SPECT in Patients With Cortical Visual Loss

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Single-photon emission computed tomography (SPECT) with ^{99m}Tc-hexamethyl propyleneamine oxime (HMPAO) was used to investigate changes in cerebral blood flow in seven patients with cortical visual impairment. Traumatic brain injury (TBI) was the cause of cortical damage in two patients, cerebral ischemia in two patients and carbon monoxide (CO) poisoning, status epilepticus and Alzheimer's Disease (AD) each in three separate patients. The SPECT scans of the seven patients were compared to T2-weighted magnetic resonance image (MRI) scans of the brain to determine the correlation between functional and anatomical findings. In six of the seven patients, the qualitative interpretation of the SPECT studies supported the clinical findings (i.e., the visual field defect) by revealing altered regional cerebral blood flow (rCBF) in the appropriate regions of the visual pathway. MR scans in all of the patients, on the other hand, were either normal or disclosed smaller lesions than those detected by SPECT. We conclude that SPECT may reveal altered rCBF in patients with cortical visual impairment of various etiologies, even when MRI studies are normal or nondiagnostic.

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Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are techniques used to determine regional physiologic activity (i.e., rCBF and glucose metabolism) in the brain. Much of the clinical research on functional imaging of the brain has focused on neuropsychiatric disorders and several neurologic conditions including cerebrovascular disease, tumors and epilepsy (*1*). PET with ^{18}F-fluoro-2-deoxyglucose (FDG) has already proven successful in demonstrating the increased metabolism of visual cortex during ictal visual hallucinations (*2*) and the hypoperfusion associated with visual cortex ischemia (*3*). By refining the visual stimulation studies (*4*), it has become possible to delineate areas of the occipital and nonoccipital cortex that are involved in complex visual functions.

The application of SPECT to understand the function and related deficits in the visual cortex is a logical step since it is more widely available than PET. It was recently demonstrated that visual stimulation increased the uptake of the SPECT radiopharmaceutical ^{99m}Tc-HMPAO in the visual cortex (*5*). In a study of patients with bilateral infarctions of the occipital lobes, residual vision was attributed to retained metabolic activity in small regions of primary visual cortex (*6*). Like PET, SPECT now holds great promise for disclosing the corresponding cortical function for a variety of visual symptoms.

We report on seven patients with clinically documented cortical visual impairment and abnormal SPECT scans. These patient reports are noteworthy in that MR scans were either normal or did not disclose the full extent of the pathologic process.

METHODS

The patient population was composed of seven subjects aged 20–67 yr (two males, five females). The patients had visual cortex damage caused by TBI (Patients 1 and 2), cerebral ischemia (Patients 3 and 4), CO poisoning (Patient 5), status epilepticus (Patient 6) and AD (Patient 7). The nature of the visual field deficits, radiological findings, etiology and the extent of the abnormality detected by SPECT versus MRI are listed in Table 1.

Cases included in this study were selected retrospectively by examining inpatient and outpatient hospital records of patients who were referred for brain SPECT scans because of suspected cortical visual field defects. All patients had a neurologic examination and all except Patient 6 had a complete neuro-ophthalmologic examination. The neuro-ophthalmologic evaluation included assessment of visual acuity, pupillary reactions, extraocular motility, visual fields and funduscopic examination. Formal fields were performed in four of seven patients and confrontation fields were performed in all patients as listed in Table 1. No patient had visual abnormalities referrable to the anterior visual pathway. Patients did not undergo any additional testing other than during the initial course of diagnosis and therapy. Because anatomical imaging is part of the normal clinical evaluation, the MR scans were obtained soon after the onset of the clinical symptomatology (i.e., performed usually within a few weeks but not sooner than three days after symptom onset). SPECT, on the other hand, is not part of the normal evaluation, and therefore the time interval between scans varied widely. The interval between the MRI and the SPECT scans ranged from a few days (Patients 4 and 7) to over 3 yr (Patient 5).

SPECT Acquisition

For all subjects except Patient 5, 20 mCi of ^{99m}Tc-HMPAO (Amersham, Inc., Arlington Heights, IL, prepared as specified by the manufacturer) was administered intravenously in a dimly lit room with the patient's eyes open and ears unoccluded. Imaging

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TABLE 1
Patient Abnormalities Detected by SPECT Versus MRI

Patient no.	Age/Sex	Etiology	Visual performance	MRI	SPECT	SPECT >, <, = MRI*
1	35/F	Trauma	BL inf. altitudinal field loss (H, C)	Normal	BL temporal lobe hypoperfusion	=
2	20/F	Trauma	Complete Lt HH (G, C)	BL basal ganglia/deep WM lacunes	Right temporal & occipital lobe hypoperfusion	>
3†	48/M	Rt postcerebral artery infarction	Complete Lt HH (G, C); subjective central field loss; visual agnosia	Large rt post-temp-occipital lobe infarction; scattered BL subcortical supratentorial WM lesions	Rt occipital lobe hypoperfusion; cerebellar hyperperfusion; Lt post visual ctx hypoperfusion	>
4	53/M	Postlateral MI and cardiac arrest	BL inf. altitudinal field loss (C); visual agnosia	Normal	BL post. visual ctx hypoperfusion anterior to occipital pole; minor BL visual assoc. ctx hypoperfusion; whole brain hypoperfusion compared to cerebellum	>
5	20/F	CO poisoning	BL congruous central scotomas (G, C)	Normal	BL postvisual ctx. hypoperfusion, greater on left	>
6	51/F	Status epilepticus	Complete Rt HH (C)	Rt post-temporal, post-parietal, occipital ctx infarct; Rt thalamic lacunar infarct; scattered BL subcortical supratentorial periventricular, deep WM lesions	Ictal left occipital-parietal hyperperfusion, interictal left occipital-folietal hyperperfusion	>
7	67/F	Alzheimer's disease	Lt inf. field neglect (C); Visual agnosia	Cerebral atrophy; BL periventricular, deep WM lesions around occipital horns of lateral ventricles	BL occipitoparietal hypoperfusion; minor BL temporal lobe hypoperfusion	>

*This column indicates whether the abnormality detected by SPECT was more (>), less (<) or equally (=) accurate in comparison to MRI in correlating the clinical findings (i.e., visual field defect) for the patient.

†Patient 3 has been reported in a clinicopathologic format (*J Nucl Med* 1993;34:1009–1012).

Key: BL = bilateral; Rt = right; Lt = left; inf. = inferior; post. = posterior; ctx = cortex; assoc. = association; MI = myocardial infarct; HH = homonymous hemianopia; WM = white matter; CO = carbon monoxide; G = Goldmann field; C = confrontation field; and H = Humphrey field.

was initiated 20–30 min after the injection of the radiopharmaceutical. The SPECT scan of the head was performed with a three-headed rotating SPECT camera (Picker Prism; Picker International, Cleveland, OH) for 40 min using high-resolution fanbeam collimators. Projection images were obtained at 3-degree angles on a 128 × 128 matrix over 360 degrees by rotating each head 120 degrees. Images were reconstructed in the transaxial, coronal and sagittal planes using a Butterworth 3.14 prefilter with ramp back-projection and Chang attenuation correction. The reconstructed slice thickness was 10.7 mm. Daily phantom acquisitions with the Data Spectrum Deluxe 5000 phantom were used to monitor overall system performance, reconstructed image uniformity and resolution.

The SPECT head scan for Patient 5 was obtained with a single-headed General Electric SPECT camera XC/T (General Electric; Milwaukee, WI). Imaging was initiated 2 hr following intravenous administration of 25.6 mCi of ^{99m}Tc-HMPAO. Images of the brain were obtained over 30 min and displayed in the transaxial, coronal, sagittal and three-dimensional surface projections. The reconstructed slice thickness was approximately 16 mm.

MRI Acquisition

MR images of the head for all subjects except Patient 4 were acquired with a 1.5-T unit with a head coil (Signa; GE Medical Systems, Milwaukee, WI). Transaxial slices, 5.0 mm thick, were obtained with a field of view of 20 cm and a pixel size of 0.781 mm. The images were displayed with a 256 × 128 matrix. T2-weighted spin echo images (TR/TE = 2,500–3,000/80) and proton density-weighted images (TR/TE = 2,500–3,000/20–30) were acquired for each patient.

The MR scan of Patient 4 was obtained with a 0.35-T unit with a head coil (Toshiba 35; San Francisco, CA). Transaxial slices, 5.5 mm thick, were collected with a field of view of 28 × 21 cm. The images were displayed with a 256 × 190 matrix. T2-weighted spin

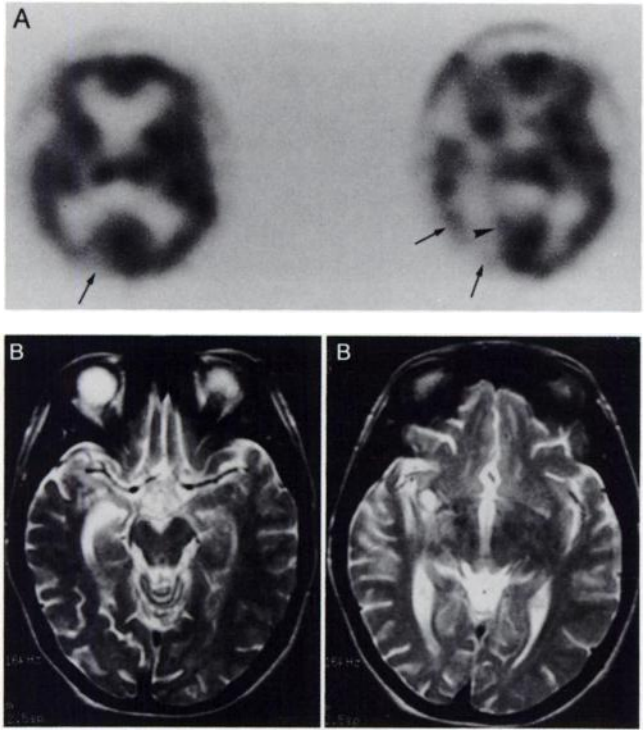

FIGURE 1. SPECT and MRI of Patient 2, who suffered a left homonymous hemianopia from trauma. (A) SPECT reveals hypoperfusion of the right lateral occipital lobe (arrows) and primary visual cortex (arrowhead) which correlated the visual field defect. (B) MRI shows only bilateral lacunes of the deep white matter and the basal ganglia.

echo images (TR/TE = 2,700/40) and gadolinium-enhanced proton density-weighted images (TR/TE = 500/25) were obtained.

Qualitative Analysis

The MRI and SPECT studies were reviewed blindly by a neuroradiologist and a nuclear medicine specialist, respectively. The reader was asked to determine the anatomic location, extent and degree of any abnormality visualized. Abnormalities in the imaging studies were subjectively interpreted based upon knowledge of the normal neuroanatomy. For the SPECT scans, abnormal activity in the visual cortex was evidenced by a relative hypoperfusion or, in Patient 6, hyperperfusion in comparison to the contralateral visual cortex and the adjacent regions of visual cortex. For the MR images, an abnormal signal was similarly detected with knowledge of the normal neuroanatomy and by regional comparison of signal intensity. Following the initial set of blind readings, both the nuclear medicine specialist and the neuroradiologist reviewed the SPECT and MR scans side by side to determine any significant difference in the extent of abnormalities in one versus the other. During this second review of the SPECT and MR scans, no changes in the initial interpretations were made.

RESULTS

Patients 2 and 3 had a complete left homonymous hemianopia. The SPECT scan of Patient 2 (Fig. 1A) showed right temporal and occipital lobe hypoperfusion which correlated with her left homonymous hemianopia, whereas an MR scan detected no abnormality in visual cortex (Fig. 1B). The SPECT scan of Patient 3 showed extensive hypoperfusion of the right primary visual cortex which extended to the right medial temporal lobe and posterior thalamic region. The lesion included the right visual association area (i.e., lateral occipital lobe) and an area of hypoperfusion in the left posterior visual cortex. The MR scan similarly detected a large right posterior occipitotemporal infarction but no lateral occipital lobe or contralateral involvement. Thus, SPECT showed a more extensive lesion that correlated well with the patient's visual associative deficits (i.e., prosopagnosia, environmental agnosia, and color agnosia).

Patient 6 had a complete right homonymous hemianopia, and her SPECT scan demonstrated hypoperfusion including the left calcarine (i.e., primary visual) cortex. Ictal SPECT scans of Patient 6 showed hyperperfusion in the left occipital-parietal cortex and in the left inferior temporal, inferior parietal and occipital lobes in a second examination. An MR scan did not reveal a focal abnormality to correspond with the visual field loss.

The other four patients had bilateral damage to the occipital cortex and displayed either bilateral visual field defects (Patients 1 and 5) or visual agnosia (Patients 4 and 7).

The SPECT scan of Patient 1 detected bilateral temporal lobe hypoperfusion, a finding more appropriate for her short-term memory impairment than her visual field defect. By contrast, her MR scan was normal.

The SPECT study of Patient 5 with congruous central scotoma disclosed bilateral posterior occipital lobe hypoperfusion which correlated well with the central scotomas of cortical origin. The MR scan, on the other hand, was normal. The location of the occipital lobe defect in SPECT correlates well with the macular representation of vision in the posterior portion of the primary visual cortex.

Patient 4 experienced numerous visual difficulties following a posterior-lateral myocardial infarct that was complicated by cardiac arrest and successful resuscitation. Although the patient was able to identify small dots of color in the range of 20/40-sized (~2mm) letters on a close card, he could not identify large objects or read the numbers on a close card. Similarly, he could see the color of a flower but was unable to recognize it. SPECT (Fig. 2A) demonstrated hypoperfusion in bilateral visual cortices most prominently anterior to the occipital poles with mild decreased perfusion in visual association areas. The MR scan (Fig. 2B) was normal.

Patient 7 had visual association deficits (i.e., object agnosia, visual disorientation, prosopagnosia and alexia with agraphia) resulting from AD. The SPECT scan (Fig. 3A) revealed diffuse hypoperfusion in bilateral occipitoparietal lobes with minor temporal lobe hypoperfusion. By contrast, the MR scan detected only extensive cerebral atrophy and bilateral periventricular deep white matter focal lesions (Fig. 3B).

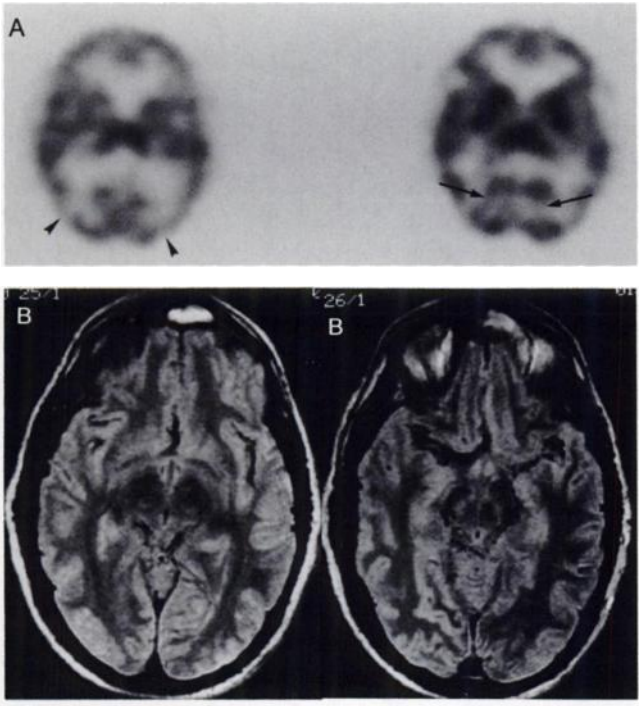

FIGURE 2. SPECT and MRI of Patient 4, who suffered visual agnosia and bilateral inferior altitudinal field loss following a posterior-lateral myocardial infarction and cardiac arrest. (A) SPECT detected bilateral posterior hypoperfusion in the visual cortex anterior to the occipital pole (arrows) as well as some minor hypoperfusion of the lateral occipital lobes (arrowheads). (B) MRI is normal. SPECT was more diagnostic than MRI for this patient's visual difficulties.

DISCUSSION

Our study demonstrates that MRI may not fully identify the pathologic substrate responsible for some visual field defects. The lesions missed by MRI seem to be of a diffuse nature as might occur in trauma, ischemic and nonvascular hypoxic events like CO poisoning, and AD. By contrast, SPECT is designed to detect minor fluctuations in rCBF for which anatomical imaging techniques are probably not as sensitive. For example, SPECT showed relative hypoperfusion of the cerebral cortex compared to the cerebellum in Patient 4 which was interpreted to be compatible with his clinical presentation of depression (*7*).

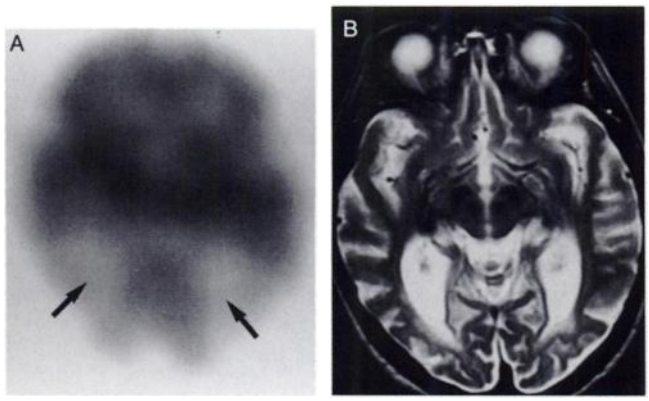

FIGURE 3. SPECT and MRI of Patient 7, whose visual agnosia was caused by Alzheimer's Disease. (A) SPECT reveals hypoperfusion most markedly in occipitoparietal regions bilaterally (arrows). (B) MRI shows only cerebral atrophy.

Diffuse axonal injury (DAI), as occurs in TBI, represents one type of lesion that MRI may underestimate the actual extent of neural damage (*8*). FDG-PET studies have revealed diffuse cortical hypometabolism, particularly in the occipitoparietal cortex, in patients with DAI (*1,9*).

In Patient 2 with TBI, the distributions of cortical hypoperfusion demonstrated by SPECT were more diagnostic for their visual field deficits than MRI. The SPECT scan of Patient 1 was not diagnostic for her visual field defect, but its detection of bilateral temporal lobe damage was not revealed by the MR scan.

Patients 3, 4 and 7 had visual agnosias with cortical lesions extending beyond the primary visual cortex. In these patients, SPECT was more capable than MRI in demonstrating the cortical defect. A prospective study comparing SPECT and MRI in a group of patients with visual associative deficits would further clarify their diagnostic roles.

Bilateral occipital lobe disease was observed in Patient 5 who suffered bilateral congruous central scotomas from hypoxia due to CO poisoning. MRI may reveal periventricular white matter and globus pallidus lesions characteristic of CO poisoning (*10,11*). In a patient with CO poisoning, Jibiki et al. (*11*) found ^{123}I-*N*-isopropyl-*p*-iodoamphetamine (IMP) SPECT to be of greater diagnostic utility than MRI. That study detected marked hypoperfusion in diffuse cortical regions and an increase in rCBF which paralleled clinical improvement.

Alzheimer's disease may also cause visual agnosia via neuronal degeneration. FDG-PET has been used to identify hypometabolic regions of visual cortex in Alzheimer's patients (*12*). Decreased glucose uptake was found bilaterally in visual association cortices and the inferior parietal cortex which correlated well with the visual agnosia observed in these patients. Later studies indicated that ^{123}I-IMP and ^{99m}Tc-HMPAO SPECT studies, though not as sensitive as FDG-PET, were useful diagnostic techniques for AD (*13*); typically, SPECT disclosed hypoperfusion in the bilateral temporoparietal regions of AD patients, including those without overt visual symptomatology (*14*). In Patient 7, the SPECT scan was more representative than MRI for the visual difficulties encountered.

Finally, recent reports of patients with status epilepticus (*15,16*) found SPECT to be as successful as MRI in revealing focal abnormalities. Both techniques are able to detect a reversible edema related to hypervascularization (*17*). In our study, SPECT disclosed left-sided occipitoparietotemporal hypoperfusion for Patient 6, while the MR scan did not reveal a lesion to account for her right homonymous hemianopia.

With the exception of Patient 1, the region of hypoperfusion detected by SPECT correlated well with the laterality and extent of the visual dysfunction. In some cases, SPECT was also able to localize altered rCBF years after

the initial event. However, in our retrospective study, the variable timing of the SPECT scan following the disease process or traumatic event confounded the predictive value of SPECT. In the case of ischemic events, for example, an uncertain amount of reperfusion may occur (*3*). In order to accurately compare anatomical imaging and SPECT, future studies should obtain both types of scans within a relatively short (e.g., 1 wk) interval of each other.

Another confounding factor is that the magnitude of hypoperfusion may be larger than the structural defect. A functional imaging technique such as SPECT would be expected to detect larger regions of abnormality in comparison to conventional MRI because of the connectivity of various regions of cerebral cortex (*1*).

Our study shows that SPECT, like PET (*3*), provides adequate resolution for corroborating regions of cerebral dysfunction in patients with cortical visual impairment. Though PET currently has greater spatial resolution, SPECT is readily accessible and less expensive. SPECT also has the flexibility to evaluate a wide range of cerebral abnormalities on short notice, which may not be practical with PET. We therefore propose that SPECT be utilized as an effective imaging procedure in the early stages of the diagnostic evaluation to define the location, extent, and nature of cortical visual loss.

Patients with cortical visual field loss may be considered functional when their MR scans are normal. In these patients, SPECT might reveal an area of dysfunction and ultimately prevent an inappropriate psychiatric diagnosis. We conclude that anatomical imaging such as MRI and functional imaging such as SPECT should be used in a complimentary fashion in the evaluation of patients with cortical visual loss.

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