Technetium-99m-HMPAO Brain SPECT in Sjögren's Syndrome

Chia-Hung Kao, Jung-Liang Lan, Sheng-Ping ChangLai and Poon-Ung Chieng
Departments of Nuclear Medicine and Internal Medicine, Taichung Veterans General Hospital, Taichung; Department of Nuclear Medicine, Chung-Shan Medical College Hospital, Taichung; and Department of Nuclear Medicine, National Taiwan University Hospital, Taipei, Taiwan, Republic of China

Technetium-99m-hexamethylpropylene amine oxime (HMPAO) brain images with fanbeam SPECT, in combination with surface three-dimensional display, were used to detect basal ganglion and cerebral cortex anomalies in Sjögren's syndrome patients. **Methods:** Forty-eight female Sjögren's syndrome patients with normal brain CT or magnetic resonance imaging findings were enrolled in this study and were investigated using ^{99m}Tc-HMPAO brain images with fanbeam SPECT and surface three-dimensional display. These patients were separated into two subgroups. Group 1 consisted of 38 patients with definite neuropsychiatric symptoms/signs and Group 2 consisted of 10 patients without any neuropsychiatric symptoms/signs. **Results:** Fanbeam SPECT demonstrated unilateral or bilateral hypoactivity of basal ganglia and thalamus in 14% and 0% of patients in Groups 1 and 2, respectively. Using surface three-dimensional display of the brain, local hypoactivity anomalies were found in the brain cortex of 53% and 20% of patients in Groups 1 and 2, respectively. In Group 1 patients, parietal lobes were the most common areas of brain involvement. The cerebellum and thalamus were the least common areas of brain involvement. In Group 2 patients, parietal and temporal lobes were the most common areas of brain involvement. **Conclusion:** This study suggests that ^{99m}Tc-HMPAO brain imaging with fanbeam SPECT, in combination with surface three-dimensional display, is a sensitive tool for detecting regional cerebral anomalies in Sjögren's syndrome patients with and without neuropsychiatric symptoms/signs.

Key Words: technetium-99m-hexamethylpropylene amine oxime; fanbeam collimator; SPECT; surface three-dimensional display; Sjögren's syndrome

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Sjögren's syndrome is a common autoimmune connective tissue disease affecting a conservatively estimated 2% of adults (*1*). It occurs most frequently in middle-aged women and is mainly characterized by dryness of the eyes (keratoconjunctivitis) and mouth (xerostomia) (*2,3*). In this disorder, the diagnosis and management of neuropsychiatric symptoms are critical. However, due to the lack of effective imaging techniques, diagnosis of brain involvement in Sjögren's syndrome patients is difficult. MRI has been considered to be highly sensitive, as it has been used to identify structural lesions in neuropsychiatric Sjögren's syndrome patients (*4–6*). PET studies of glucose metabolism with fluorine-18-fluorodeoxyglucose (FDG) have proven to be even more sensitive than MRI. Fluorine-18-fluorodeoxyglucose PET studies have been able to document the location and extent of brain involvement in patients with autoimmune connective tissue disease, even when structural lesions were not evident on MRI (*7,8*). However, PET is not suitable for routine clinical use due to its expense and lack of availability. Technetium-99m-hexamethylpropylene amine oxime (HMPAO) brain imaging is an alternative modality for studying brain involvement. Technetium-99m-HMPAO brain images have been used for the assessment of regional cerebral blood flow (rCBF) and have proven accurate in detecting many neurologic and psychiatric diseases (*9–12*).

SPECT is essential for depicting brain abnormalities, as it improves image contrast by separating overlapping structures (*13,14*). Particularly when a fanbeam collimator is used to replace the conventional parallel-hole collimator, both system resolution and sensitivity improve by approximately 20% (*15,16*). In addition, if the fanbeam collimator has an FWHM close to 6.5 mm (*17*), deeper lesions within the brain, such as lesions of the basal ganglia and thalamus, can be clearly demonstrated. However, when brain lesions are evaluated by SPECT, the interpreter must bring together every slice of the transaxial, coronal and sagittal sections to make a whole for accurate localization of lesions. To avoid this, surface three-dimensional images of the brain can be used. Surface three-dimensional images enhance continuity of structures, as well as improve understanding of spatial relationships (*17–19*). Although a standard surface three-dimensional display cannot depict lesions within the brain, such as those of the basal ganglia (*20,21*), this technique has been clinically applied to the evaluation of rCBF in patients who have suffered stroke, seizure or depression (*20–23*).

In this study, we investigated the potential of ^{99m}Tc-HMPAO brain images, in conjunction with fanbeam SPECT and surface three-dimensional display, to detect cerebral anomalies including lesions of the basal ganglia and cerebral cortex in Sjögren's syndrome patients with and without neuropsychiatric symptoms/signs.

MATERIALS AND METHODS

Patients

Forty-eight female primary Sjögren's syndrome patients (age range 23–51 yr) who fulfilled the criteria for Sjögren's syndrome were enrolled in this study. Required criteria for enrollment included ocular and oral involvement by typical symptoms/signs, histopathologic features, positive diagnostic test results and existence of autoantibodies but excluded pre-existing lymphoma, acquired immunodeficiency syndrome, sarcoidosis and graft-versus-host disease (*24*). All patients had normal CT or MRI findings. A neurologic consultant evaluated the patients for presence of neurologic symptoms/signs. Neuropsychiatric symptoms/signs due to Sjögren's syndrome were defined as those that could not be attributed to any other cause (such as uremia, hypertension or infection) and included stroke, seizure, cognition impairment, depression, mental retardation, drowsiness, syncope, vertigo, unstable gait, headaches, dizziness, insomnia and memory impairment. Thirty-eight patients (age range 23–51 yr) had definite neuropsychiatric symptoms/signs and were included in Group 1.

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For correspondence or reprints contact: Chia-Hung Kao, MD, Department of Nuclear Medicine, Taichung Veterans General Hospital, 160 Taichung Harbor Rd., Section 3, Taichung 40705, Taiwan, Republic of China.

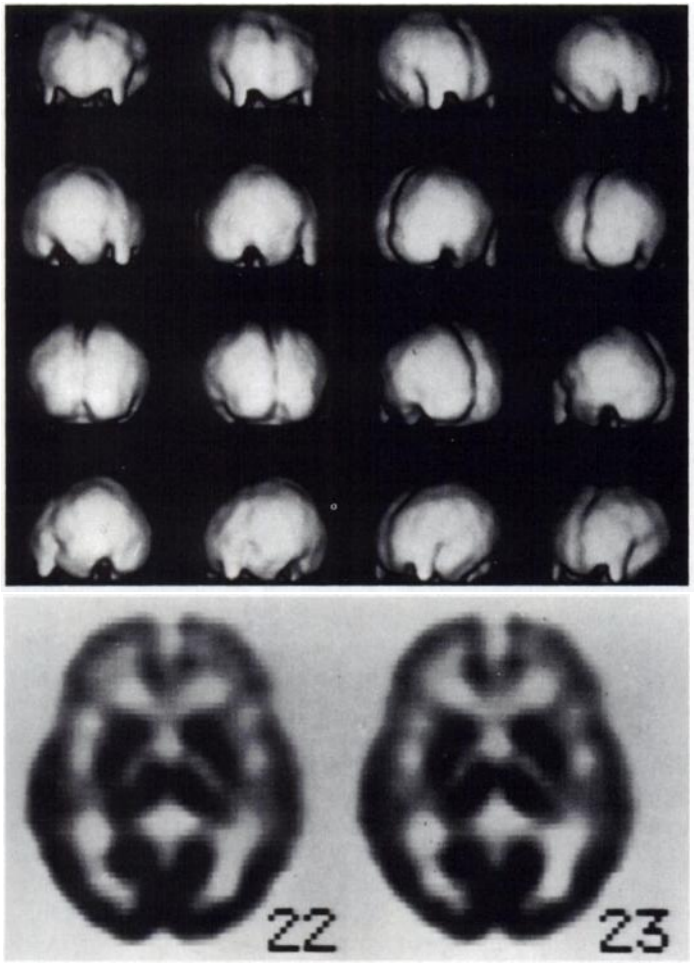

FIGURE 1. Normal ^{99m}Tc-HMPAO brain imaging findings in a 25-yr-old woman. Surface three-dimensional display of the brain (upper) and fanbeam SPECT (transaxial slices) of the brain (lower) reveal homogeneous rCBF in the gray matter of basal ganglia/thalamus and cerebral cortex without focal hypoactivity or visible asymmetry.

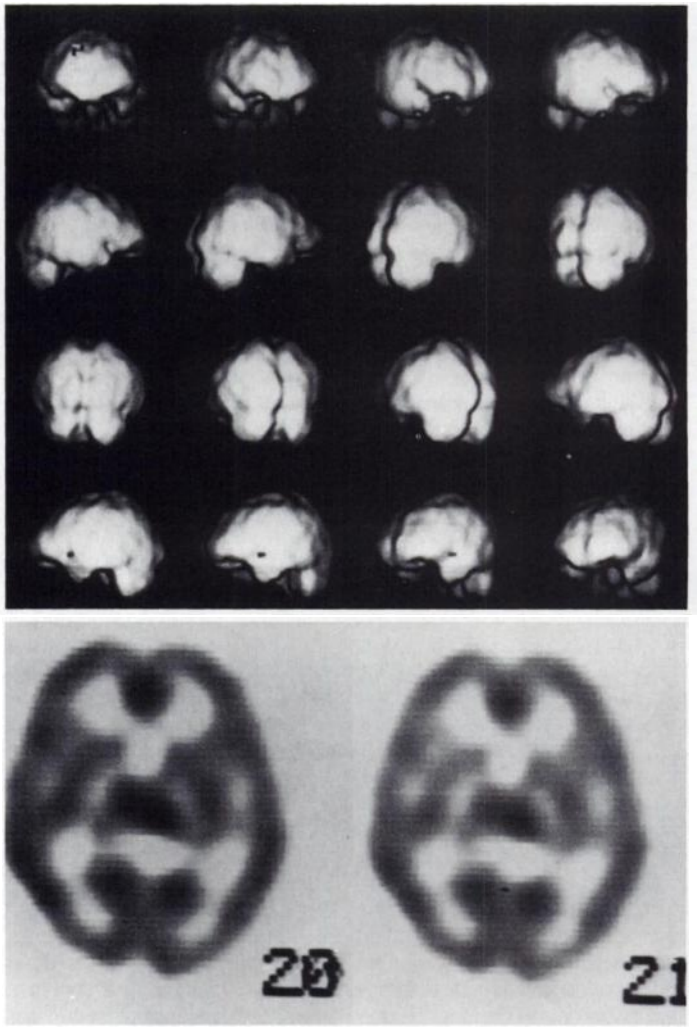

FIGURE 2. Normal ^{99m}Tc-HMPAO brain imaging findings in a 50-yr-old woman. Surface three-dimensional display of the brain (upper) and fanbeam SPECT (transaxial slices) of the brain (lower) reveal homogeneous rCBF in the gray matter of basal ganglia/thalamus and cerebral cortex without focal hypoactivity or visible asymmetry.

Ten patients (age range 23–47 yr) had no neuropsychiatric symptoms/signs and were included in Group 2.

Technetium-99m-HMPAO Brain Images

Technetium-99m-HMPAO was prepared from a freeze-dried kit (Ceretec; Amersham International, Amersham, United Kingdom) by the addition of about 1250 MBq of freshly eluted ^{99m}Tc-pertechnetate to 5 ml of saline solution. The solution was injected no more than 30 min after preparation.

Patients were placed in a supine position in a quiet room with dimmed lights and were allowed to relax with their eyes closed for 15 min prior to intravenous administration of 1110 MBq (30 mCi) of ^{99m}Tc-HMPAO. After injection of ^{99m}Tc-HMPAO, the patients were asked to not move or talk for at least 10 min. The scan was performed 90–120 min after injection, with patients positioned supine on the imaging table with their foreheads and chins restrained.

The scanning equipment consisted of a rotating, large-field-of-view, dual-head gamma camera (Helix HR; Elscint Ltd., Haifa, Israel) fitted with a fanbeam collimator. Data were collected in a 64 × 64 matrix with 1.3 zooming, through a 360° (180° for each head) rotation at three intervals, for 25 sec per arc interval. Approximately 7.5 million counts were acquired. The SPECT images (coronal, sagittal and transaxial sections) were reconstructed using a Metz filter (power 5.00), backprojection and attenuation correction. The transaxial sections were reoriented parallel to the base of the brain to obtain sagittal and coronal reconstructions. Surface three-dimensional displays were reconstructed from transaxial SPECT data, with a processing time of 3–5 min. The threshold value was set at 50% (*19,25*). The spatial resolution of the camera with fanbeam collimator was 6.3 mm FWHM.

To identify local areas of abnormal hypoperfusion, visual interpretation of the SPECT images and surface three-dimensional display results was performed by two observers who were blinded to the clinical information. Normal ^{99m}Tc-HMPAO brain imaging findings consisted of homogeneous rCBF in the gray matter of cerebral cortex and basal ganglia/thalamus without focal hypoactivity or visible asymmetry (Figs. 1 and 2). Otherwise, the findings of ^{99m}Tc-HMPAO brain imaging were considered to be abnormal (Figs. 3 and 4).

RESULTS

Detailed data for the patients are shown in Tables 1 and 2. The findings of ^{99m}Tc-HMPAO brain images are shown in Table 3. The following results were obtained from ^{99m}Tc-HMPAO brain imaging studies:

1. Fifty-eight percent (22 of 38) and 20% (2 of 10) of Group 1 and 2 patients, respectively, demonstrated focal hypoactivity or visible asymmetry;

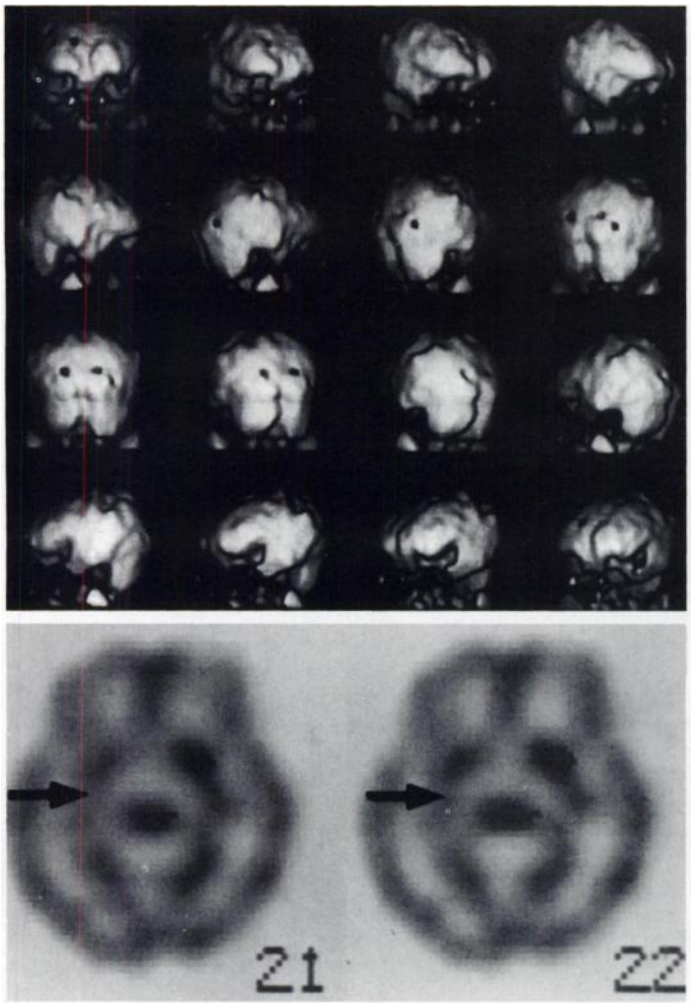

FIGURE 3. Abnormal ^{99m}Tc-HMPAO brain imaging findings in a 46-yr-old woman (Patient 3 in Group 1). Surface three-dimensional display of the brain (upper) reveals multiple small areas with hypoperfusion in the brain cortex (majority in the bilateral parietal lobes), and fanbeam SPECT of the brain (lower) demonstrates hypoperfusion in the right basal ganglia (arrows).

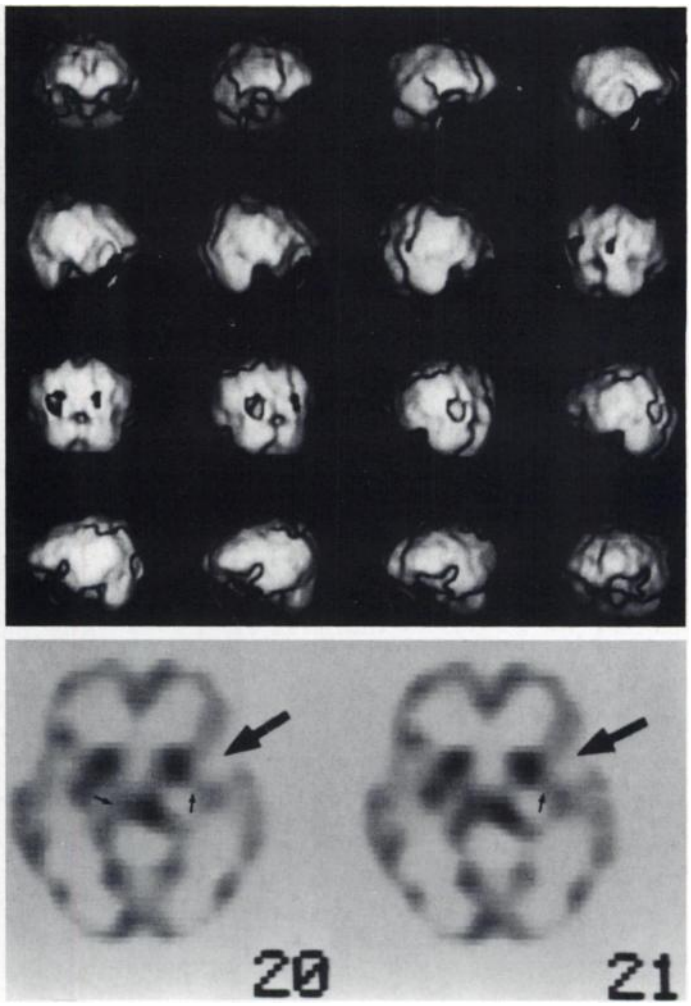

FIGURE 4. Abnormal ^{99m}Tc-HMPAO brain imaging findings in a 37-yr-old woman (Patient 22 in Group 1). Surface three-dimensional display of the brain (upper) reveals multiple small areas with hypoperfusion in the brain cortex (bilateral frontal-parietal-temporal-occipital lobes), and fanbeam SPECT of the brain (lower) demonstrates hypoperfusion in the left temporal lobe (large arrows) and bilateral basal ganglia (small arrows).

2. Surface three-dimensional display findings were abnormal in 53% (20 of 38) and 20% (2 of 10) of Group 1 and 2 patients, respectively;
3. Fanbeam SPECT was abnormal in 37% (14 of 58) and 0% (0 of 10) of Group 1 and 2 patients, respectively;
4. Parietal and temporal lobes were the most commonly involved areas in Group 1 (53%, 20 of 38; and 37%, 14 of 38, respectively) and Group 2 (10%, 1 of 10 for both regions) patients; and
5. Cerebellum and thalamus were the least common areas of involvement in Group 1 patients (0%, 0 of 38 for both regions); frontal lobes, occipital lobes, cerebellum, basal ganglia and thalamus were the least commonly involved areas in Group 2 patients (0%, 0 of 10 for all regions).

DISCUSSION

The neurologic manifestations of Sjögren's syndrome were first described in Sjögren (*26*) and include stroke, seizure, cognition impairment, depression, mental retardation, drowsiness, syncope, vertigo, unstable gait, headaches, dizziness, insomnia and memory impairment. More recently, central nervous system involvement in Sjögren's syndrome has been reported in an increasing number of reports (*1,4,24,27–29*). The overall occurrence of neuropsychiatric disturbances in Sjögren's syndrome has been estimated to be 28% (*28*). Despite increased knowledge about Sjögren's syndrome and related complications, the overall clinical picture of neurologic manifestations in Sjögren's syndrome patients remains somewhat unclear (*27–29*).

The exact sensitivity and specificity data of diagnostic modalities, for detection of brain anomalies in Sjögren's syndrome patients, have been unavailable. There has been a preliminary report concerning the use of ^{99m}Tc-HMPAO brain scans for the diagnosis of neuropsychiatric Sjögren's syndrome (*1*), but our results showed that ^{99m}Tc-HMPAO brain imaging, in conjunction with fanbeam SPECT and surface three-dimensional display, is a sensitive method for detecting brain involvement in Sjögren's syndrome patients with normal CT or MRI findings: 50% (24 of 48) of cases had hypoperfusion areas of the brain on ^{99m}Tc-HMPAO brain images. These findings are consistent with the results of the above-mentioned preliminary report (*1*) in Sjögren's syndrome patients with normal brain MRI findings. In both the previous study and in this study, it was suggested that there are cortical abnormalities in Sjögren's syndrome patients that are associated with definite neuropsychiatric symptoms/signs (cognitive or psychiatric dysfunction). However, among Group 2 patients, who do not have neuropsychiatric symptoms/signs, ^{99m}Tc-HMPAO brain imaging findings were positive in approximately 20% (2 of 10). In addition, with improved fanbeam SPECT resolution (6.3 mm FWHM),

TABLE 1
Detailed Data of Group 1 Patients

Patient no.	Age (yr)	^{99m}Tc-HMPAO (fanbeam SPECT)	Brain images (surface three-dimensional display)	Neuropsychiatric symptoms/signs
1	51	Right basal ganglia	Bilateral P	Cognition impairment
2	49	Negative	Negative	Insomnia, dizziness
3	46	Right basal ganglia	Bilateral P	Memory impairment
4	45	Negative	Negative	Mental retardation, memory impairment
5	44	Negative	Negative	Frequent syncope
6	44	Negative	Negative	Insomnia, depression
7	44	Negative	Negative	Depression
8	44	Left basal ganglia	Bilateral F-P, right T	Memory impairment
9	43	Negative	Negative	Conscious disturbance
10	43	Negative	Negative	Memory impairment
11	43	Negative	Bilateral F-P-T	Cognition impairment
12	42	Bilateral basal ganglia	Bilateral F-P-O, left T	Seizure, memory and cognition impairment
13	41	Negative	Bilateral P-O, right T	Dizziness, headache
14	40	Negative	Negative	Mental retardation, insomnia
15	40	Negative	Bilateral P-T-O	Seizure, syncope
16	39	Negative	Negative	Syncope, memory impairment
17	39	Negative	Negative	Memory impairment
18	39	Negative	Bilateral F-P-T	Cognition impairment
19	39	Left basal ganglia	Bilateral F-P, right T	Memory impairment
20	38	Negative	Negative	Conscious disturbance
21	38	Negative	Negative	Memory impairment
22	37	Bilateral basal ganglia	Bilateral F-P-O, left T	Stroke, seizure, cognition impairment
23	36	Negative	Bilateral P-O, right T	Cognition impairment
24	35	Negative	Negative	Memory impairment
25	35	Negative	Bilateral P-T-O	Seizure, headache
26	35	Left basal ganglia	Negative	Cognition impairment
27	35	Bilateral basal ganglia	Bilateral F-P-T-O	Memory impairment
28	33	Bilateral basal ganglia	Bilateral P	Drowsiness, depression
29	31	Negative	Negative	Cognition impairment
30	30	Negative	Negative	Memory impairment
31	30	Left basal ganglia	Negative	Cognition impairment
32	30	Bilateral basal ganglia	Bilateral F-P-T-O	Memory impairment
33	30	Right basal ganglia	Bilateral P	Memory and cognition impairment
34	28	Negative	Right F-P-T	Unstable gait
35	28	Bilateral basal ganglia	Bilateral P	Drowsiness, depression
36	26	Negative	Negative	Cognition and memory impairment
37	25	Right basal ganglia	Bilateral P	Memory and cognition impairment
38	23	Negative	Right F-P-T	Vertigo

F = frontal lobe; P = parietal lobe; T = temporal lobe, O = occipital lobe.

detection of deep-seated structures of the brain, such as basal ganglia, has become possible. Therefore, we were able to detect anomalies in the basal ganglia and thalamus in 37% (14 of 38) of Group 1 Sjögren's syndrome patients.

Regional cerebral cortical hypoperfusion demonstrated by surface three-dimensional display is relatively nonspecific. These abnormal features may be secondary to subclinical brain involvement. Similar hypoperfusion anomalies in the cerebral cortex can be found in a variety of acute neurologic disorders, including cerebral infarction, multi-infarct dementia and Alzheimer's and Parkinson's diseases (*30,31*). According to our results, most hypoperfused areas were found in the parietal and temporal lobes (the territory of the middle cerebral artery) because the territory of the middle cerebral artery is at higher risk for cerebral vascular abnormalities resembling embolism than are other territories (*32*). Nishimura et al. (*33*) suggested that neuropsychiatric dysfunctions associated with Sjögren's syndrome are at least in part attributable to small vessel vasculopathy, such as focal inflammation or edema. Gerraty et

TABLE 2
Detailed Data for Group 2 Patients

Patient no.	Age (yr)	^{99m}Tc-HMPAO (fanbeam SPECT)	Brain images (surface three-dimensional display)	Neuropsychiatric symptoms/signs
1	47	Negative	Negative	Negative
2	45	Negative	Negative	Negative
3	40	Negative	Negative	Negative
4	40	Negative	Negative	Negative
5	38	Negative	Negative	Negative
6	37	Negative	Left T	Negative
7	32	Negative	Bilateral P	Negative
8	30	Negative	Negative	Negative
9	28	Negative	Negative	Negative
10	23	Negative	Negative	Negative

T = temporal lobe; P = parietal lobe.

TABLE 3
Detailed Findings of Technetium-99m-HMPAO Brain Images

	Total	Surface three-dimensional display					Fanbeam SPECT	
	Brain	Frontal	Parietal	Temporal	Occipital	Total	Basal ganglia	Total
Group 1 (n = 38)	22 (58%)	10 (26%)	20 (53%)	14 (37%)	8 (21%)	20 (53%)	14 (37%)	14 (37%)
Group 2 (n = 10)	2 (20%)	0 (0%)	1 (10%)	1 (10%)	0 (0%)	2 (20%)	0 (0%)	0 (0%)

al. (*34*) suggested that cerebral vasculitis is the pathogenetic mechanism of the brain manifestations of Sjögren's syndrome. Berman et al. (*35*) described angiographic evidence of cerebral vasculitis and multiple infarcts present on neuroimaging in an Sjögren's syndrome case with brain involvement. de-la-Monte et al. (*36*) examined brain abnormalities in 11 Sjögren's syndrome patients and found cerebral vasculopathy, including necrotizing vasculitis. Alexander et al. (*37*) studied 16 patients with Sjögren's syndrome and brain disorders and suggested that an immune vasculopathy may play a role in the pathogenesis of central nervous system disease in Sjögren's syndrome. Because vasculopathy is the major pathogenesis in neuropsychiatric Sjögren's syndrome, as suggested by previous studies (*33–37*), detection of changes in rCBF may be easier than detection of structural changes.

CONCLUSION

Technetium-99m-HMPAO brain imaging, in conjunction with fanbeam SPECT and surface three-dimensional display, is a more sensitive tool than either brain CT or MRI for detecting brain abnormalities in Sjögren's syndrome patients. It can detect changes in rCBF in Sjögren's syndrome patients with and without neuropsychiatric symptoms/signs, even in Sjögren's syndrome patients with normal brain CT or MRI findings. Technetium-99m-HMPAO brain imaging should be a standard implement to evaluate both deep brain lesions and brain cortex spatial relationships in Sjögren's syndrome patients.

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REFERENCES

1. Alexander E. Central nervous system disease in Sjögren's syndrome: new insights into immunopathogenesis. *Rheum Dis Clin N Am* 1992;18:637–672.
2. Farnam J, Jorizzo JL, Grant JA, Lavastida MT, Ichikawa Y, Daniels JC. Sjögren's syndrome presenting with hypereosinophilia, lymphopenia and circulating immune complexes. *Clin Exp Rheumatol* 1984;2:41–46.
3. Fox RI, Howell FV, Bone RC, Michelson P. Primary Sjögren's syndrome: clinical and immunopathological features. *Semin Arthritis Rheum* 1984;14:77–105.
4. Alexander EL, Beall S, Provost TT, et al. Magnetic resonance imaging (MRI) in primary Sjögren's's syndrome with central nervous system disease (CNS-SS): new clues to pathogenesis. *Arthritis Rheum* 1989;29(suppl):S63.
5. Manthorpe R, Manthorpe T, Sjöberg S. Magnetic resonance imaging of the brain in patients with primary Sjögren's syndrome. *Scand J Rheumatol* 1992;21:148–149.
6. Moutsopoulos HM, Sarmas JH, Talal N. Is central nervous system involvement a systemic manifestation of primary Sjögren's syndrome? *Rheum Dis Clin N Am* 1993;19:909–912.
7. Stoppe G, Wildhagen K, Seidel JW, et al. Positron emission tomography in neuropsychiatric lupus erythematosus. *Neurology* 1990;40:304–308.
8. Stoppe G, Wildhagen K, Meyer GJ, Schober O. FDG-PET in the diagnosis of neuropsychiatric lupus erythematosus and comparison with computed tomography and magnetic resonance imaging. *Nucl Med* 1989;28:187–192.
9. Perani D, di Piero V, Vallar G, et al. Technetium-99m HMPAO-SPECT study of regional cerebral perfusion in early Alzheimer's disease. *J Nucl Med* 1988;29:1507–1514.
10. Stefan H, Kuhnen C, Biersack HJ, Reichmann K. Initial experience with ^{99m}Tc hexamethylpropylene amine oxime (HMPAO) single photon emission computed tomography (SPECT) in patients with focal epilepsy. *Epilepsy Res* 1987;1:134–138.
11. Lewis SW, Ford RA, Syed GM, Reveley AM, Toone BK. A controlled study of ^{99m}Tc HMPAO single photon emission imaging in chronic schizophrenia. *Psychol Med* 1992;22:27–35.
12. Pozzilli C, Passafiume D, Bernardi S. SPECT, MRI, and cognitive functions in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 1991;54:110–115.
13. Holman BL, Devous MD Sr. Functional brain SPECT: the emergence of a powerful clinical method. *J Nucl Med* 1992;33:1888–1904.
14. Wallis JW, Miller TR. Volume rendering in three-dimensional display of SPECT images. *J Nucl Med* 1990;31:1421–1430.
15. Denays R, Tondeur M, Noel P, Ham HR. Bilateral cerebral mediofrontal hypoactivity in ^{99m}Tc HMPAO SPECT imaging. *Clin Nucl Med* 1994;19:873–876.
16. Kim HJ, Karp JS, Mozley PD, et al. Stimulating technetium-99m cerebral perfusion studies with a three-dimensional Hoffmann brain phantom: collimator and filter selection in SPECT neuroimaging. *Ann Nucl Med* 1996;10:153–160.
17. Liew SC, Hasegawa BH. Noise, resolution, and sensitivity considerations in the design of a single-slice emission-transmission computed tomographic system. *Med Phys* 1991;18:1002–1015.
18. Keyes JW Jr. Three-dimensional display of SPECT images: advantages and problems. *J Nucl Med* 1990;31:1428–1430.
19. Wallis JW, Miller TR. Three-dimensional display in nuclear medicine and radiology. *J Nucl Med* 1991;33:534–546.
20. Ishimura J, Fukuchi M. Clinical application of three-dimensional surface display in brain imaging with ^{99m}Tc HMPAO. *Clin Nucl Med* 1991;16:343–351.
21. Shih WJ, Schleenbaker RE, Stipp V, Magoun S, Slevin JT. Surface and volume three dimensional display of ^{99m}Tc HMPAO brain SPECT in stroke patients by a three-headed camera. *Clin Nucl Med* 1993;18:945–949.
22. Devous MD Sr. Comparison of SPECT applications in neurology and psychiatry. *J Clin Psychiatry* 1992;53:13–19.
23. Okuda B, Tachibana H, Kawabata K, Sugita M, Fukuchi M. Three-dimensional surface display with ^{123}I IMP of slowly progressive apraxia. *Clin Nucl Med* 1993;18:85–87.
24. Vitali C, Bombardieri S, Moutsopoulos HM, et al. Preliminary criteria for the classification of Sjögren's syndrome: results of a prospective concerted action supported by the European community. *Arthritis Rheum* 1993;36:340–347.
25. Shih WJ, Tasdemiroglu E. Reversible hypoperfusion of the cerebral cortex in normal-pressure hydrocephalus on technetium-99m-HMPAO brain SPECT images after shunt operation. *J Nucl Med* 1995;36:470–473.
26. Sjögren H. Zur kenntnis der keratoconjunctivitis sicca II. Allgemeine symptomatologie und atiologie. *Acta Ophthalmol (Copenh)* 1935;13:1–39.
27. Drosos AA, Andonopoulos AP, Lagos G, Angelopoulos NV, Moutsopoulos HM. Neuropsychiatric abnormalities in primary Sjögren's syndrome. *Clin Exp Rheumatol* 1989;7:207–209.
28. Hietaharju A, Yli-Kerttula U, Hakkinen V, Frey H. Nervous system manifestations in Sjögren's syndrome. *Acta Neurol Scand* 1990;81:144–152.
29. Malinow KL, Molina R, Gordon B, et al. Neuropsychiatric dysfunction in primary Sjögren's syndrome. *Ann Intern Med* 1985;103:344–350.
30. Kuwabara Y, Ichiya Y, Otsuka M, et al. Differential diagnosis of bilateral parietal abnormalities in ^{123}I IMP SPECT imaging. *Clin Nucl Med* 1990;15:893–899.
31. DeVolder AG, Goffinet AM, Bol A, Michel C, de-Barsy T, Laterre C. Brain glucose metabolism in postanoxic syndrome. Positron emission tomographic study. *Arch Neurol* 1990;47:197–204.
32. Devinsky O, Petito CK, Alonso DR. Clinical and neuropathological findings in systemic lupus erythematosus: the role of vasculitis, heart emboli and thrombotic thrombocytopenia purpura. *Amm Neurol* 1988;23:380–384.
33. Nishimura H, Tachibana H, Makiura N, Okuda B, Sugita M. Corticosteroid-responsive parkinsonism associated with primary Sjögren's syndrome. *Clin Neurol Neurosurg* 1994;96:327–331.
34. Gerraty RP, McKelvie PA, Byrne E. Aseptic meningoencephalitis in primary Sjögren's syndrome. Response to plasmapheresis and absence of CNS vasculitis at autopsy. *Acta Neurol Scand* 1993;88:309–311.
35. Berman JL, Kashii S, Trachtman MS, Burde RM. Optic neuropathy and central nervous system disease secondary to Sjögren's syndrome in a child. *Ophthalmology* 1990;97:1606–1609.
36. de-la-Monte SM, Hutchins GM, Gupta PK. Polymorphous meningitis with atypical mononuclear cells in Sjögren's syndrome. *Ann Neurol* 1983;14:455–461.
37. Alexander EL, Provost TT, Stevens MB, Alexander GE. Neurologic complications of primary Sjögren's syndrome. *Medicine* 1982;61:247–257.