

# Transient global amnesia: Diffusion MRI findings

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## Abstract

**Introduction:** Aim of this study is to identify and describe the MRI findings in patients with Transient Global Amnesia (TGA), specifically on Diffusion Weighted Imaging (DWI) sequence. **Methods:** MRI findings in 12 patients with clinical diagnosis of TGA were retrospectively analysed. MRI brain was performed with a 3T scanner on 11 patients and 1.5T scanner on 1 patient. DWI were acquired at B value of 1000 s/mm<sup>2</sup> in 4 patients, 2000 s/mm<sup>2</sup> in 2 patients and both 1000 and 2000 s/mm<sup>2</sup> in 6 patients. **Results:** There were 7 female and 5 male patients. The mean age was 65.67 years (range 61-74 years). The median time interval between the onset of symptom and MRI scan was 47.5 hours, range 25-114 hours. 11 of the 12 patients showed punctate foci of restricted diffusion in hippocampus (mean size 3.7 mm (range 2-6.5 mm). 10 patients showed foci in left hippocampus. Nine patients showed a single focus, 1 patient showed three foci and 1 patient showed four foci. In 6 patients who had DWI MRI at both B values, scans at B value of 1000 s/mm<sup>2</sup> revealed abnormality in 4 patients, while higher B value imaging improved sensitivity in one patient and one patient had a negative scan at both B values. **Conclusion:** We have highlighted the MRI finding of typical punctate foci of bright signal in hippocampus seen on DWI in patients diagnosed with TGA. Detection on a routine stroke MRI protocol can avoid need for dedicated TGA protocols or repeat scan, improving the workflow.

**Key words:** Amnesia; diffusion MRI; transient global amnesia; hippocampus; neuroimaging

## Introduction

Transient global amnesia (TGA) is a reversible, benign, mostly nonrecurrent clinical syndrome of anterograde amnesia lasting up to 24 hours, manifesting as repetitive questioning and occasionally retrograde amnesia, without any gross neurological deficit.<sup>[1]</sup>

TGA affects middle-aged to elderly patients with reported annual incidence of 3.4–10.4 per 100,000 in general population. This increases to 23–32 per 100,000 per year for patients older than 50 years.<sup>[2]</sup> We describe magnetic resonance imaging (MRI) findings in 12 patients with TGA.

## Materials and Methods

MRI findings of 12 consecutive TGA patients who presented to a tertiary level teaching hospital with clinical findings of TGA between October 2013 and October 2106 were retrospectively analyzed. Diagnosis of TGA was established in all patients using Hodges and Warlow criteria.<sup>[3]</sup> Approval from ethics institutional review board was obtained.

MRI brain was performed with a 3T scanner on 11 patients and 1.5T scanner on 1 patient (Ingenua, Philips Healthcare, Netherlands). The MRI protocol included diffusion weighted imaging (DWI), T1- and T2-weighted imaging,

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fluid-attenuated inversion recovery (FLAIR) imaging (4 mm slices at 5 mm intervals), conventional gradient-echo imaging in the transverse plane, T1-weighted imaging, 3D time-of-flight (TOF) angiography of the intracranial Circle of Willis. Single-shot spin-echo echo-planar imaging was used for DWI with the following parameters: TR = 3700–8050 ms; TE = 82–105 ms; FOV = 220 mm; SENSE factor = 2, and number of acquisitions = 2; DWI were acquired at B value of 1000 s/mm<sup>2</sup> in 4 patients, 2000 s/mm<sup>2</sup> in 2 patients, and both 1000 and 2000 s/mm<sup>2</sup> in 6 patients. In the 6 patients with scans at B values of both 1000 and 2000 s/mm<sup>2</sup>, scans were performed consecutively at the same head position. The signal-to-noise ratio (SNR) was improved on 1.5T by increasing the number of signal acquisitions (NSA) from 2 on 3T to 3.

An area of restricted diffusion was defined as area of signal brighter than adjacent brain parenchyma on DWI images and signal lower than adjacent brain parenchyma on apparent diffusion coefficient (ADC) images. The number, location, and size of the DWI abnormality was recorded. The ADC was not measured.

## Results

There were 7 female and 5 male patients. The mean age was 65.67 years (range 61–74 years). The median time interval between the onset of symptom and MRI scan was 47.5 hours (range 25–114 hours). Eleven of the 12 patients diagnosed clinically with TGA showed DWI abnormalities. A total of 16 punctuate areas of DWI restriction were identified in hippocampus. Out of the 11 patients with positive MRI finding, 10 patients showed foci in left hippocampus. Nine patients showed only a single focus, 8 on the left side, while 1 patient showed a focus on the right side. One patient showed two foci on the left side and one focus on the right side. One patient showed three foci on the left side and one on the right side [Figure 1]. The mean size of the foci was 3.7 mm (range 2–6.5 mm). No other area of brain showed DWI abnormality in any patient.

In 6 patients who had DWI images acquired at B values of both 1000 and 2000 s/mm<sup>2</sup>, abnormal DWI focus was

identified on both B values in 4 patients. In one patient, abnormal focus was identified only on DWI with high B value of 2000 s/mm<sup>2</sup>, while it was not seen on DWI with B value of 1000, which was acquired with same slice thickness of 3 mm [Figure 2]. No abnormality was visualized on both the B values in 1 patient. This patient had his MRI performed at 25 hours after symptom onset on the 3T scanner.

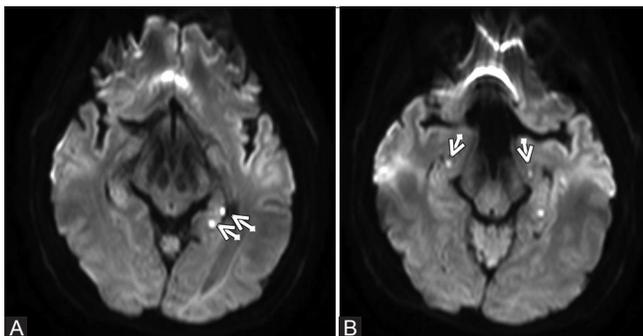
In three lesions, corresponding small bright spot was visible on FLAIR images, while in the rest of the lesions with DWI abnormality, no FLAIR signal abnormality was seen.

## Discussion

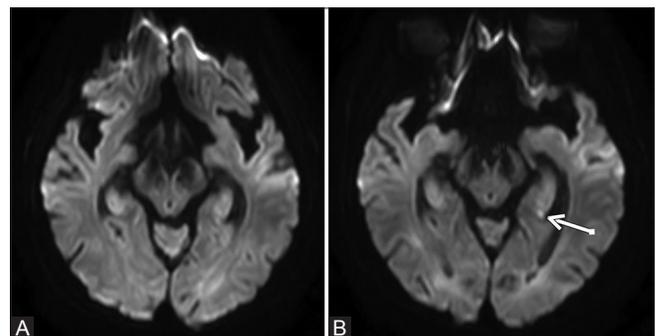
We present MRI findings of TGA in 12 patients. TGA presents with a distinct typical history with a known time of onset and symptoms lasting for less than 24 hours. Anterograde amnesia with inability to form new memories is the hallmark of TGA.<sup>[1]</sup> The etiology and pathogenesis of TGA are uncertain, although several different causes suggested include ischemia, migraine, epileptic seizure, venous congestion, and psychological disturbances.<sup>[4]</sup> The syndrome is of unknown cause but can be closely imitated by disorders of known aetiology such as partial complex seizures, migraine, and possibly transient ischemia of the hippocampus on one or both sides. A possible explanation for transient ischemia is that of venous congestion and venous reflux.<sup>[5]</sup> Anterograde amnesia gradually diminishes within the course of a few hours and patients return to their baseline status, though they may retain a dense amnesic gap for the duration of the episode.<sup>[6]</sup>

TGA typically affects patients between 50 and 80 years of age at an average age of 61 years.<sup>[6]</sup> All our patients had acute-onset confusion and amnesia and the mean age of patients in our series was 65.67 years (range 61–74 years).

Diffusion weighted abnormalities on MRI were initially reported as far back as 1998 by Strupp *et al.* in 7 of 10 patients imaged during episodes of transient global amnesia.<sup>[7]</sup> Abnormal diffusion MRI signal was seen in the left hippocampus; 3 of these had bilateral hippocampal



**Figure 1 (A and B):** DWI images showing four typical punctate foci (arrows) in hippocampus, three on the left side (A and B) and one on the right side (B)



**Figure 2 (A and B):** DWI image at 1000 s/mm<sup>2</sup> was unremarkable (A), while DWI image at 2000 s/mm<sup>2</sup> showed the typical punctate focus in left hippocampus (B)

abnormalities. Permanent infarctions were not found. Yang *et al.* reported similar hippocampal lesions in the lateral or CA1 region in 17 of 20 cases of TGA.<sup>[8]</sup> Other investigators have found frontal lobe abnormalities by diffusion-weighted MRI or PET.<sup>[9]</sup> Ten patients in our series had lesions in the left hippocampus, with 2 patients also showing a lesion on the right side. While one patient showed a lesion only on the right side. This left-sided predominance has been reported earlier also.<sup>[10]</sup> Further investigation would be required to ascertain the pathophysiology and significance behind this left-sided preponderance. Three lesions were also visible on FLAIR images as similar punctate dot-like bright lesions. However, visibility was best on DWI images in all patients. All the reports in the literature have relied on the bright appearance of the punctate foci on DWI images and role of measurement of ADC or normalized ADC values has not been reported.

The median time between the onset of symptoms and the MRI scan was 47.5 hours. Other studies have described that MRI is more sensitive for TGA lesions after 2 days<sup>[11]</sup> or 3 days of symptom onset.<sup>[12,13]</sup> Kim *et al.* even performed a separate MRI scan at day 3 to improve sensitivity.<sup>[12]</sup>

There was 1 patient in whom the abnormal lesion was not seen on B value of 1000 s/mm<sup>2</sup> and was visible only on DWI with B value of 2000 s/mm<sup>2</sup>. In 4 other patients, who had DWI scan with B values of both 1000 and 2000 s/mm<sup>2</sup>, there was no change in visibility or size of the bright spot.

The factors improving the conspicuity of the lesions on MRI have been reported to be thin slice images (2–3 mm),<sup>[11,12]</sup> 2–3 days delay from symptom onset,<sup>[10-12]</sup> resolution of the DWI images,<sup>[10]</sup> and high B values (2000 or 3000 s/mm<sup>2</sup>).<sup>[11,12]</sup> One patient in our series who had negative MRI had his scan performed at 25 hours after symptom onset. This patient did not undergo any follow-up scan to enable us to comment whether a delayed MRI would have been more sensitive. The detection rate has been reported to be higher at 3T than at 1.5T scanners.<sup>[13]</sup> Use of a modified specific TGA protocol has been suggested to improve lesion detection.<sup>[12]</sup>

Confusional migraine, partial epilepsy, drug intoxication, alcoholic “blackouts,” stroke, and minor head injuries can also produce transient amnesic syndromes and should be considered in the clinical differential diagnosis when patients present to the emergency department.<sup>[10,14]</sup> Hence, prospectively planning a TGA protocol can be difficult. If the initial MRI scan is normal and there is strong clinical suspicion of TGA, then additional images with thinner sections and higher B values according to a dedicated TGA protocol, repeat MRI on a higher strength MRI scanner, or repeat MRI after 3 days of symptom onset can be acquired.

Abnormal signal in hippocampus can also occur in posterior cerebral artery stroke, after prolonged seizures, limbic

encephalitis. These can be differentiated on the basis of clinical presentation and the characteristic punctate dot-like focus of abnormality in TGA.<sup>[15]</sup>

Despite distinct MRI findings, TGA remains a clinical diagnosis. MRI may be warranted in patients with an atypical presentation, symptoms lasting for more than 24 hours, or patients having vascular risks factors for stroke or structural lesions. As the punctate DWI abnormality in hippocampus may possibly be regarded as pathognomonic of TGA, it may be reasonable to include it as an additional criterion in addition to Hodges and Warlow’s criteria for TGA after further validation in larger studies or series.<sup>[15]</sup> TGA does not have an impact on mortality or morbidity in affected patients and does not represent a risk factor for stroke or ischemic disease. Treatment is generally not required, and the condition usually does not recur.<sup>[16]</sup> However, a timely diagnosis helps in reassuring the patients and their relatives of the benign character of this subjectively disturbing disorder.<sup>[11]</sup> Especially in cases with uncertain onset or less characteristic clinical presentation, MRI finding of typical punctate areas of DWI bright signal in hippocampus is useful to confirm the clinical diagnosis.

A major imitation of our study is the relatively small number of patients and retrospective analysis of MRI images.

## Conclusion

In conclusion, we have highlighted the MRI finding of typical punctate foci of bright signal in hippocampus seen on DWI in patients diagnosed with TGA. Detection on a routine stroke MRI protocol can avoid need for dedicated TGA protocols or repeat scan after 2–3 days of symptom onset. Our case series will add to the growing evidence of characteristic DWI lesions in TGA.

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## Conflicts of interest

There are no conflicts of interest.

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