories [24].

Testing patients at a mean of 3 years post-TGA, Uttner et al. found no differences in neuropsychological assessment between TGA patients and controls [12]. In a subsequent study, no differences were found in patients with or without acute MR-DWI changes versus healthy controls 2 years after TGA [13].

Jäger et al. administered a recognition memory task for faces and words to eleven TGA patients during the post-acute phase and to eleven matched controls. They

sought to examine dual-process models of recognition memory, which posit that recollection and familiarity are mediated by hippocampal and extra-hippocampal brain regions, respectively, hypothesising that because of the changes seen in the hippocampus on diffusion-weighted magnetic resonance imaging (MR-DWI) in TGA patients (Sect. 5.1.2), the former may be more impaired than the latter. They found impaired recollection in the TGA patients' memory for words, but no difference between TGA patients and controls in familiarity-based recognition memory, suggesting that TGA has selective effects on specific recognition memory subprocesses, consistent with a dual-process model [25].

Noël et al. studied 19 patients one year after TGA and found that mild anterograde memory deficits could be detected. As might be anticipated, patients with evidence for depression or anxiety (see Sect. 6.3.5) did worse. Although the mild post-TGA episodic memory disorder may be a consequence of TGA, the authors suggested that patients' emotional state might slow recovery processes [26].

Schöberl et al. used sophisticated tests of hippocampal function which indicated selective and prolonged deficits in allocentric (hippocampus-dependent) spatial navigation in patients following TGA, suggesting that damage had occurred within hippocampal circuits [27].

Fewer follow-up studies have been reported in possible variants of TGA (see Sect. 2.3 for descriptions of these phenotypes). Neuropsychological evaluation in transient topographical amnesia (TTA; Sect. 2.3.1) 6–12 months after recovery 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 [28]. One patient in the series of patients with TTA reported by Naranjo-Fernandez et al. [29] developed dementia six years after the acute episode.

In view of the mild impairment in verbal memory following TGA reported in some studies, the possibility that these patients may be at risk for long-term cognitive decline, manifesting as mild cognitive impairment or dementia, has been examined (Sect. 6.3.1).

6.2 Recurrence

In one of the earliest published reports of TGA, Morris Bender described isolated or single episodes of confusion with amnesia [30] and later emphasised the absence of recurrence [31]. However, the possibility of recurrence of TGA was mentioned in the early literature, for example by Guyotat and Courjon [32] and by Fisher and Adams [33]. However, it was the paper by Lou in 1968 which first made the possibility of recurrence of TGA explicit, although at least one patient in this series was almost certainly having ischaemic events [34].

Many subsequent reports of recurrent TGA have appeared (although not all can be accepted as such, especially those predating widespread application of Hodges and Warlow's 1990 diagnostic criteria [35]). Accounts include recurrence

associated with sexual activity [36–38], at high altitude [39], as well as detail from the patient's perspective [40]. Recurrence has also been reported in transient topographical amnesia (TTA), a possible variant form of TGA (Sect. 2.3.1). Occurrence of up to three episodes was noted in 3/10 patients [41], with a mean number of episodes of 1.75, range 1–3 [29], although some patients are reported to have many episodes over many years [42].

6.2.1 Annual Recurrence Rate

Although numbers of studies have cited a "recurrence rate" for TGA, fewer have taken into account the duration and extent of patient follow-up and are thus able to calculate an annual recurrence rate (Table 6.1). These are for the most part prospective studies, and their findings suggest an annual TGA recurrence rate of around 3–6%. Mueller reviewed eight "representative" studies from the literature encompassing 622 TGA patients and 122 patients from a personal survey to produce a risk of recurrence of 3.4%/year [8].

Low recurrence rate is one factor which may assist in the differential diagnosis of TGA from transient epileptic amnesia (TEA) and from transient ischaemic attack (TIA) (see Table 3.3). Although occasional patients undoubtedly do suffer recurrent episodes of TGA (Case Study 2.1) [45], frequent recurrence of events labelled as TGA should certainly prompt careful diagnostic consideration, and possibly concern, for example the case reported by Rumpl and Rumpl [46], also associated with epileptic seizures, unilateral visual loss, hemiparesis and dysarthria (see also [47, 48]). Questions about the differential diagnosis, especially from epilepsy, may need to be reassessed (e.g. [49, 50]).

6.2.2 Recurrent TGA

Do patients with recurrent (definite or pure) TGA differ from those who experience only a single episode? A number of lines of evidence, both clinical and radiological, suggest this possibility, although the caveats concerning adequate differentiation from TEA must be borne in mind when assessing these accounts.

Table 6.1 Reports of annual recurrence rates of TGA

Reference	Study location	Annual recurrence rate
Hinge et al. (1986) [5]	Danish multicentre	4.7%
Hodges (1991) [22]	Oxford, UK	ca. 3%
Toledo et al. (2005) [43]	Barcelona, Spain	4.4%
Quinnette et al. (2006) [44]	Caen, France	5.8%

Gallassi et al. undertook neuropsychological tests in patients with single ($n = 31$) or multiple ($n = 10$) TGA episodes compared with matched controls ($n = 41$) and found that patients with multiple attacks showed more impairment in tasks addressing memory and visuoperceptual abilities than patients with single attacks who showed only immediate and long-term verbal memory impairments with respect to controls [51].

Lampl et al. found that acute brain hypoperfusion seen on SPECT imaging (Sect. 5.2.1) in 16 TGA patients returned to normal after 3 months in those patients experiencing a first episode of TGA, whereas perfusion remained abnormal at 3 and 12 months in three patients with recurrent TGA [52].

Toledo et al. compared "unique-TGA" cases ($n = 98$) with "recurrent-TGA" cases ($n = 26$) and found that the latter had the same vascular risk factors (Sect. 7.11) as a comparison group of TIA patients. Moreover, the recurrent-TGA patients had a significantly more frequent history of stroke and a trend to suffer new ischaemic events than patients in the unique-TGA group, prompting the authors to suggest that recurrent TGA should be considered a manifestation of ischaemic cerebrovascular disease [43]. However, in a later study these authors revised their view, finding no perfusion abnormalities, arterial stenoses or underlying cardioembolic disease in a series of 28 TGA patients [53].

Agosti et al. studied 85 TGA patients recruited over a 3-year period of whom 73 had a single episode and 12 (14.1%) had two episodes. A risk factor sum of recognised TGA triggers was calculated for each patient and this was higher for the recurrent group, who also had a higher frequency of carotid atheroma (41.8% vs. 15.1%, $p < 0.05$) and ischaemic heart disease (6.8% vs. 3.3%, $p < 0.02$) [54].

A magnetic resonance imaging study of TGA patients ($n = 27$) looking at diffusion-weighted abnormalities in the hippocampus (Sect. 5.1.2) found these in nine patients, with a higher association observed in patients with a second TGA attack compared to a first event. These authors concluded that patients with recurrent TGA had a significantly higher association of reversible MR-DWI abnormality [55].

Moon et al. undertook diffusion tensor imaging (Sect. 5.1.3) in seven patients with recurrent TGA and fourteen with single-episode TGA to examine the hypothesis that the former might have more disrupted structural connectivity and hence greater pre-existing vulnerability to TGA attacks. The study found no disruptions in the structural connectivity of the memory pathway in recurrent-TGA patients, suggesting that repeated hippocampal lesions associated with TGA do not affect the microstructure of the brain [56]. However, volumetric analyses (Sect. 5.1.3) have suggested the possibility of network alterations in connectivity in recurrent TGA [57, 58].

Summarising these disparate studies, there does appear to be some tentative, but not uniform, evidence that prognosis following recurrent TGA may differ from that following single-event or unique TGA, being less benign. Whether this subgroup can be recognised from the outset, i.e. after their first episode, on the basis of risk factor profiles or biomarkers, remains to be determined, but this might have implications for management.

6.2.3 Possible Risk Factors for Recurrent TGA

Are there specific risk factors for recurrence of TGA? Morris et al. examined over 1000 patients with TGA, of whom 13.7% had had at least one recurrence (maximum 9). They found a significant difference in age at first TGA episode between individuals with a single-episode (65.2 ± 10.0 years) compared to those with recurrent episodes (58.8 ± 10.3 years). In addition, a personal or family history of migraine was more prevalent in recurrent compared to isolated cases [59].

Alessandro et al. [60] reported that 8% of 203 TGA patients seen in Buenos Aires had a recurrence over a mean follow-up of 24 months. A personal history of migraine was more frequent in patients with than without recurrence.

Tynas and Panegyres followed up a cohort of 93 TGA cases of whom 16% had recurrence. Risk factors for recurrence were depression, previous head injury and a family history of dementia. Typical MR-DWI changes, observed in 24 patients, were not associated with outcomes in this patient cohort [61].

In a cohort of 70 TGA patients followed up for mean of 16.5 months, Oliveira et al. found TGA recurrence in 27%, and associated with female sex, depression, shorter duration of TGA episode and hippocampus hyperintensity on MR-DWI (although only 5 patients in the cohort had this change). Of these, a history of depression was the most important predictor [62].

Ganeshan et al. reported recurrence in 13/126 patients in their study, with no difference in percentage recurrence between those patients with and without additional non-hippocampal (silent) ischaemic lesions [63].

A systematic review by Liampas et al. found evidence for a relationship between recurrence risk and a personal or family history of migraine and a personal history of depression. Weaker evidence was found for a relationship with family history of dementia, personal history of head injury and MR-DWI hippocampal lesions. However, no relationship was found with EEG abnormalities, impaired jugular venous drainage, cardiovascular risk factors, atrial fibrillation or cardiovascular events [64].

6.2.4 Is Family History of TGA a Risk Factor for Recurrent TGA?

A small number of patients reported in the TGA literature give a history of TGA episodes in other family members (Sect. 7.8). A patient reported from the author's clinic who had recurrent TGA and whose father reportedly also had recurrent TGA prompted the question as to whether or not a positive family history of TGA is a risk factor for recurrent-TGA episodes [65]. Following this publication, the author has received emails from other families with recurrent and familial TGA [66], which are summarised along with cases reported in the published literature in Table 6.2.

Table 6.2 Reports of familial cases of TGA with history of TGA recurrence (see Table 7.3 for reports of familial TGA cases)

Reference	TGA patient details	Recurrence history
Corston and Godwin-Austen (1982) [67]	Four male siblings, aged in 60s and 70s; three had TGA attacks in the context of exercise	2–3 attacks each
Munro and Loizou (1982) [68]	Two siblings (M:F) and their father, in 50s to 60s	2 attacks in index case (M), 3 in father
Dupuis et al. (1987) [69]	Twin sisters (probably monozygotic), attacks in 60s	2 attacks in first sister, aged 64 and 69, both attacks followed by severe migraine
Vyhnalek et al. (2008) [70]	Male, father and sister. Proband had migraine without aura from adolescence; no migraine in father or sister	Male had 2 episodes aged 52 and 54. Father and sister had single episodes
Segers-van Rijn and de Bruijn (2010) [71]	Four siblings (3F:1M) and possibly their mother, attacks after exercise (3) and air travel (1), and on birthday; attacks between 50s and 70s	One of the female siblings had history of two episodes
Maggioni et al. (2011) [72]	Two monozygotic twin brothers aged 50 and 49 at onset	Elder brother had 5-6 attacks per year during migraine without aura (MO) attacks; younger had four episodes all during MO
Larner 2017 [65]	Male; father also reportedly had TGA	Index case had two episodes, aged 61and 64; father 2–3 episodes (uncertain)
Larner (2018) [66]	Two male siblings and their mother	Younger male sibling had three events, aged 60, 63, 66, first two after exercise (cycling)
Larner (2018) [66]	Two female siblings, both had history of migraine	Younger female sibling had two events, aged 54 and 55, second after sexual activity. Older sibling had single event, aged 60, after sexual activity
Larner (2019) (unpublished, personal communication)	Three siblings (1F:2M)	Female had 3 events aged 63, 68, 70, first after emotional upset, second after exercise. Single events in male siblings

In addition, Dupuis et al. [73] reported (in abstract) a higher recurrence rate (and history of migraine) in those TGA patients with a positive family history of TGA (21) compared to the whole cohort of 219 patients (24% vs 12.6%) seen over an extended period of time (1999–2016). Morris et al. reported a family history of TGA in 1.3% of their cohort with single-episode TGA and in 2.8% with recurrent TGA [59]. Liampas et al. found no relationship between TGA recurrence and family history of TGA [64]. However, given that both familial history and recurrence of TGA are likely to be underascertained, this possible link may merit further examination in prospective population-based studies.

6.3 Future Risk

Generally, TGA has been regarded as a benign event with respect to long-term prognosis. But in light of some of the aforementioned clinical and imaging findings (Sects. 6.1 and 6.2), it is pertinent to ask whether or not an episode or episodes of TGA may put patients at risk for future neurological problems. In other words, is the long-term prognosis of TGA entirely benign or not? This has been examined particularly for cognitive decline, stroke and epilepsy.

6.3.1 Cognitive Decline: Dementia and Mild Cognitive Impairment (MCI)

Because cognitive decline becomes increasingly prevalent with ageing, it is not surprising to encounter patients with cognitive impairment who have a prior history of an episode of TGA (especially so in view of the typical age at which TGA occurs; Sect. 7.4), without there necessarily being an implication that subsequence is consequence (see Case Studies 6.1 and 6.2), or in other words that dementia is "presenting" as TGA [74].

Case Study 6.1: Dementia Subsequent, but not Consequent, to TGA
A 73-year-old man was referred with a two-year history of progressive memory difficulties, corroborated by family members. On the Mini-Mental State Examination, he scored 22/30 and on the Addenbrooke's Cognitive Examination-Revised 60/100. MR brain imaging showed bilateral temporal lobe atrophy. A diagnosis of Alzheimer's disease was made. Nine years earlier, he had had an episode of memory loss after going for a swim one morning whilst on holiday, with resolution after about 7 h. He was subsequently well. A diagnosis of TGA had been made. He had no further amnesic episodes or memory issues until the onset of his progressive memory problems seven years later, which was felt to be entirely distinct from his previous episode of TGA.

Case Study 6.2: Subjective Memory Complaint Subsequent, but not Consequent, to TGA?
A 72-year-old academic complained of difficulties recalling peoples' names and their associations, perhaps dating back a couple of years. Her concerns stemmed in part from the family history of Alzheimer's disease in her mother with onset in her late 70s. Furthermore, the patient had had an episode of

transient global amnesia for which she had been briefly hospitalised some nine years earlier. She reported that brain imaging had not been undertaken at that time, but pursuing the clinical records proved this not to be the case (presumably a reflection of her acute amnesic state), she had had a CT brain scan which was normal. She now scored at ceiling on both the Montreal Cognitive Assessment and the Mini-Addenbrooke's Cognitive Examination.

However, since TGA likely represents functional change in the hippocampus (Sect. 9.7), as suggested by diffusion-weighted magnetic resonance imaging (Sect. 5.1.2), is it possible that TGA might predispose to future hippocampal pathology?

Nausieda and Sherman reported dementia in 6% of 32 TGA patients followed up for 3 years [9]. Gandolfo et al. reported only 3 of 102 TGA patients with intellectual deterioration in a prospectively identified group followed up for a mean of 82 months [4].

One study has suggested that TGA may be a risk factor for the syndrome of mild cognitive impairment (MCI). Although MCI has been variously defined, it may represent a prodromal phase of dementing disorder, most frequently Alzheimer's disease. Borroni et al. undertook neuropsychological assessment in 55 TGA patients at least one year after the attack and also in 80 age-matched controls, finding worse performance on tests evaluating verbal and non-verbal long-term memory and attention in the former group but with comparable global cognitive functions [1]. Applying then current criteria for amnestic MCI (aMCI; [75]), nearly one-third of the TGA subjects (18/55 = 32.7%) fulfilled the criteria. It was concluded that objective memory deficits fulfilling aMCI criteria may persist over time in TGA patients [1]. To my knowledge, no subsequent study has been reported which corroborates this finding.

Arena et al. followed up 221 TGA cases for a mean of 12 years and found no evidence of increased risk of subsequent cognitive impairment compared to a matched control group [76].

The systematic review of long-term TGA prognosis reported by Liampas et al. found contradictory results for dementia, with evidence for both a similar and increased risk compared to healthy controls [14]. Hence, the issue of long-term cognitive outcome in TGA requires further long-term follow-up studies in large cohorts, which might also profitably address whether or not cognitive outcomes differ between patients with single-episode and recurrent TGA.

6.3.2 Cognitive Decline: Progressive Aphasia

Graff-Radford and Josephs reported three patients diagnosed with primary progressive aphasia (PPA) who had had episodes of TGA prior to their presentation with linguistic problems and speculated that the conditions might be related [77]. Of

possible relevance, all three patients had recurrent attacks of TGA (Sect. 6.2.2). This paper prompted a response from Nitrini and colleagues [78] drawing attention to an abstract they had published some years previously describing two patients with the semantic variant of PPA (or semantic dementia) who had both had recurrent episodes of TGA prior to the development of aphasia, in one case predating it by 7 and 6 years ([79], p.332, Abstract 34). I am not aware of any further publications on this possible association and have not observed it in any patient in my TGA case series, or examples of prior TGA in patients with progressive aphasia syndromes. Hence, Glannon's assertion that "a significant number of people diagnosed with TGA … have been subsequently diagnosed with primary progressive aphasia" ([80], p.64) does not currently bear scrutiny.

6.3.3 Stroke

In light of the generally favourable vascular risk factor profile in TGA patients as compared to TIA patients (Sect. 7.11), future stroke risk in TGA patients may be anticipated to be low. Miller et al. found no increased risk for subsequent stroke in their report of 277 TGA patients with average follow-up of 80 months [7]. Gandolfo et al. reported only four instances of stroke in 102 TGA patients identified in a prospective study and followed up for a mean of 82 months [4]. Hodges [22] and Pantoni et al. [10] found a lower risk of stroke at follow-up in TGA compared to TIA patients. Arena et al. [76] found no evidence of increased risk of subsequent cerebrovascular events in 221 TGA patients followed up for a mean of 12 years in comparison with a matched control group. The systematic review of TGA prognosis by Liampas et al. found similar vascular (and mortality) risks in TGA and healthy controls [14]. Of course, these reassuring data do not obviate addressing vascular risk factors in TGA patients should they be identified.

Recently, however, a propensity-matched cohort study from Korea (>10,000 patients) has suggested an increased risk [81], in direct contradiction to the findings of another propensity-matched study from the USA (>21,000 patients) [82]. Attempting to explain these differences, Romoli and Muccioli noted the increased frequency of cardiovascular risk factors in the American population and the female predominance in the Korean cohort, with risk emerging over longer follow-up [83]. This subject area remains one of active research.

6.3.4 Epilepsy

The Oxford TGA study reported that 7% of patients with apparent TGA subsequently developed epilepsy, usually of complex partial type ([22], p.41,46–7,56,121,123,124–5137). This suggested to the investigators that the original "TGA" attacks were in fact due to seizures. Another possible explanation is that TGA attacks may predispose to epileptic attacks as a consequence of microstructural

damage to the hippocampus (Sect. 3.2.2). The occasional emergence of TEA in patients with prior episodes of TGA (Sect. 3.2.2) might also be pertinent to this argument.

Although the case–control study of Arena et al. did not suggest any increased risk of subsequent epileptic seizures in TGA patients followed up for a mean of 12 years [76], a population-based cohort study has reported an association of TGA with increased long-term risk of epilepsy. The adjusted hazard ratio for epilepsy in TGA cohorts was 6.50 (95% confidence interval 1.87–22.68, $p = 0.003$) compared with non-TGA cohorts after adjusting for age, gender and comorbidities [84]. A systematic review of long-term TGA prognosis could not exclude an increased risk of epilepsy in TGA patients [14].

6.3.5 Depression

The finding of depression as a risk factor for recurrent TGA [61, 62] was previously mentioned. In a population-based cohort study, Hsieh et al. found no increase in the long-term risk of depression in TGA patients versus matched non-TGA subjects (adjusted hazard ratio 1.67; 95% confidence interval 0.85–3.25, $p = 0.139$) [85]. Whilst TGA patients may have anxious personality traits (Sect. 7.10) and experience depressive mood during an attack (Sect. 2.1.2), long-term risk for depression does not appear to be increased.

6.4 Management

Once the diagnosis of TGA has been established, there is no specific treatment other than patient explanation and reassurance. As TGA episodes are self-limiting, there is no indication for acute medication.

Future management is expectant, since there is currently no compelling evidence of increased risk of future stroke, epilepsy or other cognitive impairments (see Sect. 6.3). No specific lifestyle advice is indicated, unless attacks have come on during specific activities (e.g. exercise) which might be avoided or moderated.

6.4.1 Driving

A particular management issue relates to driving after TGA. Advice to stop driving is not infrequently issued by clinicians unfamiliar with TGA who encounter these patients, probably because of concerns about stroke and epilepsy [86].

Different jurisdictions have different rules relating to fitness to drive, which should be consulted and adhered to. In the United Kingdom, the Driver and Vehicle Licencing Authority (DVLA) has placed no restriction on driving following a single

episode of TGA, and there is no statutory obligation to inform DVLA following a single episode [87], and this remains the case at time of writing (31/12/2021). This contrasts with previous DVLA recommendations, prior to 1991, in which TGA was regarded as equivalent to TIA and driving for 3 months was not permitted ([22], p.59).

Reports of patients driving safely over long distances during attacks of TGA (e.g. [88, 89].), sometimes referred to as the "unconscious driving phenomenon" (see Case Study 3.3), may be taken to indicate that driving skills, an aspect of procedural memory, are not impaired. Memory impairment does not necessarily impair most aspects of driving performance, as shown by a study of two experienced drivers with bilateral hippocampal lesions causing severe amnesia [90].

6.4.2 Pharmacotherapy

The low recurrence rate of TGA, meaning that most patients suffer only a single attack, currently obviates routine prophylactic treatment, although one report claiming successful prophylaxis with a beta-blocker, metoprolol, has appeared [91]. Recurrent-TGA attacks following withdrawal and change of beta-blocker therapy for migraine has also been reported [70]. In a patient reported to have 5–6 TGA attacks per year during attacks of migraine without aura, verapamil and valproate were said to reduce the frequency of TGA [72].

It may be that those with recurrent TGA do require more than simple reassurance, but further studies will be required to address this question.

6.5 Summary and Recommendations

Generally, TGA is a benign condition and patients can be reassured about long-term outcome. Nevertheless, some deficits in verbal memory, beyond the amnesia for the attack itself, and in spatial navigation may persist although the practical consequences seem to be few. Long-term risk of dementia remains uncertain. There is a distinct but low recurrence rate for TGA to which migraine may predispose. Some patients may develop partial epilepsy but whether this reflects initial misdiagnosis or the consequence of TGA remains to be fully defined. Further studies focussing particularly on outcome in patients with recurrent TGA are required.

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