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Magnetic Resonance Imaging in Transient Global Amnesia

Lessons Learned from 198 Cases

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Abstract
Purpose Patients with transient global amnesia (TGA) present with a characteristic clinical syndrome although other differential diagnoses have to be considered. Diffusion-weighted imaging (DWI) represents a highly specific diagnostic tool in the context of TGA; however, standard clinical DWI often fails to detect the small characteristic hippocampal lesions. The diagnostic success of DWI sequences in TGA patients was analyzed with respect to slice thickness and time interval between symptom onset.
Methods Magnetic resonance imaging (MRI) studies of 198 patients with clinically diagnosed TGA were retrospectively analyzed. All DWI studies were grouped according to the slice thickness applied (3 mm, 5 mm and 6 mm). The three groups were assessed for group-specific detection rates of hippocampal lesions with diffusion restriction. In addition the detection rates were evaluated with respect to the time interval between TGA symptom onset and MRI examination.
Results A significant increase in detection rates (about 8.4% per mm) was found when thinner slices were acquired (44.7% for 3 mm, 27.1% for 5 mm and 19.6% for 6 mm slice thickness). The detection rate was highest (up to 80%) when MRI was performed 2 days after TGA symptom onset.
Conclusions The MRI protocol in patients with TGA should include a DWI sequence with a slice thickness of 3 mm or less. The examination should be performed on day 2 after symptom onset to fully exploit the diagnostic value of DWI which represents a sensitive and specific diagnostic tool for patients with TGA.

Keywords Transient global amnesia · Diffusion-weighted imaging · Retrospective studies · Ischemic attacks · Hippocampus

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Introduction

Transient global amnesia (TGA) is still an enigmatic disease and patients present with a remarkable and characteristic clinical syndrome. A TGA episode is often described as a threatening experience by patients and their relatives for the profound and disturbing clinical symptoms. The disease TGA was first defined by Fisher and Adams as the temporary loss of anterograde and recent retrograde memory lasting less than 24 h with preservation of alertness, attention and self-identity and without other neurological deficits [1]. Various etiologies for TGA episodes have been suggested including ischemic insult [2], transient mesiotemporal ischemia induced by venous congestion [3–5], migraine [6], spreading depression [7] and epileptic seizures [8]. An involvement of temporomesial structures, such as the hippocampus has been suggested by several studies [9, 10]. Episodes of TGA have a relatively unique clinical presentation and diagnosis can often be made based solely on the clinical symptoms. In cases of equivocal clinical findings diffusion-weighted imaging (DWI) represents a valuable diagnostic adjunct in establishing the diagnosis of TGA. Initial reports on magnetic resonance imaging (MRI) chan-

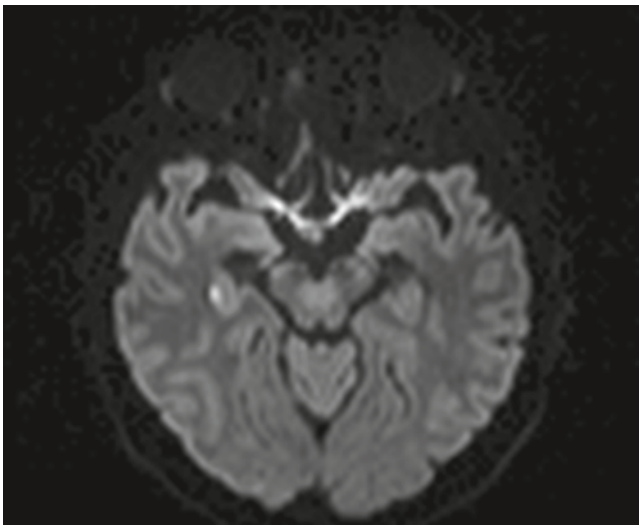

Fig. 1 Example of a characteristic hippocampal lesion in diffusion-weighted imaging (b = 1000 s/mm²)

ges in TGA were contradictory in some studies [11–25] demonstrating diffusion restriction (hyperintense) in lesions of temporomesial structures by DWI, while other studies did not confirm these findings [26–29]. It is now generally accepted that a substantial proportion of TGA patients have characteristic small punctuate hyperintense lesions in DWI studies (Fig. 1) although the published detection rates vary broadly. A recent study showed that these lesions are located exclusively in the lateral portion of the hippocampus, i.e. the CA1 region [11]. Comparable punctuate hippocampal DWI hyperintensities may be very rarely seen in posterior cerebral artery (PCA) stroke (see pattern 4 in Szabo et al. [30]) but these patients do not present with TGA symptoms. Hence in the context of TGA DWI can be regarded as a diagnostic tool with a very high specificity. With respect to sensitivity the published reports vary widely (12–86%) regarding the proportion of patients in whom the characteristic DWI lesions were detected.

To improve sensitivity and detection rates previous reports investigated the impact of slice thickness, diffusion-weighting factor and timing of the MRI examination relative to TGA symptom onset [11–14, 24, 25]. Almost all previously published results were acquired in relatively small patient populations. A recently published study in a large sample of 200 TGA patients who were examined with a DWI protocol (1.5 T, 5 mm slice thickness with 90% of all patients being examined in less than 24 h) showed a low diagnostic yield when performed early in the course of TGA [24].

These and previous results have now been extended by a retrospective MRI data analysis in a large population of 198 TGA patients, comparing the detection of DWI lesions for different slice thicknesses, field strengths and detection rates are related to the time interval between TGA symptom onset and MRI examination. The aim of this study was to identify and affirm factors which increase detection rates and if possible to derive imaging protocol recommendations to fully exploit the diagnostic capabilities of DWI in the context of patients with suspected TGA but equivocal clinical findings.

Methods

Following approval from the institutional review board for this retrospective study a comprehensive data base search was performed to identify all MRI studies performed in this institution (major university hospital in Berlin, Germany) throughout the last decade (January 2000 to July 2011). The aim was to retrieve all studies performed including patients with clinically suspected TGA who were referred for MRI assessment by the neurology department and 239 patients were identified. Emergency reports and discharge letters of these patients were scrutinized to corroborate the diagnosis of TGA. Patients where the discharge letter revealed that TGA was not the final diagnosis (n = 12) and for whom no DWI study was available (MRI study not retrievable n = 10, DWI not performed n = 19) were excluded. A total of 198 patients were included (123 women, 75 men, mean age ± SD = 64.7 ± 8.5 years) in the further analysis. For these TGA patients DWI studies with a slice thickness of 3 mm, 5 mm, or 6 mm in the institutes picture archiving and communication system (PACS) were retrieved. After grouping the studies according to DWI slice thickness a total of 47 DWI studies were identified with 3 mm slice thickness, 59 with 5 mm and 92 with 6 mm. The time span in days between onset of TGA symptoms and MRI examination was recorded with day 0 being the day of symptom onset.

The DWI studies were reviewed by two raters (MS and CM) independently for the characteristic small punctuate hyperintensities in the hippocampus on a standard PACS workstation (GE Centricity RA 1000, GE Healthcare Munich, Germany). Both raters noted the occurrence of these signal abnormalities as well as the lesion side (left, right or bilateral), lesion number (single, multiple) and lesion diameter. In six cases the two raters differed regarding the occurrence of a lesion. In all six cases the lesion suspected by one of the raters was small and not well defined. As all six cases were inconclusive the consensus rating was “no hyperintense lesion present”. The raters also noted the type and field strength of the MR scanner used. Most DWI studies (21 out of 27) on the 3 T scanners were performed with a slice thickness (ST) of 3 mm and most of the studies on the 1 T scanner (58 out of 60) were performed with 6 mm ST. Consequently, there was a high correlation between magnetic field strength and slice thickness. Therefore, three different subset analyses were performed. The

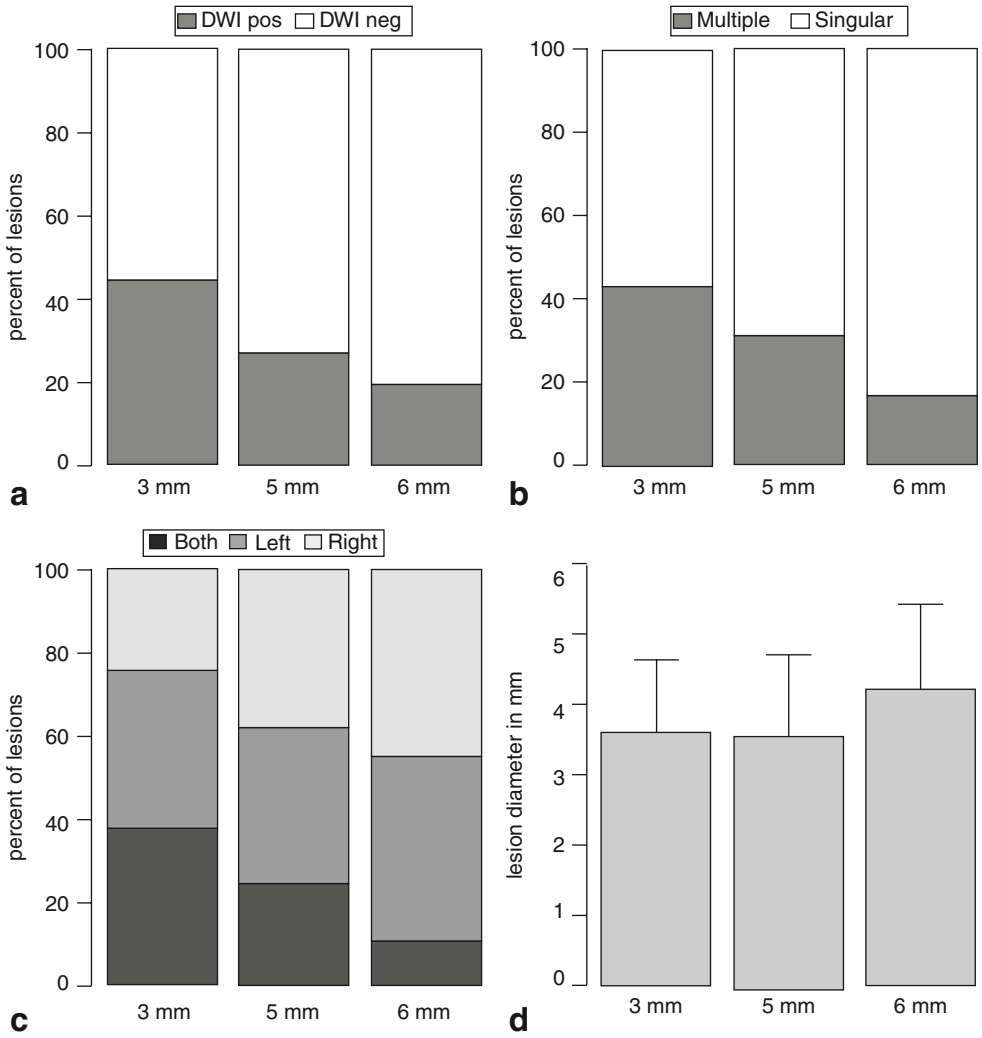

Fig. 2 Comparison of detection rate (**a**), rate of singular versus multiple lesions (**b**), lesion side (**c**) and lesion diameter with mean ± SD (**d**) for the different slice thicknesses

first subset analysis included the data from 1.5 T scanners only (n = 26/54/31 with respect to 3/5/6 mm ST) and another two subset analyses compared the detection rates between 1.5 and 3 T at 3 mm ST and between 1 T and 1.5 T at 6 mm ST.

Statistics

Tests were carried out for the presence of DWI hyperintense lesions, the occurrence of single versus multiple lesions, lesion side as well as for differences in lesion diameter between the three groups. The χ^2-test was used for testing the rate of DWI hyperintense lesions. Due to the small number of observations ($n < 5$) in some cells of the contingency table the Freeman-Halton extension of the Fisher exact test was used for testing group differences with respect to single versus multiple lesions and lesion side. A one-way ANOVA was chosen to test differences in lesion diameter. A p-value < 0.05 was regarded as being significant for all tests.

Results

The group comparison showed a significant increase of detection rates (i.e. approximately 8.4% per millimeter reduction in slice thickness) when smaller slice thicknesses were used. The DWI hyperintense lesions were detected in 44.7% when using an ST of 3 mm, in 27.1% when using 5 mm and in 19.6% when using 6 mm. The detection of bilateral and multiple lesions on a descriptive level increased with smaller slice thickness but did not reach statistical significance. The comparison of lesion diameters also did not reveal a significant difference between groups (Table 1, Fig. 2).

Subset Analysis

A subset analysis of the data from all 1.5 T scanners was performed to rule out magnetic field strength as the decisive factor for the findings. The results of the subset analysis

Table 1 Occurrence rates of diffusion-weighted imaging lesions (number of patients) and lesion diameter (mean±SD) for different slice thicknesses, p-values (uncorrected for multiple comparison)s for χ^2-tests detection rate), Fisher exact test (multiple lesions and lesion side) and one-way ANOVA (lesion diameter)

Patients	Slice thickness			
	3 mm	5 mm	6 mm	*P*-value
With/without diffusion-weighted imaging lesions (detection rate in %)	21/26 (44.7)	16/43 (27.1)	18/74 (19.6)	0.007
Multiple lesions/singular lesion	9/12	5/11	3/15	0.200
Right/left/bilateral lesions	5/8/8	6/6/4	8/8/2	0.392
Lesion diameter (mm)	4.5±1.8	5.1±1.6	5.5±1.2	0.167

Table 2 Results for the subset of studies performed at 1.5 T. Occurrence rates of diffusion-weighted imaging lesions (number of patients) and lesion diameter (mean±SD) for different slice thicknesses, p-values (uncorrected for multiple comparisons) for χ^2-test(detection rate), Fisher exact test (multiple lesions and lesion side) and one-way ANOVA (lesion diameter)

Patients	Slice thickness			
	3 mm	5 mm	6 mm	*P*-value
With/without diffusion-weighted imaging lesions (detection rate %)	13/13 (50.0)	14/40 (25.9)	6/25 (19.4)	0.029
With multiple lesions/with singular lesion	6/7	4/10	2/4	0.720
With right/left/bilateral lesions	3/4/6	5/6/3	0/4/2	0.365
Lesion diameter (mm)	3.8±1.0	3.8±1.1	3.8±1.3	0.930

(Table 2) were very similar to the results for the whole data set (Table 1).

The comparison of 3 mm ST at 1.5 T versus 3 T showed no significant difference in detection rates: 1.5 T (DWI pos/DWI neg=13/13) and 3 T (DWI pos/DWI neg=8/13, χ^2 p=0.60). The same was true for the comparison of 1 T and 1.5 T at 6 mm ST: 1 T (DWI pos/DWI neg=11/47) and 1.5 T (DWI pos/DWI neg=6/25, χ^2 p=0.81). The subset analysis confirmed that reduced slice thickness but not increase in magnetic field strength was responsible for the increased detection rate.

Optimal Time Interval

Regarding the time interval between symptom onset and imaging, the lesion detection rate was highest on day 2 after TGA onset in this data set (Fig. 3).

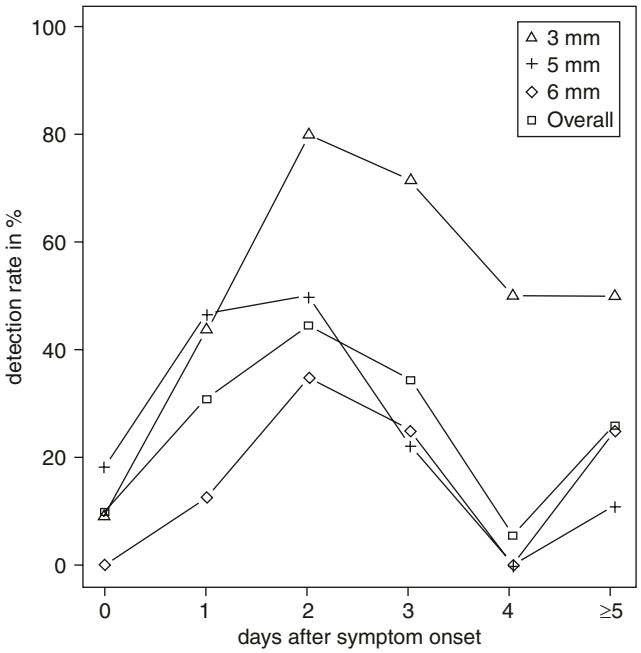

Fig. 3 Detection rate of diffusion-weighted imaging hyperintense lesions for the different slice thicknesses with respect to time, day 0 being the day of symptom onset

Discussion

This study demonstrated the significant impact on detection rates for TGA lesions when adapting slice thickness (approximately 8.4% increase per millimeter reduction in slice thickness) and timing of the MRI study. Transient global amnesia does not have an impact on mortality or morbidity in affected patients and does not represent a risk factor for stroke or ischemic disease [6]. However, a timely diagnosis will help in reassuring the patients and their relatives of the benign character of this subjectively disturbing disorder. The diagnosis of TGA can be established with much greater confidence if the patient shows the characteristic DWI lesions, as comparable punctuate hippocampal DWI hyperintensities may only be rarely seen in PCA stroke [30] but these patients do not present with TGA symptoms and often show further lesions outside the hippocampus.

The overall detection rate in this population with MRI studies using different slice thicknesses as well as varying time spans between symptom onset and MRI studies was only 28%. However, considering the subgroup with 3 mm slice thickness and a 2-day time interval a detection rate as high as 80% was encountered (Fig. 3) which compares well with previous studies using the 3 mm approach [11, 12, 25]. In contrast the use of slices >3 mm and the use of different study time points have resulted in varying detection rates ranging from 0% to 86%. It has been recently shown in a large dataset of 200 TGA patients that DWI has a low diagnostic yield when performed early in the course of TGA [24]. These varying detection rates were more questioning than confirming the evidence of a clear TGA-DWI lesion association and questioning the value of DWI as a diagnostic procedure. This study demonstrated the different influencing factors when using DWI as a diagnostic tool in TGA.

The main limitation of this study is the retrospective analysis of MRI studies obtained outside a controlled prospective study setting. By evaluating all available clinical data (emergency reports and discharge letters) the aim was to include "pure" TGA patients only. Another limitation is that the DWI studies were collected using different scanners from different manufacturers and these factors might have influenced the results. Regarding field strength in the subset analysis a significantly increased detection rate could not be found in the DWI studies performed at higher field strengths. However, an advantage of higher magnetic field strengths to detect small lesions would still be expected due to a higher signal-to-noise ratio. This has been shown in recently published study where the detection rate was significantly higher at 3.0 T compared to 1.5 T [25].

The authors are not aware of any studies investigating TGA with slice thicknesses below 3 mm; however, with an increasing number of imaging centers performing DTI allowing higher resolution studies with slice thicknesses of 2 mm are to be expected. Future work will show if detection rates and sensitivity can be further improved when using slice thicknesses below 3 mm and if hippocampal DWI lesions can be found in almost every TGA patient.

Conclusions

In the context of TGA DWI can be a diagnostic tool with high specificity and high sensitivity. This study corroborates the call for an optimized imaging protocol in order to improve the sensitivity of DWI. It was also shown that MRI should be performed on day 2 after symptom onset and the DWI sequence should have a slice thickness of no more than 3 mm.

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Conflict of Interest No potential conflict of interest relevant to this article is reported.

References

1. Fisher CM, Adams RD. Transient global amnesia. Acta Neurol Scand. 1964;40(Suppl 9):1–83.
2. Santos S, López del Val J, Tejero C, Iñiguez C, Lalana JM, Morales F. Transient global amnesia: a review of 58 cases. Rev Neurol. 2000;30:1113–7.
3. Schreiber SJ, Doepp F, Klingebiel R, Valdueza JM Internal jugular vein valve incompetence and intracranial venous anatomy in transient global amnesia. J Neurol Neurosurg Psychiatr. 2005;76:509–13.
4. Akkawi NM, Agosti C, Rozzini L, Anzola GP, Padovani A. Transient global amnesia and venous flow patterns. Lancet. 2001;357:639.
5. Sander D, Winbeck K, Etgen T, Knapp R, Klingelhöfer J, Conrad B. Disturbance of venous flow patterns in patients with transient global amnesia. Lancet. 2000;356:1982–4.
6. Hodges JR, Warlow CP. The aetiology of transient global amnesia. A case-control study of 114 cases with prospective follow-up. Brain. 1990;113:639–57.
7. Gorji A. Spreading depression: a review of the clinical relevance. Brain Res Brain Res Rev. 2001;38:33–60.
8. Melo TP, Ferro JM, Paiva T. Are brief or recurrent transient global amnesias of epileptic origin? J Neurol Neurosurg Psychiatr. 1994;57:622–5.
9. Hodges JR, Warlow CP. Syndromes of transient amnesia: towards a classification. A study of 153 cases. J Neurol Neurosurg Psychiatr. 1990;53:834–43.
10. Bartsch T, Deuschl G. Transient global amnesia: functional anatomy and clinical implications. Lancet Neurol. 2010;9:205–14.
11. Bartsch T, Alfke K, Stingele R, Rohr A, Freitag-Wolf S, Jansen O, et al. Selective affection of hippocampal CA-1 neurons in patients with transient global amnesia without long-term sequelae. Brain. 2006;129:2874–84.
12. Weon Y, Kim J, Lee J, Kim S. Optimal diffusion-weighted imaging protocol for lesion detection in transient global amnesia. AJNR Am J Neuroradiol. 2008;29:1324–8.
13. Sedlaczek O, Hirsch JG, Grips E, Peters CNA, Gass A, Wöhrle J, et al. Detection of delayed focal MR changes in the lateral hippocampus in transient global amnesia. Neurology. 2004;62:2165–70.
14. Toledo M, Pujadas F, Grivé E, Alvarez-Sabin J, Quintana M, Rovira A. Lack of evidence for arterial ischemia in transient global amnesia. Stroke. 2008;39:476–9.
15. Enzinger C, Thimary F, Kapeller P, Ropele S, Schmidt R, Ebner F, et al. Transient global amnesia: diffusion-weighted imaging lesions and cerebrovascular disease. Stroke. 2008;39:2219–25.
16. Lee HY, Kim JH, Weon Y-C, Lee JS, Kim SY, Youn SW, et al. Diffusion-weighted imaging in transient global amnesia exposes the CA1 region of the hippocampus. Neuroradiology. 2007;49:481–7.
17. Strupp M, Brüning R, Wu RH, Deimling M, Reiser M, Brandt T. Diffusion-weighted MRI in transient global amnesia: elevated signal intensity in the left mesial temporal lobe in 7 of 10 patients. Ann Neurol. 1998;43:164–70.
18. Winbeck K, Etgen T, von Einsiedel HG, Röttinger M, Sander D. DWI in transient global amnesia and TIA: proposal for an ischaemic origin of TGA. J Neurol Neurosurg Psychiatr. 2005;76:438–41.
19. Woolfenden AR, O'Brien MW, Schwartzberg RE, Norbash AM, Tong DC. Diffusion-weighted MRI in transient global amnesia precipitated by cerebral angiography. Stroke. 1997;28:2311–4.
20. Ay H, Furie KL, Yamada K, Koroshetz WJ. Diffusion-weighted MRI characterizes the ischemic lesion in transient global amnesia. Neurology. 1998;51:901–3.
21. Greer DM, Schaefer PW, Schwamm LH. Unilateral temporal lobe stroke causing ischemic transient global amnesia: role for diffusion-weighted imaging in the initial evaluation. J Neuroimaging. 2001;11:317–9.
22. Matsui M, Imamura T, Sakamoto S, Ishii K, Kazui H, Mori E. Transient global amnesia: increased signal intensity in the right hippocampus on diffusion-weighted magnetic resonance imaging. Neuroradiology. 2002;44:235–8.
23. Cianfoni A, Tartaglione T, Gaudino S, Pilato F, Saturno E, Tonali PA, et al. Hippocampal magnetic resonance imaging abnormalities in transient global amnesia. Arch Neurol. 2005;62:1468–9.

24. Ahn S, Kim W, Lee Y-S, Kim WY, Lee JH, Oh BJ, et al. Transient global amnesia: seven years of experience with diffusion-weighted imaging in an emergency department. Eur Neurol. 2011;65:123–8.
25. Ryoo I, Kim JH, Kim S, Choi BS, Jung C, Hwang SI. Lesion detectability on diffusion-weighted imaging in transient global amnesia: the influence of imaging timing and magnetic field strength. Neuroradiology. 2011. http://www.ncbi.nlm.nih.gov/pubmed/21603902.
26. Gass A, Gaa J, Hirsch J, Schwartz A, Hennerici MG. Lack of evidence of acute ischemic tissue change in transient global amnesia on single-shot echo-planar diffusion-weighted MRI. Stroke. 1999;30:2070–2.
27. Huber R, Aschoff AJ, Ludolph AC, Riepe MW. Transient global amnesia. Evidence against vascular ischemic etiology from diffusion weighted imaging. J Neurol. 2002;249:1520–4.
28. Ay H, Buonanno FS, Rordorf G, Schaefer PW, Schwamm LH, Wu O, et al. Normal diffusion-weighted MRI during stroke-like deficits. Neurology. 1999;52:1784–92.
29. Budson AE, Schlaug G, Briemberg HR. Perfusion- and diffusion-weighted magnetic resonance imaging in transient global amnesia. Neurology. 1999;53:239–40.
30. Szabo K, Förster A, Jäger T, Kern R, Griebe M, Hennerici MG, et al. Hippocampal lesion patterns in acute posterior cerebral artery stroke: clinical and MRI findings. Stroke. 2009;40:2042–5.