

- fissure on axial CT: II. Recognition and differentiation of interhemispheric subarachnoid hemorrhage and subdural hemorrhage. *Am J Neuroradiol* 1982;3:635-642
7. Spiegel SM, Fox AJ, Vinuela F, et al. Increased density of tentorium and falx: a false positive CT sign of subarachnoid hemorrhage. *J Can Assoc Radiol* 1986;37:243-247
 8. Mendelson DB, Moss ML, Chason DP, et al. Acute purulent leptomenigitis mimicking subarachnoid hemorrhage on CT. *J Computer Assisted Tomography* 1994;18:126-128
 9. Eckel TS, Beiter SN, Monsein LH. Subarachnoid contrast enhancement after spinal angiography mimicking diffuse subarachnoid hemorrhage. *AJR* 1998;170:503-505
 10. Noguchi K, Ogawa T, Seto H, et al. Subacute and chronic subarachnoid hemorrhage: diagnosis with fluid-attenuated inversion-recovery MR imaging. *Radiology*. 1997;203:257-262
 11. Singer MB, Atlas SW, Drayer BP. Subarachnoid space disease: diagnosis with fluid-attenuated inversion-recovery MR imaging and comparison with gadolinium-enhanced spin-echo MR imaging—blinded reader study. *Radiology*. 1998;208:417-422
 12. Ishii K, Onuma T, Kinoshita T, et al. Brain death: MR and MR angiography. *Am J Neuroradiol* 1996;17:731-735
 13. Orrison WW Jr, Champlin AM, Kesterson OL, et al. MR 'hot nose sign' and 'intravascular enhancement sign' in brain death. *Am J Neuroradiol* 1994;15:913-916

Evolution of Temporal Lobe Hypoperfusion in Transient Global Amnesia: A Serial Single Photon Emission Computed Tomography Study

Tudor G. Jovin, MD
Richard A. Vitti, MD
Leo F. McCluskey, MD

ABSTRACT

Previous functional neuroimaging studies performed during transient global amnesia (TGA) have not answered the central

question regarding the etiology of TGA, namely: whether the observed hypoperfusion in the mesial temporal lobe structures reflects a primarily ischemic process or whether it represents a secondary phenomenon resulting from locally decreased metabolism. The authors performed Tc 99m-bicisate brain single photon-emission computed tomography (SPECT) scanning in a 66-year-old man during an episode of TGA, 24 hours after the episode and 3 months after the episode. To the authors' knowledge, this is the only reported study in which a follow-up SPECT scan was performed within 24 hours. The initial study showed bilateral mesial temporal lobe hypoperfusion that partially resolved after 24 hours and returned to normal at 3 months. Resolution of the SPECT scan abnormalities correlated well with resolution of the memory loss. These findings agree with previously reported SPECT, positron-emission tomography (PET), and diffusion magnetic resonance imaging (MRI) studies that indicate the mesial temporal lobe structures as the major site of pathology in TGA. The authors suggest that a process causing decreased local metabolism, such as cortical spreading depression, constitutes the primary pathophysiologic mechanism in this case.

Key words: Transient global amnesia, brain SPECT, bilateral medial temporal lobe hypoperfusion.

Jovin TG, Vitti RA, and McCluskey LF. Evolution of Temporal Lobe Hypoperfusion in Transient Global Amnesia: A Serial Single Photon Emission Computed Tomography Study. *J Neuroimaging* 2000;10:238-241.

Received January 24, 1999; accepted April 13, 2000.

From the Departments of Neurology (T.G.J., L.F.M.) and Nuclear Medicine (R.A.V.), University of Pennsylvania Health System, Pennsylvania Hospital, Philadelphia PA.

Address correspondence to T Jovin, M.D., UPMC Health System, Stroke Institute, UPMC Presbyterian, Suite C400, 200 Lothrop St., Pittsburgh, PA 15213-2582.

The etiology of transient global amnesia is still unclear. The most widely accepted of the mechanisms proposed so far are Leao's spreading depression, thromboembolic cerebrovascular disease, and epilepsy (1).

Recent advances in understanding the pathophysiology of TGA have been possible largely because of functional neuroimaging studies (single photon-emission computed tomography (SPECT), positron-emission tomography (PET) and diffusion magnetic resonance imaging (MRI)) performed acutely during episodes of transient global amnesia (2-13). Most of the reported studies seem to indicate the left mesial temporal lobe structures as the main site of the pathologic process in TGA. Other accompanying abnormal areas have also been described.

Because none of the previous reports describe early follow-up imaging, a correlation between the imaging abnormalities and the clinical course has not been firmly established. We present a case study of a patient in whom perfusion deficits in the mesial temporal lobes resolved in parallel to his clinical course.

Case Presentation

A 66-year-old, right-handed man was seen in the emergency room because of acute onset of memory loss. He was well until the morning of admission. He had sexual intercourse, and shortly thereafter his wife noticed that he did not recall any events of the previous 2 days. He was then taken to the hospital where he arrived approximately 2 hours after the onset of his memory impairment.

He was fully awake and alert, appeared perplexed, and was asking repetitive questions about his immediate circumstances. He was oriented to person and place but not to time. He had a dense retrograde amnesia for events that had occurred within the last 2 days and patchy memory loss for events prior to that. Immediate memory was intact, but he could not recall any of the three words presented to him after 1 minute even after multiple repetitions of the same three words. Calculations, abstractions, and reasoning were intact. The results for the rest of the neurologic examination and the general physical examination were normal.

He had a history of a myocardial infarction (MI) and coronary bypass surgery in the distant past. There was no history of migraine, epilepsy, head trauma, or any other neurologic disease.

He was generally enjoying excellent health prior to his presentation. He denied excessive alcohol consumption or any recreational drug intake.

The patient thus fulfilled all the diagnostic criteria for transient global amnesia defined as follows (14):

1. The attack must be witnessed.
2. Clear-cut anterograde amnesia during the attack must be present.
3. Clouding of consciousness and loss of personal identity must be absent and the cognitive impairment must be limited to amnesia.
4. There should be no accompanying focal neurologic symptoms.
5. Epileptic seizures must be absent
6. Attacks must be resolved within 24 hours.
7. Patients with recent head injury or known active epilepsy are excluded.

He underwent radionuclide brain SPECT scanning 4 hours after presentation while he was still severely amnesic (Figure 1, Day 1). Approximately 8 hours after onset of his symptoms, his memory started resolving gradually with more distant memories returning first. He had a

dense persistent memory loss for the duration of the amnesic episode. By the next morning when he underwent the second radionuclide brain SPECT scan (Figure 1, Day 2), all the mental state abnormalities noted on the previous day were resolved except for mild impairment of short-term memory recall (one out of three objects missed at 5 minutes).

A cranial computed tomographic (CT) scan performed acutely did not show any acute lesions. Results of a brain MRI consisting of sagittal and axial T1-weighted images, axial and coronal proton-density and T2-weighted images, and axial fluid attenuated inversion recovery (FLAIR) scans performed the following day revealed a very small old cerebellar infarct and were otherwise unremarkable. Specifically, the temporal lobe areas and hippocampi appeared normal bilaterally. Results of a magnetic resonance angiographic (MRA) scan of the Circle of Willis were normal. Results of carotid, vertebral, and transcranial Doppler examinations were normal.

The patient was seen in follow-up in the office at 3 months. He subjectively continued to do well and had a normal

mental state examination. Around that time, the third radionuclide brain SPECT scan was performed (Figure 1, Day 90).

SPECT Imaging

Cerebral SPECT was performed as follows: peripheral intravenous access was obtained using a small-gauge angiocatheter. The patient was placed supine in a dimly lit room for at least 5 minutes and was then injected with 925 mBq (25 mCi) technetium-99m-bicisate dihydrochloride (Neurolite) (DuPont; Billerica, MA) and allowed to rest for another 5 minutes. The patient then underwent cerebral imaging using a dual-headed gamma camera (ADAC Vertex system) (ADAC; San Jose, CA), 128 images at 30 seconds per image, 3° arc. The raw images were filtered and attenuation-corrected, and 1-centimeter slices were reconstructed along the orbital-meatal line in the transaxial, coronal, and sagittal planes (Figure 1).

Isovolume regions of interest were drawn according to anatomic templates, and the mean count rates for each region of interest (ROI) were obtained in the following areas: mesial temporal lobe, frontal lobe, caudate nucleus for each hemisphere, and cerebellum (Figure 2). Because comparison to the contralateral ROI was not possible, the cerebellum was used as a reference and the ratios of the ROI mean counts:cerebellum mean counts were obtained (Table 1). The mesial temporal lobe area, because of its normally low perfusion and its poor delineation with dual-headed SPECT cameras, was considered normal when the ratio was >0.7 . This corresponds to findings reported by previous investigators (15), who have found mean ratios of 0.76 in healthy individuals.

Findings

There is severe hypoperfusion within the mesial temporal areas during the attack. The observed hypoperfusion resolves only partially at 24 hours. At 90 days the uptake in the left mesial temporal lobe has normalized, whereas on the contralateral side, it remains slightly below the normal range (Table 1). This borderline abnormal uptake in the right mesial temporal lobe may reflect the previously reported decline with age of regional cerebral blood flow in the inferior temporal lobe in healthy persons, which can be asymmetric (16). Alternatively, it may be caused by a structural abnormality not detected by MRI or by a slower recovery process of the right mesial temporal lobe than of the left.

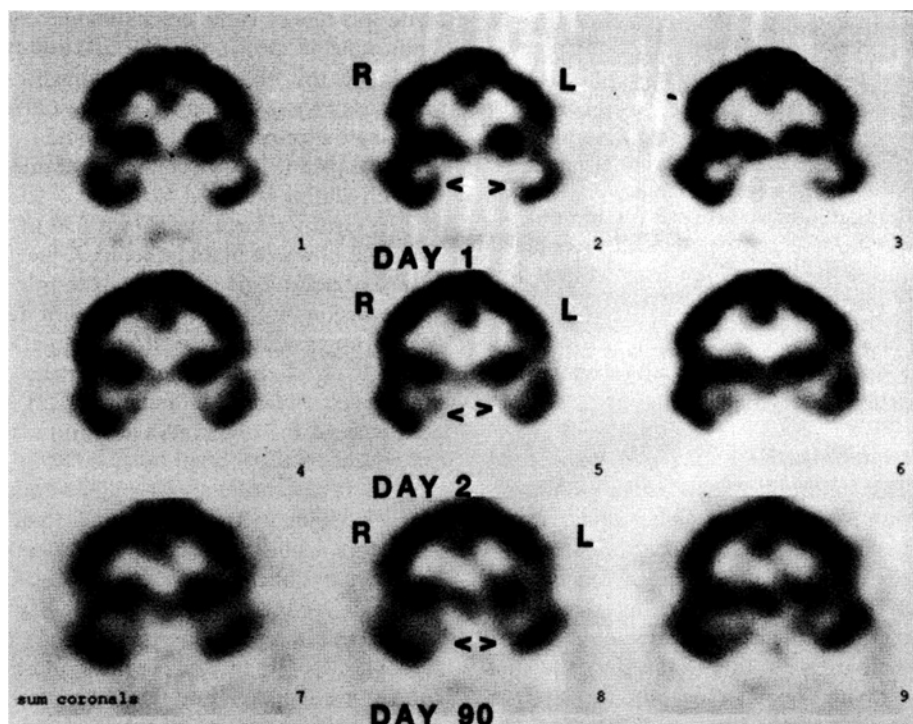


Figure 1. Brain SPECT coronal 1-cm sections through the brain from anterior to posterior. Day 1. There is diminished radiotracer uptake within the temporal lobes bilaterally, most prominently in the mesial temporal areas (open arrows), representing diminished perfusion. The remainder of the cerebral hemispheres, basal ganglia, and cerebellum is normal. Day 2. Repeat study obtained 24 hours later. Coronal sections in the same projection. There is improvement of uptake in both temporal lobes. Day 90. Follow-up study at 3 months. Coronal sections in the same projection. Uptake has normalized in the temporal lobes.

CHART A

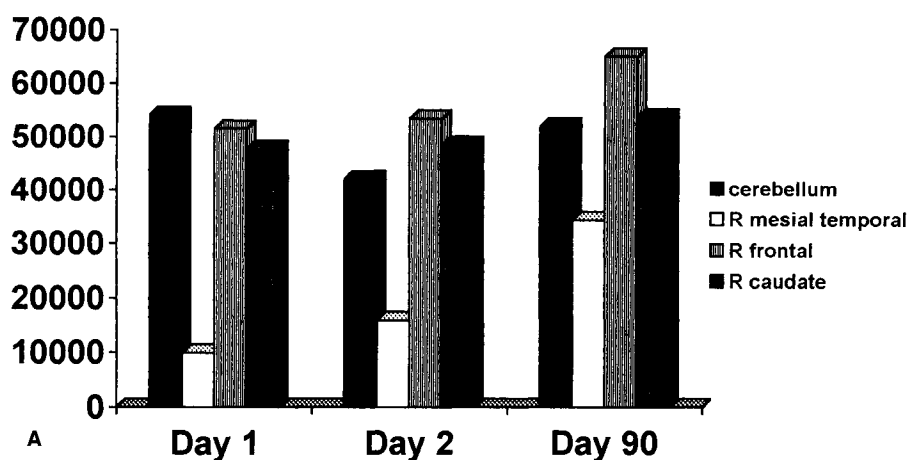


CHART B

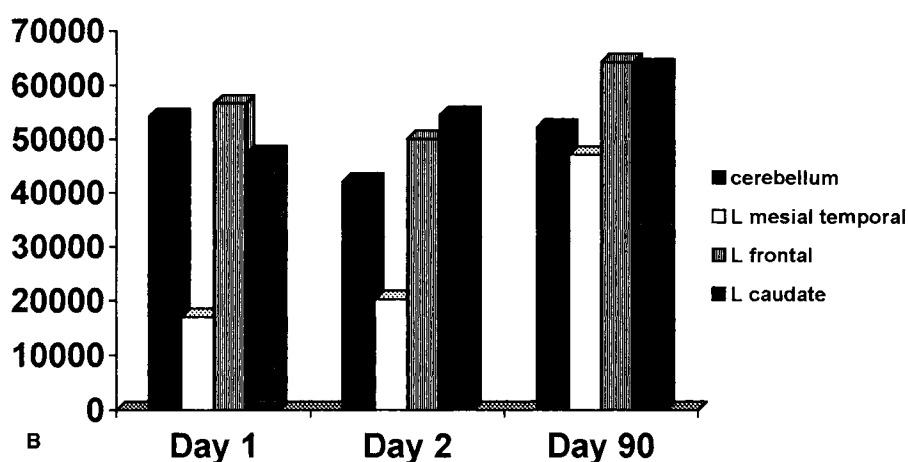


Figure 2. (A) Tc-99 uptake in the right hemisphere compared to the cerebellum. (B) Tc-99 uptake in the left hemisphere compared to the cerebellum. The numbers on the y-axis represent mean counts for each region of interest (ROI).

The increased uptake in the frontal lobes may reflect frontal lobe hyperperfusion, which has been reported previously (17). Alternatively, it may represent an artifact, because artifactually increased frontal lobe uptake with dual-headed

Table 1. Mean Counts for Each ROI Are Expressed as Ratio to Cerebellar Mean Counts

	Day 1	Day 2	Day 90
Left mesial temporal	0.31	0.48	0.90
Right mesial temporal	0.18	0.37	0.66
Left frontal	1.04	1.19	1.23
Right frontal	0.95	1.27	1.25
Left caudate	0.87	1.29	1.21
Right caudate	0.88	1.15	1.03

ROI = region of interest.

SPECT scanning is a well-recognized problem (18).

Discussion

This report characterizes the pathologic process in transient global amnesia for two reasons. First, it identifies an anatomic site for the described functional deficit, and second, it defines the time course of the observed anatomic abnormalities in relation to the clinical course.

With regard to location, this study is in agreement with findings reported from previous functional neuroimaging studies that identify the medial structures of the left temporal lobe as the major site of pathology in TGA (Table 2). Our results are similar to those reported by Stilhard et al (4), Evans et al (9), and Tanabe et al (11) and is the fourth report of bilateral mesial temporal lobe hypoperfusion

on brain SPECT during TGA, supporting the idea that the pathologic process is bilateral in TGA. In contrast, most of the other functional neuroimaging studies performed during TGA have shown decreased perfusion only in the left temporal lobe, accompanied in some cases by abnormal perfusion in areas other than the temporal lobes (Table 2). The predominance of abnormalities in the left mesial temporal lobes is of unclear significance. The generally accepted view is that for amnesia to occur, dysfunction of bilateral medial temporal lobe structures is required. It has been postulated that bilateral mesial temporal lobe dysfunction does in fact occur, but that, for unknown reasons, the abnormalities in the left temporal lobe last longer (13).

Regarding the nature of the initiating event in TGA, there are currently two major hypotheses; one hypothesis favors ischemia as the primary process. However, epidemiologic data showing that vascular risk factors are no more frequently present in TGA patients than in the general population is not in favor of this hypothesis (14,19). The second hypothesis favors spreading depression as the initiating event in TGA. Compatible with this theory is the epidemiologic data indicating an association of TGA with migraine, the aura of which is thought to be caused by spreading depression (20).

Single positron-emission computed tomographic (SPECT) studies performed acutely during transient ischemic attacks (TIAs) and strokes have shown that in patients in which brain ischemia is the cause of neurologic deficits, severe hypoperfusion on SPECT (<70% count densities compared to the contralateral ROI) as early as 6 hours after onset of symptoms is predictive of infarction (21,22). In our patient, the observed hypoperfusion of both medial temporal lobes on SPECT and its persistence after 24 hours without corresponding MRI abnormalities argues therefore against ischemia as the cause of memory dysfunction. Also arguing against ischemia are the normal flow velocities in all vascular territories on transcranial Doppler, the absence of carotid stenosis on carotid Doppler, and the fact that observed hypoperfusion did not respect any vascular territory.

The method we used for assessment of cerebral blood flow does not permit any conclusions as to whether the observed hypoperfusion reflects primarily ischemia versus primarily hypometabolism. However, our findings of prolonged hypoperfusion in the absence of structural lesions

Table 2. Findings From the Literature on Neuroimaging Studies Performed During Transient Global Amnesia, With Respect to Temporal Lobe Hypoperfusion*

	PET	DW MRI	SPECT
Number of reported cases	1	1	17
No. cases with decreased perfusion in L temporal lobe and normal R temporal lobe	1/1	0/1	9/17
No. cases with decreased perfusion in R temporal lobe and normal L temporal lobe	0/1	0/1	1/17
No. of cases with abnormal bilateral temporal lobes	0/1	1/1	3/17
No. cases with decreased perfusion in other areas (cortex, thalamus, striatum)	1/1	0/1	8/17

PET = positron emission tomography; DW MRI = diffusion-weighted magnetic resonance imaging; SPECT = single photon emission computed tomography; L = left; R = right.

*The present case report is not included in the table.

could be better explained by a primarily hypometabolic event such as spreading depression, which consists of a short lasting depolarization wave, followed by neuronal depression and regionally decreased blood flow (20). The dynamic nature of spreading depression could explain why areas in the brain other than the temporal lobe displayed abnormalities on SPECT, PET, and diffusion-weighted MRI scanning in other reported studies. The depolarization wave is known to travel across the cortex at a rate of 3–5 mm/min. Therefore, it is likely that each of those reported studies represents a snapshot of the same process at different stages.

References

- Hodges JR. Unraveling the enigma of transient global amnesia. *Ann Neurol* 1998;43:151–3
- Schmidtke K, Reinhardt M, Krause T. Cerebral perfusion during transient global amnesia: findings with HM-PAO SPECT. *J Nucl Med* 1998;39:155–9
- Sakashita Y, Sugimoto T, Taki S, et al. Abnormal cerebral blood flow following transient global amnesia. *J Neurol Neurosurg Psychiatry* 1993;56:1327
- Stillhard G, Landis T, Schiess R, et al. Bitemporal hypoperfusion in transient global amnesia: 99m-Tc-HM-PAO SPECT and neuropsychological findings during and after an attack. *J Neurol Neurosurg Psychiatry* 1990;53:339–42
- Jung HH, Baumgartner RW, Burgunder JM, et al. Reversible hyperperfusion of the right medial temporal lobe in transient global amnesia. *J Neurol Neurosurg Psychiatry* 1996;61:654–5
- Matsuda H, Higashi S, Tsuji S, et al. High resolution Tc-99m HMPAO SPECT in a patient with transient global amnesia. *Clin Nucl Med* 1993;18:46–9
- Lin KN, Liu RS, Yeh TP, et al. Posterior ischemia during an attack of transient global amnesia. *Stroke* 1993;24:1093–5
- Goldenberg G, Podreka I, Pfaffelmeyer N, et al. Thalamic ischemia in transient global amnesia: a SPECT study. *Neurology* 1991;41:1748–52
- Evans J, Wilson B, Wraight EP, et al. Neuropsychological and SPECT scan findings during and after transient global amnesia: evidence for the differential impairment of remote episodic memory. *J Neurol Neurosurg Psychiatry* 1993;56:1227–30
- Sakashita Y, Kanai M, Sugimoto T, et al. Changes in cerebral blood flow and vasoreactivity in response to acetazolamide in patients with transient global amnesia. *J Neurol Neurosurg Psychiatry* 1997;63:605–10
- Tanabe H, Hashikawa K, Nakagawa Y, et al. Memory loss due to transient hypoperfusion in the medial temporal lobes including hippocampus. *Acta Neurol Scand* 1991;84:22–7
- Eustache F, Desgranges B, Petit-Taboue MC, et al. Transient global amnesia: implicit/explicit memory dissociation and PET assessment of brain perfusion and oxygen metabolism in the acute stage. *J Neurol Neurosurg Psychiatry* 1997;63:357–67
- Strupp M, Bruning R, Wu RH, et al. 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
- Hodges JR, Warlow CP. Syndromes of transient amnesia: towards a classification. A study of 153 cases. *J Neurol Neurosurg Psychiatry* 1990;53:834–43
- Ohnishi T, Hoshi H, Nagamachi S, et al. High-resolution SPECT to assess hippocampal perfusion in neuropsychiatric diseases. *J Nucl Med* 1995;36:1163–9
- Shaw TG, Mortel KF, Meyer JS, et al. Cerebral blood flow changes in benign aging and cerebrovascular disease. *Neurology* 1984;34:855–62
- Matsuda H, Tsuji S, Shuke N, et al. Noninvasive measurements of regional cerebral blood flow using technetium-99m hexamethylpropylene amine oxime. *Eur J Nucl Med* 1993;20:391–401
- Mathew RJ. Hyperfrontality of regional cerebral blood flow distribution in normals during resting wakefulness: fact or artifact? *Biol Psychiatry* 1989;26:717–24
- Zorzon M, Antonutti L, Mase G, et al. Transient global amnesia and transient ischemic attack. Natural history, vascular risk factors and associated conditions. *Stroke* 1995;26:1536–42
- Lauritzen M. Pathophysiology of the migraine aura. The spreading depression theory. *Brain* 1994;117(Pt 1):199–210
- Berrouschot J, Barthel H, Hesse S, et al. Differentiation between transient ischemic attack and ischemic stroke within the first six hours after onset of symptoms by using 99mTc-ECD-SPECT. *J Cereb Blood Flow Metab* 1998;18:921–9
- Shimosegawa E, Hatazawa J, Inugami A, et al. Cerebral infarction within six hours of onset: prediction of completed infarction with technetium-99m-HMPAO SPECT. *J Nucl Med* 1994;35:1097–103

Reduction of Carotid Arterial Blood Flow in Ventricular Septal Defect Associated With Severe Congestive Heart Failure

Masanobu Kojo
Katsuhiko Yamada
Shinnosuke Akiyoshi
Miwako Maeda
Keisuke Sato
Tatsuro Izumi

ABSTRACT

After diagnosing abnormality of cardiac and carotid–cerebral circulation in an infant with isolated ventricular septal defect