therapy may also suggest that the first course of chemotherapy in these patients served to sensitize them to the drugs.

Our observations suggest that treatment with both 5-FU and cisplatin could be responsible for ischemic stroke in patients with oropharyngeal carcinoma, but this suggestion should be taken cautiously because it is based on anecdotal observations, and not all patients had intracranial vessel examination and none were connected to a cardiac monitor at the time of drug infusion to detect transient atrial fibrillation. However, due to the wide use of cisplatin and 5-FU, detailed prospective studies should be performed to determine factors that may be responsible for this potential complication of chemotherapy for head and neck cancer.

Received March 25, 1997. Accepted in final form May 16, 1998.

Address correspondence to Dr. Pierre Amarenco, Service de Neurologie, Hôpital Lariboisière, 2 rue Ambroise Paré, 75475 Paris Cedex 10, France.

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# Diffusion-weighted MRI characterizes the ischemic lesion in transient global amnesia

Article abstract—We present a patient with transient global amnesia (TGA) whose diffusion-weighted MRI (DWI) showed increased signal in the splenium of the corpus callosum and in the left parahippocampal gyrus. The absence of high signal on the corresponding apparent diffusion coefficient (ADC) images supports the diagnosis of an acute infarction. This finding provides a temporal relation between cerebral ischemia and infarction in the territory of posterior cerebral artery and in certain cases of TGA. An early means of detecting ischemia in TGA by DWI may influence clinical decisions made in patient evaluation and management.

NEUROLOGY 1998;51:901-903

Hakan Ay, MD; Karen L. Furie, MD, MPH; Kei Yamada, MD; and Walter J. Koroshetz, MD

Transient global amnesia (TGA) is a syndrome involving temporary loss of anterograde and retrograde memory, usually accompanied by repetitive questioning and temporal disorientation.<sup>1</sup> Alertness, attention, self-identity, and the ability to carry out complex manual tasks are preserved with no other focal neurologic accompaniments. The amnesia usually starts and ends abruptly, leaving a lapse in memory for the events that occurred during the attack.

Although ischemic insult to the memory-related structures is one of the most commonly proposed mechanisms, it has not been possible to demonstrate radiographically an infarction in every case. Moreover, neither CT scan nor standard MRI are able to establish a temporal or causal relation between infarction and symptoms accurately. Diffusion-weighted imaging (DWI), however, detects ischemic lesions in the hyperacute phase and thereby provides a rapid and accurate means of diagnosis. In this report, we describe a patient with pure TGA in whom DWI showed an acute ischemic lesion. DWI appears useful in documenting the etiology and clinicoanatomic correlates of this multifactorial syndrome.

**Case report.** The patient was a 62-year-old, righthanded man with no vascular risk factors who after skiing for 4 hours was unable to recall where he was. The family

From the Departments of Neurology (Drs. El Amrani, Bousser, and Amarenco), Saint-Antoine Hospital, and Tenon Hospital (Drs. Heinzlef and Roullet), Pierre and Marie Curie University, Paris; Delafontaine Hospital (Dr. Debroucker), Saint-Denis; and the Department of Neurology (Drs. El Amrani, Bousser, and Amarenco), Lariboisière Hospital, Paris, France.

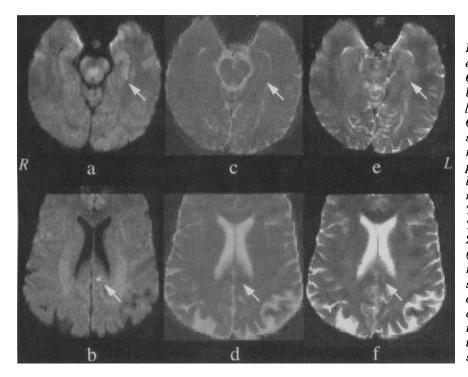


Figure. (a) Axial single-shot isotrophic echo-planar DWI (time to repeat [TR], 6,000 ms; time to echo [TE], 118 ms; b-value, 1,221 s/mm<sup>2</sup>; field of view [FOV],  $40 \times 20$  cm; matrix,  $256 \times 128$ ; 6-mm slice with 1-mm gap; 1 NEX) shows a region of slightly increased signal intensity in the left parahippocampal gyrus. There was no corresponding lesion on (c), the axial ADC map (parameters as in DWI), or (e), the axial T2-weighted MR image (TR, 4,200 ms; TE, 102 ms; FOV,  $20 \times 20$  cm; matrix,  $256 \times 256$ ; 5-mm slice with 1-mm gap). (b) Axial DWI shows a hyperintense signal in the splenium of the corpus callosum on the left. (d) The ADC map is apparently normal and does not show any increased signal in the corresponding region. (f) T2-weighted image is notable for a subtle hyperintensity in the splenium.

reported that he anxiously repeated questions about where he was and how he had gotten there. He was able to identify himself and immediate family members, and otherwise seemed normal, not registering any other neurologic complaints. The patient had no preceding illness or emotional stress, nor had he witnessed trauma while skiing. Taken immediately to a local hospital, his inability to retain new information persisted. A noncontrast head CT scan was reported as normal. He could not remember what he was told during the following 5 hours.

The patient arrived at the Massachusetts General Hospital approximately 12 hours after he had started skiing. The neurologic examination was normal, and he had regained the ability to make new memories. However, he never retrieved memory for any event during the 4 hours of skiing.

An immediate MRI study showed a small region of increased signal intensity on T2-weighted images in the left splenium of the corpus callosum (figure, f). There was a corresponding hyperintense signal on DWI (figure, b). The lesion was not large enough for apparent diffusion coefficient (ADC) calculations, but there was no increased signal intensity on the ADC maps (figure, d). A subtle hyperintensity in the left parahippocampal gyrus was also present on DWI (figure, a), but it was not possible to identify a corresponding lesion on either ADC or T2 images (figure, c and e). Magnetic resonance angiography (MRA) of the Circle of Willis and phase contrast MRA through the neck were unremarkable. Transthoracic echocardiography, 24holter monitoring, and hypercoagulable workup were negative. The deficit was presumed secondary to an embolus from a cryptogenic source. The patient was anticoagulated acutely and remained completely asymptomatic. He was discharged taking aspirin, 325 mg/day.

**Discussion.** Ischemia in the territory of the posterior cerebral artery (PCA) has been proposed as one cause of TGA. Infarctions most often involve the

thalamus<sup>2</sup> or the hippocampus, but a single case of occipital lobe infarction also has been reported.<sup>3</sup> In addition to the very subtle parahippocampal lesion in our patient, the more prominent splenial lesion must also be considered as clinically relevant. Retrograde and anterograde amnesia due to a small hemorrhage in this region has previously been described.<sup>4</sup> The retrosplenial cortex provides an alternative route for the reciprocal connections between the medial temporal structures involved in memory and the anterior thalamus (Papez circuit).<sup>4</sup>

Previous CT and MRI studies showed an association between TGA and cerebral infarction, but were unable to establish a direct causal relation because of their relative inability to detect small lesions within the first 24 hours. It is also difficult to determine the age of a small infarction in the subacute phase accurately. This limitation may be mitigated by the advent of physiologic imaging by diffusionand perfusion-weighted MRI.

In ischemic lesions, DWI signal intensity increases due to both an increase in T2 and a decrease in the ADC of water protons.<sup>5</sup> The ADC begins to decrease as energy stores are depleted in cerebral ischemia. Low ADC leads to DWI brightness within minutes of cytotoxic edema and neural dysfunction.<sup>5</sup> DWI signal intensity in infarction increases over hours as T2 signal intensity increases. This leads to a very high signal-to-noise ratio, improving the detection of small lesions. In our patient, increased signal intensity on DWI, isointensity on the ADC maps, and subtle hyperintensity on T2 images in the left splenium support the occurrence of an ischemic event around the onset of amnesia.

Woolfenden et al.<sup>6</sup> reported a patient with TGA and acute bilateral mesial temporal infarctions

shown by DWI. In contrast to the focal abnormalities in both our case and Woolfenden et al.'s, Strupp et al.<sup>7</sup> reported a widespread and subtle increase in the DWI signal intensity in the hippocampus in 7 of 10 TGA patients, bilaterally in 3. Concurrent T2weighted sequences were normal, even in those scanned during the subacute phase. DWI abnormalities completely reversed on follow-up scans. ADC changes were not reported. In our case, we described different DWI characteristics in a TGA patient that are more consistent with focal ischemia. In light of our case and that of Woolfenden et al. with focal lesions, and Strupp at al.'s disparate diffuse temporal findings, we propose that TGA is a pathophysiologically heterogenous syndrome.

In patients presenting with acute, focal, neurologic deficits conforming to a specific vascular territory, a corresponding lesion bright on DWI and dark on ADC strongly favors a diagnosis of ischemic stroke.<sup>8</sup> However, such reversible MRI lesions have been reported in some paroxysmal events such as focal status epilepticus and spreading depression in animals, but not in patients during a migrainous visual aura.9 Reversibility of DWI signal after clinical improvement in stroke patients is very rare, especially when the ischemic stroke has progressed to the stage of increased T2 signal intensity. In our patient, persistence of increased signal intensity on DWI (almost 6 hours after the resolution of amnesia); corresponding T2 hyperintensity; localization mainly in the white matter (splenium); no history of migraine, epilepsy, or previous episodes; prolonged duration of amnesia (more than 1 hour); and absence of any impairment of consciousness or focal seizure activity make a primary migrainous or epileptic etiology seem less likely.

It is conceivable that ischemia may cause neurologic symptoms by generating waves of spreading depression or by serving as an epileptic focus. Regarding the former possibility, Eustache et al.<sup>10</sup> reported a patient in whom PET findings were consistent with spreading depression in the left lateral frontal cortex at the time of a TGA attack. However, there was also a small region of oligemia in the left occipital cortex, suggesting that an infarction was the underlying event.

Because both lesions in our case occurred in the PCA territory, a reversible widespread hypoperfusion in the medial temporal cortex may have been present when the patient was symptomatic. In some stroke patients, we have seen small DWI-bright lesions appear in brain regions where perfusion MR demonstrates more widespread, slowed passage of gadolinium.

Future reports of TGA patients combining diffusion- with perfusion-weighted imaging are necessary to delineate the exact clinicoanatomic location of the lesion and the pathophysiology in this heterogenous syndrome. Functional MRI may become a useful tool for identifying the subset of patients with TGA due to ischemia from those with a more benign cause.

Received March 3, 1998. Accepted in final form May 1, 1998. Address correspondence and reprint requests to Dr. Karen L. Furie, Department of Neurology-Stroke Service, VBK-802, Massachusetts General Hospital, 32 Fruit Street, Boston, MA 02114.

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From the Stroke Service of the Neurology Department (Drs. Ay, Furie, and Koroshetz) and Neuroradiology Division (Dr. Yamada), Massachusetts General Hospital, Harvard Medical School, Boston, MA.



### Diffusion-weighted MRI characterizes the ischemic lesion in transient global amnesia Hakan Ay, Karen L. Furie, Kei Yamada, et al. *Neurology* 1998;51;901-903 DOI 10.1212/WNL.51.3.901

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